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**LITERATURE SEARCH**

**“Vocal Biomarkers and Artificial  
Intelligence”**

**Prepared by  
The Royal Society of Medicine Library  
for**

**Dr M Pedersen**

**2 March 2023**

## **Database(s) Searched**

Medline (Dialog): 1946 – 1 March 2023

Embase (Dialog): 1947 – 1 March 2023

## **Summary of the Search**

Vocal biomarkers and artificial intelligence

### **Search Parameters**

All Years

All Languages

Human Studies

Includes Conference Abstracts in Embase

### **Overview**

The search strategy was devised using three main concepts: (1) Vocal, voice or speech -AND- (2) Biomarkers -AND- (3) Artificial intelligence (including machine learning, deep learning and artificial neural networks). Both thesaurus terms (i.e. MeSH terms in Medline and EMB terms in Embase), where available and textwords (i.e. words or phrases appearing in the Title, Abstract or Author Keywords fields of references; including any synonyms) were identified to describe each concept. It's not possible to search for these terms in the full text of articles using these databases.

Set S14 (745 references) represents the final results of this search. These references were then manually scanned for relevancy, identifying a total of 332 references as the closest match to your search question.

### **Search undertaken by**

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**January 2022**  
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# Search Strategy

Databases: Embase®, MEDLINE®

(results downloaded on 1 March 2023)

Set#	Searched for	Results
S1	MESH.EXACT("Voice Quality") OR MESH.EXACT("Voice") OR MESH.EXACT.EXPLODE("Voice Disorders") OR MESH.EXACT.EXPLODE("Vocal Cord Dysfunction") OR MESH.EXACT("Vocal Cord Paralysis") OR MESH.EXACT("Vocal Cords") OR MESH.EXACT("Glottis") OR MESH.EXACT("Phonation") OR MESH.EXACT.EXPLODE("Speech") OR MESH.EXACT.EXPLODE("Speech Production Measurement") OR MESH.EXACT.EXPLODE("Speech Disorders") OR MESH.EXACT("Phonetics")	107972*
S2	EMB.EXACT("voice") OR EMB.EXACT("voice analysis") OR EMB.EXACT("voice change") OR EMB.EXACT.EXPLODE("voice disorder") OR EMB.EXACT.EXPLODE("voice parameter") OR EMB.EXACT("vocal cord") OR EMB.EXACT("vocal cord paralysis") OR EMB.EXACT.EXPLODE("vocal cord disorder") OR EMB.EXACT("glottis") OR EMB.EXACT("phonation") OR EMB.EXACT.EXPLODE("speech") OR EMB.EXACT("speech analysis") OR EMB.EXACT("speech development") OR EMB.EXACT.EXPLODE("speech disorder") OR EMB.EXACT("phonetics")	307070*
S3	ti,ab,if(vocal* or glotti* or glottal* or voice or dysphoni* or dysarthri* or dysarthos* or aphony* or hoarseness or phonat* or phonet* or speech)	492965*
S4	MESH.EXACT("Biomarkers")	343430*
S5	EMB.EXACT("biological marker") OR EMB.EXACT("biomarker detection kit")	482890*
S6	ti,ab,if(biomarker[*1] or "bio marker[*1]" or "biologic[*2] marker[*1]")	1133945*
S7	(s1 or s2 or s3) and (s4 or s5 or s6)	3369°
S8	MESH.EXACT.EXPLODE("Artificial Intelligence") OR MESH.EXACT.EXPLODE("Neural Networks, Computer") OR MESH.EXACT.EXPLODE("Machine Learning") OR MESH.EXACT("Deep Learning") OR MESH.EXACT("Pattern Recognition, Automated") OR MESH.EXACT("Digital Technology")	192991*
S9	EMB.EXACT("artificial general intelligence") OR EMB.EXACT.EXPLODE("artificial intelligence") OR EMB.EXACT("automated reasoning") OR EMB.EXACT("ambient intelligence") OR EMB.EXACT("artificial intelligence software") OR EMB.EXACT.EXPLODE("machine learning") OR EMB.EXACT("feature learning (machine learning)") OR EMB.EXACT("deep learning") OR EMB.EXACT.EXPLODE("artificial neural network") OR EMB.EXACT("convolutional neural network") OR EMB.EXACT.EXPLODE("deep neural network") OR EMB.EXACT("machine learning software") OR EMB.EXACT("automated pattern recognition") OR EMB.EXACT("digital imaging") OR EMB.EXACT("digital technology")	407684*
S10	ti,ab,if("artificial intelligen*" or AI or "computational intelligen*" or "computer reasoning" or "automated reasoning" or "automated inference" or "machine reasoning" or "computer vision system*" or "machine intelligen*" or "computer knowledge	1041046*

	acquisition*" or "computer knowledge representation*" or "ambient intelligen*" or "deep learning" or "hierarchical learning" or "machine learning" or "transfer learning" or "learning machine*" or "support vector machine*" or "support vector network*" or SVC or SVR or SVM or SVMs or "neural network model*" or ANN or ANNs or CNN or CNNs or DNN or DNNs or perceptron* or "automated pattern recognition" or "automatic pattern recognition" or "pattern recognition system*" or "automatic speech recognition" or "automated speech recognition" or "affective computing" or "artificial emotional intelligen*" or digital or digitally) or ti,ab,if((deep or convolutional or artificial or computer* or computational) near/5 "neural network*") or ti,ab,if(connectionist near/5 (model* or network* or system*))	
S11	(s1 or s2 or s3) and (s4 or s5 or s6) and (s8 or s9 or s10)	399°
S12	EMB.EXACT("marker") or ti,ab,if(marker or markers or signature or signatures)	2724659*
S13	(s1 or s2 or s3) and s12 and (s8 or s9 or s10)	571°
<b>S14</b>	<b>s11 or s13</b>	<b>745°</b>

\* The search strategy retrieved a number of references that were then hand searched to find the most relevant. The details of 332 references have been provided in accordance with your original request.

## Search Results

The full text of any of these articles may be ordered from the Royal Society of Medicine Library by either contacting the Enquiry Desk on Tel: +44 (0)20 7290 2940 or emailing [library@rsm.ac.uk](mailto:library@rsm.ac.uk)

Document 1

### Development and validation of a machine learning-based vocal predictive model for major depressive disorder

**Author:** Wasserzug, Yael 1 ; Degani, Yoav 2 ; Bar-Shaked, Mili 1 ; Binyamin, Milana 1 ; Klein, Amit 2 ; Hershko, Shani 2 ; Levkovitch, Yechiel 1

1 Merhavim Beer Yaakov-Ness Ziona Mental Health Center, Israel, Israel [yaelwasserzug@gmail.com](mailto:yaelwasserzug@gmail.com)  
2 VoiceSense Ltd., Herzliya, Israel, Israel

**Publication info:** Journal of affective disorders 325 : 627-632. (Mar 15, 2023)

#### Abstract (summary): BACKGROUND

Variations in speech intonation are known to be associated with changes in mental state over time. Behavioral vocal analysis is an algorithmic method of determining individuals' behavioral and emotional characteristics from their vocal patterns. It can provide biomarkers for use in psychiatric assessment and monitoring, especially when remote assessment is needed, such as in the COVID-19 pandemic. The objective of this study was to design and validate an effective prototype of automatic speech analysis based on algorithms for classifying the speech features related to MDD using a remote assessment system combining a mobile app for speech recording and central cloud processing for the prosodic vocal patterns.

#### METHODS

Machine learning compared the vocal patterns of 40 patients diagnosed with MDD to the patterns of 104 non-clinical participants. The vocal patterns of 40 patients in the acute phase were also compared to 14 of these patients in the remission phase of MDD.

#### RESULTS

A vocal depression predictive model was successfully generated. The vocal depression scores of MDD patients were significantly higher than the scores of the non-patient participants ( $p < 0.0001$ ). The vocal depression scores of the MDD patients in the acute phase were significantly higher than in remission ( $p < 0.02$ ).

#### LIMITATIONS

The main limitation of this study is its relatively small sample size, since machine learning validity improves with big data.

## CONCLUSIONS

The computerized analysis of prosodic changes may be used to generate biomarkers for the early detection of MDD, remote monitoring, and the evaluation of responses to treatment.

**Accession number:** 36586600

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**Correspondence author:** Wasserzug, Yael Merhavim Beer Yaakov-Ness Ziona Mental Health Center, Israel.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2023-02-13

**Date created:** 2022-12-31

**Date revised:** 2023-02-13

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1016/j.jad.2022.12.117>

**First available:** 2023-01-01

**Identifier (keyword):** Depression screening, Machine learning, Predictive analytics, Remote patient monitoring, Speech prosody, Voice analysis

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Humans; Depressive Disorder, Major (major) -- diagnosis; Depressive Disorder, Major (major) - - epidemiology; Pandemics; COVID-19 (major); Speech; Machine Learning

**Notes:** Conflict of interest The study was funded by VoiceSense. Yoav Degani, Amit Klein and Shani Hershko are VoiceSense employees. Dr. Wasserzug declares no financial interests or potential conflicts of interest. Dr. Bar-Shaked declares no financial interests or potential conflicts of interest. Dr. Binyamin declares no financial interests or potential conflicts of interest. Dr. Levkovitch declares no financial interests or potential conflicts of interest.; Indexing method: Automated;; Publication model: Print-Electronic;; Cited medium: Internet

**Publication date:** Mar 15, 2023



**Publication type:** Journal

**Publisher location:** NETHERLANDS

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**Updates:** 2023-01-012023-01-242023-01-262023-01-272023-01-282023-01-292023-01-302023-01-312023-02-022023-02-102023-02-13

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Document 2

## **DystoniaBoTXNet: Novel Neural Network Biomarker of Botulinum Toxin Efficacy in Isolated Dystonia**

**Author:** Yao, Dongren 1 ; O'Flynn, Lena C. 2 ; Simonyan, Kristina 3

1 Department of Otolaryngology—Head and Neck Surgery, Massachusetts Eye and Ear and Harvard Medical School, Boston, MA, United States 2 Department of Otolaryngology—Head and Neck Surgery, Massachusetts Eye and Ear and Harvard Medical School, Boston, MA, United States, Program in Speech Hearing Bioscience and Technology, Harvard University, Boston, MA, United States 3 Department of Otolaryngology—Head and Neck Surgery, Massachusetts Eye and Ear and Harvard Medical School, Boston, MA, United States, Program in Speech Hearing Bioscience and Technology, Harvard University, Boston, MA, United States, Department of Neurology, Massachusetts General Hospital, Boston, MA, United States kristina\_simonyan@meei.harvard.edu

**Publication info:** Annals of Neurology 93.3: 460-471. John Wiley and Sons Inc. (Mar 2023)

**Abstract (summary):** Objective: Isolated dystonia is characterized by abnormal, often painful, postures and repetitive movements due to sustained or intermittent involuntary muscle contractions. Botulinum toxin (BoTX) injections into the affected muscles are the first line of therapy. However, there are no objective predictive markers or standardized tests of BoTX efficacy that can be utilized for appropriate candidate selection prior to treatment initiation. Methods: We developed a deep learning algorithm, DystoniaBoTXNet, which uses a 3D convolutional neural network architecture and raw structural brain magnetic resonance images (MRIs) to automatically discover and test a neural network biomarker of BoTX efficacy in 284 patients with 4 different forms of focal dystonia, including laryngeal dystonia, blepharospasm, cervical dystonia, and writer's cramp. Results: DystoniaBoTXNet identified clusters in superior parietal lobule, inferior and middle frontal gyri, middle orbital gyrus, inferior temporal gyrus, corpus callosum, inferior fronto-occipital fasciculus, and anterior thalamic radiation as components of the treatment biomarker. These regions are known to contribute to both dystonia pathophysiology across a broad clinical spectrum of disorder and the central effects of botulinum toxin treatment. Based on its biomarker, DystoniaBoTXNet achieved an overall accuracy of 96.3%, with 100% sensitivity and 86.1% specificity, in predicting BoTX efficacy in patients with isolated dystonia. The algorithmic decision was computed in 19.2 seconds per case. Interpretation: DystoniaBoTXNet and its treatment biomarker have a high translational potential as an objective,

accurate, generalizable, fast, and cost-effective algorithmic platform for enhancing clinical decision making for BoTX treatment in patients with isolated dystonia. **ANN NEUROL** 2023;93:460–471.

**Accession number:** 2020591839

**Author e-mail address:** kristina\_simonyan@meei.harvard.edu

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**Correspondence author:** Simonyan, Kristina Department of Otolaryngology—Head and Neck Surgery, Harvard Medical School and Massachusetts Eye and Ear, 243 Charles Street, Suite 421, Boston, MA, 02493, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-12-21

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**DOI:** <http://dx.doi.org/10.1002/ana.26558>

**Embase document status:** In Process; Publisher (MEDLINE in Embase)

**First available:** 2022-12-21

**Grant:** R01DC011805. , NIDCD. National Institute on Deafness and Other Communication Disorders.

R01DC012545. , NIDCD. National Institute on Deafness and Other Communication Disorders.

R01NS088160. , NINDS. National Institute of Neurological Disorders and Stroke.

R01NS124228. , NINDS. National Institute of Neurological Disorders and Stroke.

The authors thank Azadeh Hamzehei Sichani, MA, for her assistance with data collection. This study was supported by the National Institutes of Health (grants R01DC012545, R01DC011805, R01NS088160, R01NS124228, and P50DC019900 to K.S.), the Mass General Brigham Innovation Discovery Grant (K.S.), and the Amazon Web Services Machine Learning Research Award (K.S.). We acknowledge the use of the Medical Imaging Informatic Bench to Bedside (mi2b2) workbench for image retrieval.

**Language:** English

**Language of abstract:** English

**Number of references:** 38

**Publication date:** Mar 2023

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;alprazolam;biological marker (major);botulinum toxin (major);adult;article;artificial neural network;blepharospasm;cervical dystonia;clinical decision making;comparative effectiveness;convolutional neural network (major);corpus callosum;deep learning;drug efficacy (major);dystonia (major);female;focal dystonia;human;inferior fronto-occipital fasciculus;inferior temporal gyrus;major clinical study;male;middle frontal gyrus;nuclear magnetic resonance;orbital cortex;sensitivity and specificity;spasmodic dysphonia;superior parietal lobule;thalamocortical tract;writer's cramp

**Updates:** 2022-12-212023-02-27

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Document 3

## **Artificial Intelligence and Laryngeal Cancer: From Screening to Prognosis: A State of the Art Review**

**Author:** Bensoussan, Yael 1 ; Vanstrum, Erik B. 2 ; Johns, Michael M., III 3 ; Rameau, Anaïs 4

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anr2783@med.cornell.edu

**Publication info:** Otolaryngology - Head and Neck Surgery (United States) 168.3: 319-329. John Wiley and Sons Inc. (Mar 2023)

**Abstract (summary):** Objective: This state of the art review aims to examine contemporary advances in applications of artificial intelligence (AI) to the screening, detection, management, and prognostication of laryngeal cancer (LC). Data Sources: Four bibliographic databases were searched: PubMed, EMBASE, Cochrane, and IEEE. Review Methods: A structured review of the current literature (up to January 2022) was performed. Search terms related to topics of AI in LC were identified and queried by 2 independent reviewers. Citations of selected studies and review articles were also evaluated to ensure comprehensiveness. Conclusions: AI applications in LC have encompassed a variety of data modalities, including radiomics, genomics, acoustics, clinical data, and videomics, to support screening, diagnosis, therapeutic decision making, and prognosis. However, most studies remain at the proof-of-concept level, as AI algorithms are trained on single-institution databases with limited data sets and a single data modality. Implications for Practice: AI algorithms in LC will need to be trained on large multi-institutional data sets and integrate multimodal data for optimal performance and clinical utility from screening to prognosis. Out of the data types reviewed,

genomics has the most potential to provide generalizable models thanks to available large multi-institutional open access genomic data sets. **Voice** acoustic data represent an inexpensive and accurate **biomarker**, which is easy and noninvasive to capture, offering a unique opportunity for screening and monitoring of LA, especially in low-resource settings.

**Accession number:** 2018166028

**Author e-mail address:** anr2783@med.cornell.edu

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**Correspondence author:** Rameau, Anaïs Department of Otolaryngology–Head and Neck Surgery, Sean Parker Institute for the Voice, Weill Cornell Medical College, 240 East 59th St, New York, NY, 10022, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-07-10

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1177/01945998221110839>

**Embase document status:** In Process; Publisher (MEDLINE in Embase)

**First available:** 2022-07-11

**Identifier (keyword):** **artificial intelligence**, **deep learning**, laryngeal cancer, **machine learning**

**Language:** English

**Language of abstract:** English

**Number of references:** 45

**Publication date:** Mar 2023

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;**biological marker**;acoustics;algorithm (major);article;**artificial intelligence** (major);bibliographic database;cancer prognosis (major);decision making;**deep learning** (major);Embase;genomics;human;larynx cancer (major);**machine learning** (major);Medline;multicenter study (topic);prognosis (major);proof of concept;radiomics;systematic review;**voice**

**Updates:** 2022-07-112023-02-27

## **Artificial Intelligence-Based Voice Assessment of Patients with Parkinson's Disease Off and On Treatment: Machine vs. Deep-Learning Comparison**

**Author:** Costantini, Giovanni 1 ; Cesarini, Valerio 1 ; Di Leo, Pietro 1 ; Amato, Federica 2 ; Suppa, Antonio 3 ; Asci, Francesco 3 ; Pisani, Antonio 4 ; Calculli, Alessandra 4 ; Saggio, Giovanni 1

1 Department of Electronic Engineering, University of Rome Tor Vergata, 00133 Rome, Italy, Italy 2 Department of Control and Computer Engineering, Polytechnic University of Turin, 10129 Turin, Italy, Italy 3 Department of Human Neurosciences, Sapienza University of Rome, 00185 Rome, Italy, IRCCS Neuromed Institute, 86077 Pozzilli, Italy, Italy 4 Department of Brain and Behavioral Sciences, University of Pavia, 27100 Pavia, Italy, IRCCS Mondino Foundation, 27100 Pavia, Italy, Italy

**Publication info:** Sensors (Basel, Switzerland) 23.4 (Feb 18, 2023)

**Abstract (summary):** Parkinson's Disease (PD) is one of the most common non-curable neurodegenerative diseases. Diagnosis is achieved clinically on the basis of different symptoms with considerable delays from the onset of neurodegenerative processes in the central nervous system. In this study, we investigated early and full-blown PD patients based on the analysis of their **voice** characteristics with the aid of the most commonly employed **machine learning** (ML) techniques. A custom dataset was made with hi-fi quality recordings of **vocal** tasks gathered from Italian healthy control subjects and PD patients, divided into early diagnosed, off-medication patients on the one hand, and mid-advanced patients treated with L-Dopa on the other. Following the current state-of-the-art, several ML pipelines were compared using different feature selection and classification algorithms, and **deep learning** was also explored with a custom **CNN** architecture. Results show how feature-based ML and **deep learning** achieve comparable results in terms of classification, with KNN, **SVM** and naïve Bayes classifiers performing similarly, with a slight edge for KNN. Much more evident is the predominance of CFS as the best feature selector. The selected features act as relevant **vocal biomarkers** capable of differentiating healthy subjects, early untreated PD patients and mid-advanced L-Dopa treated patients.

**Accession number:** 36850893

**Correspondence author:** Costantini, Giovanni Department of Electronic Engineering, University of Rome Tor Vergata, 00133 Rome, Italy.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2023-02-28

**Date revised:** 2023-02-28

**Document status:** New

**Document type:** Journal Article

DOI: <http://dx.doi.org/10.3390/s23042293>

First available: 2023-02-28

Identifier (keyword): CNN, F0, L-Dopa, Parkinson's disease, SVM, artificial intelligence, deep learning, speech, voice

Language: English

Language of abstract: English

Medline document status: In-Process

Notes: Publication model: Electronic;; Cited medium:Internet

Publication date: Feb 18, 2023

Publication type: Journal

Publisher location: SWITZERLAND

Source attribution: Medline, © Publisher specific

Updates: 2023-02-28

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Document 5

## Distinguish the Severity of Illness Associated with Novel Coronavirus (COVID-19) Infection via Sustained Vowel **Speech** Features

Author: Omiya, Yasuhiro 1 ; Mizuguchi, Daisuke 2 ; Tokuno, Shinichi 3

1 PST Inc., Yokohama 231-0023, Japan, Department of Bioengineering, Graduate School of Engineering, The University of Tokyo, Tokyo 113-8656, Japan, Japan 2 PST Inc., Yokohama 231-0023, Japan, Japan 3 Department of Bioengineering, Graduate School of Engineering, The University of Tokyo, Tokyo 113-8656, Japan, Graduate School of Health Innovation, Kanagawa University of Human Services, Yokosuka 210-0821, Japan, Japan

**Publication info:** International journal of environmental research and public health 20.4 (Feb 15, 2023)

**Abstract (summary):** The authors are currently conducting research on methods to estimate psychiatric and neurological disorders from a **voice** by focusing on the features of **speech**. It is empirically known that numerous psychosomatic symptoms appear in **voice biomarkers**; in this study, we examined the effectiveness of distinguishing changes in the symptoms associated with novel coronavirus infection using **speech** features. Multiple **speech** features were extracted from the **voice** recordings, and, as a countermeasure against overfitting, we selected features using statistical analysis and feature selection methods utilizing pseudo data and built and verified **machine learning** algorithm models using LightGBM. Applying 5-fold cross-validation, and using three types of sustained vowel sounds of /Ah/, /Eh/, and /Uh/, we achieved a high performance (accuracy and AUC)

of over 88% in distinguishing "asymptomatic or mild illness (symptoms)" and "moderate illness 1 (symptoms)". Accordingly, the results suggest that the proposed index using **voice (speech)** features) can likely be used in distinguishing the symptoms associated with novel coronavirus infection.

**Accession number:** 36834110

**Correspondence author:** Omiya, Yasuhiro PST Inc., Yokohama 231-0023, Japan. , Department of Bioengineering, Graduate School of Engineering, The University of Tokyo, Tokyo 113-8656, Japan.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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Document 6

## **Development of digital **voice biomarkers** and associations with cognition, cerebrospinal **biomarkers**, and neural representation in early Alzheimer's disease**

**Author:** Hajjar, Ihab 1 ; Okafor, Maureen 2 ; Choi, Jinho D 3 ; Moore, Elliot, 2nd 4 ; Abrol, Anees 5 ; Calhoun, Vince D 5 ; Goldstein, Felicia C 2

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**Publication info:** Alzheimer's & dementia (Amsterdam, Netherlands) 15.1: e12393. (Feb 5, 2023)

## **Abstract (summary): Introduction**

Advances in natural language processing (NLP), **speech** recognition, and **machine learning** (ML) allow the exploration of linguistic and acoustic changes previously difficult to measure. We developed processes for deriving lexical-semantic and acoustic measures as Alzheimer's disease (AD) digital **voice biomarkers**.

## **Methods**

We collected connected **speech**, neuropsychological, neuroimaging, and cerebrospinal fluid (CSF) AD **biomarker** data from 92 cognitively unimpaired (40 A $\beta$ +) and 114 impaired (63 A $\beta$ +) participants. Acoustic and lexical-semantic features were derived from audio recordings using ML approaches.

## **Results**

Lexical-semantic (area under the curve [AUC] = 0.80) and acoustic (AUC = 0.77) scores demonstrated higher diagnostic performance for detecting MCI compared to Boston Naming Test (AUC = 0.66). Only lexical-semantic scores detected amyloid- $\beta$  status ( $p = 0.0003$ ). Acoustic scores associated with hippocampal volume ( $p = 0.017$ ) while lexical-semantic scores associated with CSF amyloid- $\beta$  ( $p = 0.007$ ). Both measures were significantly associated with 2-year disease progression.

## **Discussion**

These preliminary findings suggest that derived digital **biomarkers** may identify cognitive impairment in preclinical and prodromal AD, and may predict disease progression.

## **Highlights**

This study derived lexical-semantic and acoustics features as Alzheimer's disease (AD) digital **biomarkers**. These features were derived from audio recordings using **machine learning** approaches. **Voice biomarkers** detected cognitive impairment and amyloid- $\beta$  status in early stages of AD. **Voice biomarkers** may predict Alzheimer's disease progression. These markers significantly mapped to functional connectivity in AD-susceptible brain regions.

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Document 7

## **Speech as a Biomarker for Depression**

**Author:** Koops, Sanne 1 ; Brederoo, Sanne G. 2 ; de Boer, Janna N. 3 ; Nadema, Femke G. 1 ; Voppel, Alban E. 1 ; Sommer, Iris E. 1

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**Publication info:** CNS and Neurological Disorders - Drug Targets 22.2: 152-160. Bentham Science Publishers. (Feb 1, 2023)

**Abstract (summary):** Background: Depression is a debilitating disorder that at present lacks a reliable **bio-marker** to aid in diagnosis and early detection. Recent advances in computational analytic approaches have opened up new avenues in developing such a **biomarker** by taking advantage of the wealth of information that can be extracted from a person's **speech**. Objective: The current review provides an overview of the latest findings in the rapidly evolving field of computational language analysis for the detection of depression. We cover a wide range of both acoustic and content-related linguistic features, data types (i.e., spoken and written language), and data sources (i.e., lab settings, social media, and smartphone-based). We put special focus on the current methodological advances with regard to feature extraction and computational modeling techniques. Furthermore, we pay attention to potential hurdles in the implementation of automatic **speech** analysis. Conclusion: Depressive **speech** is characterized by several anomalies, such as lower **speech** rate, less pitch variability and more self-referential **speech**. With current computational modeling techniques, such features can be used to detect depression with an accuracy of up to 91%. The performance of the models is optimized when **machine learning** techniques are implemented that suit the type and amount of data. Recent studies now work towards further optimization and generalizability of the computational language models to detect depression. Finally, privacy and ethical issues are of paramount importance to be addressed when automatic **speech** analysis techniques are further implemented in, for example, smartphones. Altogether, computational **speech** analysis is well underway towards becoming an effective diagnostic aid for depression.

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**Subject:** Embase;MEDLINE;biological marker -- endogenous compound;smartphone;Alzheimer disease;attention;classification algorithm;computer model;depression -- diagnosis (major);disease severity;feature extraction;health care personnel;human;interview;machine learning;mental disease;mental health service;natural language processing;pitch;psychosis;Short Survey;social media;speech analysis (major);speech discrimination;speech rate;written language

**Updates:** 2022-12-202023-01-03

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Document 8

## **The SPEAK study rationale and design: A linguistic corpus-based approach to understanding thought disorder**

**Author:** Bayer, J M M 1 ; Spark, J 1 ; Krcmar, M 1 ; Formica, M 1 ; Gwyther, K 1 ; Srivastava, A 2 ; Selloni, A 2 ; Cotter, M 2 ; Hartmann, J 1 ; Polari, A 1 ; Bilgrami, Z R 3 ; Sarac, C 2 ; Lu, A 2 ; Yung, Alison R 4 ; McGowan, A 2 ; McGorry, P 1 ; Shah, J L 5 ; Cecchi, G A 6 ; Mizrahi, R 5 ; Nelson, B 1 ; Corcoran, C M 7

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Kingdom, United Kingdom 5 McGill Department of Psychiatry & Douglas Research Hospital, Montreal, Canada, Canada 6 IBM TJ Watson Research Center, Yorktown Heights, NY, USA, USA 7 Icahn School of Medicine at Mount Sinai, New York, NY, USA; James J. Peters Veterans Administration, Bronx, NY, USA, USA

**Publication info:** Schizophrenia research (Jan 31, 2023)

### **Abstract (summary):** AIM

Psychotic symptoms are typically measured using clinical ratings, but more objective and sensitive metrics are needed. Hence, we will assess thought disorder using the Research Domain Criteria (RDoC) heuristic for language production, and its recommended paradigm of "linguistic corpus-based analyses of language output". Positive thought disorder (e.g., tangentiality and derailment) can be assessed using word-embedding approaches that assess semantic coherence, whereas negative thought disorder (e.g., concreteness, poverty of **speech**) can be assessed using part-of-**speech** (POS) tagging to assess syntactic complexity. We aim to establish convergent validity of automated linguistic metrics with clinical ratings, assess normative demographic variance, determine cognitive and functional correlates, and replicate their predictive power for psychosis transition among at-risk youths.

## METHODS

This study will assess language production in 450 English-speaking individuals in Australia and Canada, who have recent onset psychosis, are at clinical high risk (CHR) for psychosis, or who are healthy volunteers, all well-characterized for cognition, function and symptoms. **Speech** will be elicited using open-ended interviews. Audio files will be transcribed and preprocessed for automated natural language processing (NLP) analyses of coherence and complexity. Data analyses include canonical correlation, multivariate linear regression with regularization, and **machine-learning** classification of group status and psychosis outcome.

## CONCLUSIONS

This prospective study aims to characterize language disturbance across stages of psychosis using computational approaches, including psychometric properties, normative variance and clinical correlates, important for **biomarker** development. SPEAK will create a large archive of language data available to other investigators, a rich resource for the field.

**Accession number:** 36732110

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Document 9

## **Automated measurement of inter-arytenoid distance on 4D laryngeal CT: A validation study**

**Author:** Ma, Andrew 1 ; Desai, Nandakishor 2 ; Lau, Kenneth K 3 ; Palaniswami, Marimuthu 2 ; O'Brien, Terence J 4 ; Palaniswami, Paari 5 ; Thyagarajan, Dominic 1

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Melbourne, Victoria, Australia, Department of Neurology, Alfred Health, Melbourne, Victoria, Australia, Australia 5 School of Computing and Information Systems, Faculty of Engineering and Information Technology, The University of Melbourne, Melbourne, Victoria, Australia, Australia

**Publication info:** PloS one 18.1: e0279927. (Jan 18, 2023)

**Abstract (summary):** Changes to the **voice** are prevalent and occur early in Parkinson's disease. Correlates of these **voice** changes on four-dimensional laryngeal computed-tomography imaging, such as the inter-arytenoid distance, are promising **biomarkers** of the disease's presence and severity. However, manual measurement of the inter-arytenoid distance is a laborious process, limiting its feasibility in large-scale research and clinical settings. Automated methods of measurement provide a solution. Here, we present a **machine-learning** module which determines the inter-arytenoid distance in an automated manner. We obtained automated inter-arytenoid distance readings on imaging from participants with Parkinson's disease as well as healthy controls, and then validated these against manually derived estimates. On a modified Bland-Altman analysis, we found a mean bias of 1.52 mm (95% limits of agreement -1.7 to 4.7 mm) between the automated and manual techniques, which improves to a mean bias of 0.52 mm (95% limits of agreement -1.9 to 2.9 mm) when variability due to differences in slice selection between the automated and manual methods are removed. Our results demonstrate that estimates of the inter-arytenoid distance with our automated **machine-learning** module are accurate, and represents a promising tool to be utilized in future work studying the laryngeal changes in Parkinson's disease.

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Document 10

## Screening for Mild Cognitive Impairment Using a **Machine Learning Classifier** and the Remote **Speech Biomarker** for Cognition: Evidence from Two Clinically Relevant Cohorts

**Author:** Schäfer, Simona 1 ; Mallick, Elisa 1 ; Schwed, Louisa 1 ; König, Alexandra 2 ; Zhao, Jian 1 ; Linz, Nicklas 1 ; Bodin, Timothy Hadarsson 3 ; Skoog, Johan 3 ; Possemis, Nina 4 ; Ter Huurne, Daphne 4 ; Zettergren, Anna 3 ; Kern, Silke 3 ; Sacuiu, Simona 3 ; Ramakers, Inez 4 ; Skoog, Ingmar 3 ; Tröger, Johannes 1

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**Publication info:** Journal of Alzheimer's Disease 91.3: 1165-1171. IOS Press BV. (2023)

**Abstract (summary):** Background: Modern prodromal Alzheimer's disease (AD) clinical trials might extend outreach to a general population, causing high screen-out rates and thereby increasing study time and costs. Thus, screening tools that cost-effectively detect mild cognitive impairment (MCI) at scale are needed. Objective: Develop a screening algorithm that can differentiate between healthy and MCI participants in different clinically relevant populations. Methods: Two screening algorithms based on the remote ki:e **speech biomarker** for cognition (ki:e SB-C) were designed on a Dutch memory clinic cohort (N=121) and a Swedish birth cohort (N=404). MCI classification was each evaluated on the training cohort as well as on the unrelated validation cohort. Results: The algorithms achieved a performance of AUC 0.73 and AUC 0.77 in the respective training cohorts and AUC 0.81 in the unseen validation cohorts. Conclusion: The results indicate that a ki:e SB-C based algorithm

robustly detects MCI across different cohorts and languages, which has the potential to make current trials more efficient and improve future primary health care.

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**Subject:** Embase;MEDLINE;biological marker (major);aged;algorithm (major);Alzheimer disease;Article;birth cohort;classifier (major);cognition (major);cohort analysis;controlled study;data analysis;data protection;episodic memory;human;language;machine learning (major);major clinical study;mild cognitive impairment (major);primary health care;processing speed;Rey auditory verbal learning test;speech (major);speech analysis;support vector machine;validation process

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Document 11



## Screening over **Speech** in Unselected Populations for Clinical Trials in AD (PROSPECT-AD): Study Design and Protocol

**Author:** König, Alexandra 1 ; Linz, N. 2 ; Baykara, E. 2 ; Tröger, J. 2 ; Ritchie, C. 3 ; Saunders, S. 3 ; Teipel, S. 4 ; Köhler, S. 5 ; Sánchez-Benavides, G. 6 ; Grau-Rivera, O. 6 ; Gispert, J.D. 7 ; Palmqvist, S. 8 ; Tideman, P. 8 ; Hansson, O. 8

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**Publication info:** Journal of Prevention of Alzheimer's Disease Serdi-Editions. (2023)

**Abstract (summary):** Background: **Speech** impairments are an early feature of Alzheimer's disease (AD) and consequently, analysing **speech** performance is a promising new digital **biomarker** for AD screening. Future clinical AD trials on disease modifying drugs will require a shift to very early identification of individuals at risk of dementia. Hence, digital markers of language and **speech** may offer a method for screening of at-risk populations that are at the earliest stages of AD, eventually in combination with advanced **machine learning**. To this end, we developed a screening battery consisting of **speech**-based neurocognitive tests. The automated test performs a remote primary screening using a simple telephone. Objectives: PROSPECT-AD aims to validate **speech biomarkers** for identification of individuals with early signs of AD and monitor their longitudinal course through access to well-phenotyped cohorts. Design: PROSPECT-AD leverages ongoing cohorts such as EPAD (UK), DESCRIBE and DELCODE (Germany), and BioFINDER Primary Care (Sweden) and Beta-AARC (Spain) by adding a collection of **speech** data over the telephone to existing longitudinal follow-ups. Participants at risk of dementia are recruited from existing parent cohorts across Europe to form an AD 'probability-spectrum', i.e., individuals with a low risk to high risk of developing AD dementia. The characterization of cognition, **biomarker** and risk factor (genetic and environmental) status of each research participants over time combined with audio recordings of **speech** samples will provide a well-phenotyped population for comparing novel **speech** markers with current gold standard

**biomarkers** and cognitive scores. Participants: N= 1000 participants aged 50 or older will be included in total, with a clinical dementia rating scale (CDR) score of 0 or 0.5. The study protocol is planned to run according to sites between 12 and 18 months. Measurements: The **speech** protocol includes the following neurocognitive tests which will be administered remotely: Word List [Memory Function], Verbal Fluency [Executive Functions] and spontaneous free **speech** [Psychological and/ or behavioral symptoms]. **Speech** features on the linguistic and paralinguistic level will be extracted from the recordings and compared to data from CSF and blood **biomarkers**, neuroimaging, neuropsychological evaluations, genetic profiles, and family history. Primary candidate marker from **speech** will be a combination of most significant features in comparison to **biomarkers** as reference measure. **Machine learning** and computational techniques will be employed to identify the most significant **speech biomarkers** that could represent an early indicator of AD pathology. Furthermore, based on the analysis of **speech** performances, models will be trained to predict cognitive decline and disease progression across the AD continuum. Conclusion: The outcome of PROSPECT-AD may support AD drug development research as well as primary or tertiary prevention of dementia by providing a validated tool using a remote approach for identifying individuals at risk of dementia and monitoring individuals over time, either in a screening context or in clinical trials.

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Document 12

## Harmonic-to-noise ratio as speech biomarker for fatigue: K-nearest neighbour machine learning algorithm

**Author:** Gaur, Savita 1 ; Kalani, Priti 2 ; Mohan, M. 3

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**Publication info:** Medical Journal Armed Forces India Elsevier B.V. (2023)

**Abstract (summary):** Background: Vital information about a person's physical and emotional health can be perceived in their voice. After sleep loss, altered voice quality is noticed. The circadian rhythm controls the sleep cycle, and when it is askew, it results in fatigue, which is manifested in speech. Using MATLAB statistical techniques and the k-nearest neighbour (KNN) machine learning algorithm, this study assessed the efficacy of the harmonic-to-noise ratio (HNR) as a speech biomarker in differentiating fatigued and normal voice after sleep deprivation of one night. Methods: After one night of sleep deprivation, acoustic samples for sustained vowel/a/and visual reaction time were recorded from n = 32 healthy young Indian male volunteers (20–40 yrs). One-way ANOVA established significant changes in voice characteristics with progressive sleep deprivation. The effectiveness of speech HNR as a biomarker for the detection of healthy and fatigued voice was researched, using the KNN classifier in a machine learning algorithm. Results: The HNR voice feature was taken from an acoustic sample for three times: baseline (Time 1), 3 AM (Time 2), and 7 AM (Time 3) towards an incremental one-night sleep loss. At 3AM, the HNR changed significantly  $p < 0.05$ . Utilizing an iterative signal extrapolation approach, the KNN classifier divided the submitted voice signal sample into normal and fatigued categories. Conclusion: The findings imply that the HNR can be used to link fatigue from sleep deprivation with vocal alterations by classifying voice samples in a KNN classifier.

Along with the multimodal diagnostic features, this method may also offer an additional acoustic **biomarker** for the diagnosis of fatigue post sleep loss.

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**Identifier (keyword):** Harmonic-to-noise ratio, K-nearest neighbour, **Machine learning**, **Speechbiomarker**

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**Subject:** Embase;biological marker (major);adult;algorithm (major);analysis of variance;article;classifier;clinical article;comparative effectiveness;controlled study;data analysis software;diagnosis;fatigue (major);human;human tissue;Indian;k nearest neighbor (major);machine learning (major);male;night sleep;noise (major);sleep deprivation;speech (major);visual reaction time;voice;vowel

**Updates:** 2023-01-23

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Document 13

## Detecting subtle signs of depression with automated speech analysis in a non-clinical sample

**Author:** König, Alexandra 1 ; Tröger, Johannes 2 ; Mallick, Elisa 2 ; Mina, Mario 2 ; Linz, Nicklas 2 ; Wagnon, Carole 3 ; Karbach, Julia 4 ; Kuhn, Caroline 5 ; Peter, Jessica 3

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### Abstract (summary): BACKGROUND

Automated speech analysis has gained increasing attention to help diagnosing depression. Most previous studies, however, focused on comparing speech in patients with major depressive disorder to that in healthy volunteers. An alternative may be to associate speech with depressive symptoms in a non-clinical sample as this may help to find early and sensitive markers in those at risk of depression.

## METHODS

We included n = 118 healthy young adults (mean age: 23.5 ± 3.7 years; 77% women) and asked them to talk about a positive and a negative event in their life. Then, we assessed the level of depressive symptoms with a self-report questionnaire, with scores ranging from 0-60. We transcribed speech data and extracted acoustic as well as linguistic features. Then, we tested whether individuals below or above the cut-off of clinically relevant depressive symptoms differed in speech features. Next, we predicted whether someone would be below or above that cut-off as well as the individual scores on the depression questionnaire. Since depression is associated with cognitive slowing or attentional deficits, we finally correlated depression scores with performance in the Trail Making Test.

## RESULTS

In our sample, n = 93 individuals scored below and n = 25 scored above cut-off for clinically relevant depressive symptoms. Most **speech** features did not differ significantly between both groups, but individuals above cut-off spoke more than those below that cut-off in the positive and the negative story. In addition, higher depression scores in that group were associated with slower completion time of the Trail Making Test. We were able to predict with 93% accuracy who would be below or above cut-off. In addition, we were able to predict the individual depression scores with low mean absolute error (3.90), with best performance achieved by a **support vector machine**.

## CONCLUSIONS

Our results indicate that even in a sample without a clinical diagnosis of depression, changes in **speech** relate to higher depression scores. This should be investigated in more detail in the future. In a longitudinal study, it may be tested whether **speech** features found in our study represent early and sensitive **markers** for subsequent depression in individuals at risk.

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Document 14

## **Predicting dementia from spontaneous speech using large language models**

**Author:** Agbavor, Felix 1 ; Liang, Hualou 1

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**Publication info:** PLOS digital health 1.12: e0000168. (Dec 22, 2022)

**Abstract (summary):** Language impairment is an important biomarker of neurodegenerative disorders such as Alzheimer's disease (AD). Artificial intelligence (AI), particularly natural language processing (NLP), has recently been increasingly used for early prediction of AD through speech. Yet, relatively few studies exist on using large language models, especially GPT-3, to aid in the early diagnosis of dementia. In this work, we show for the first time that GPT-3 can be utilized to predict dementia from spontaneous speech. Specifically, we leverage the vast semantic knowledge encoded in the GPT-3 model to generate text embedding, a vector representation of the transcribed text from speech, that captures the semantic meaning of the input. We demonstrate that the text embedding can be reliably used to (1) distinguish individuals with AD from healthy controls, and (2) infer the subject's cognitive testing score, both solely based on speech data. We further show that text embedding considerably outperforms the conventional acoustic feature-based approach and even performs competitively with prevailing fine-tuned models. Together, our results suggest that GPT-3 based text embedding is a viable approach for AD assessment directly from speech and has the potential to improve early diagnosis of dementia.

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Document 15

## **Association Between Acoustic Features and Neuropsychological Test Performance in the Framingham Heart Study: Observational Study**

**Author:** Ding, Huitong 1 ; Mandapati, Amiya 2 ; Karjadi, Cody 3 ; Ang, Ting Fang Alvin 4 ; Lu, Sophia 5 ; Miao, Xiao 6 ; Glass, James 7 ; Au, Rhoda 8 ; Lin, Honghuang 9

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## **Abstract (summary):** BACKGROUND

Human **voice** has increasingly been recognized as an effective indicator for the detection of cognitive disorders. However, the association of acoustic features with specific cognitive functions and mild cognitive impairment (MCI) has yet to be evaluated in a large community-based population.

## OBJECTIVE

This study aimed to investigate the association between acoustic features and neuropsychological (NP) tests across multiple cognitive domains and evaluate the added predictive power of acoustic composite scores for the classification of MCI.

## METHODS

This study included participants without dementia from the Framingham Heart Study, a large community-based cohort with longitudinal surveillance for incident dementia. For each participant, 65 low-level acoustic descriptors were derived from **voice** recordings of NP test administration. The associations between individual acoustic descriptors and 18 NP tests were assessed with linear mixed-effect models adjusted for age, sex, and education. Acoustic composite scores were then built by combining acoustic features significantly associated with NP tests. The added prediction power of acoustic composite scores for prevalent and incident MCI was also evaluated.

## RESULTS

The study included 7874 voice recordings from 4950 participants (age: mean 62, SD 14 years; 4336/7874, 55.07% women), of whom 453 were diagnosed with MCI. In all, 8 NP tests were associated with more than 15 acoustic features after adjusting for multiple testing. Additionally, 4 of the acoustic composite scores were significantly associated with prevalent MCI and 7 were associated with incident MCI. The acoustic composite scores can increase the area under the curve of the baseline model for MCI prediction from 0.712 to 0.755.

## CONCLUSIONS

Multiple acoustic features are significantly associated with NP test performance and MCI, which can potentially be used as digital biomarkers for early cognitive impairment monitoring.

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**MeSH:** Humans;Female;Middle Aged;Male;Cognitive Dysfunction (major) -- diagnosis;Cognitive Dysfunction (major) -- epidemiology;Cognitive Dysfunction (major) -- psychology;Cognition Disorders (major) -- diagnosis;Longitudinal Studies;Neuropsychological Tests;Dementia (major) -- psychology

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Document 16

## **Linguistic and non-linguistic markers of disorganization in psychotic illness**

**Author:** Liebenthal, Einat 1 ; Ennis, Michaela 2 ; Rahimi-Eichi, Habiballah 1 ; Lin, Eric 3 ; Chung, Yoonho 1 ; Baker, Justin T 1

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**Publication info:** Schizophrenia research (Dec 21, 2022)

### **Abstract (summary): BACKGROUND**

Disorganization, presenting as impairment in thought, language and goal-directed behavior, is a core multidimensional syndrome of psychotic disorders. This study examined whether scalable computational measures of spoken language, and smartphone usage pattern, could serve as **digital biomarkers** of clinical disorganization symptoms.

## **METHODS**

We examined in a longitudinal cohort of adults with a psychotic disorder, the associations between clinical measures of disorganization and computational measures of 1) spoken language derived from monthly, semi-structured, recorded clinical interviews; and 2) smartphone usage pattern derived via passive sensing technologies over the month prior to the interview. The language features included

speech quantity, rate, fluency, and semantic regularity. The smartphone features included data missingness and phone usage during sleep time. The clinical measures consisted of the Positive and Negative Symptom Scale (PANSS) conceptual disorganization, difficulty in abstract thinking, and poor attention, items. Mixed linear regression analyses were used to estimate both fixed and random effects.

## RESULTS

Greater severity of clinical symptoms of conceptual disorganization was associated with greater verbosity and more disfluent speech. Greater severity of conceptual disorganization was also associated with greater missingness of smartphone data, and greater smartphone usage during sleep time. While the observed associations were significant across the group, there was also significant variation between individuals.

## CONCLUSIONS

The findings suggest that digital measures of speech disfluency may serve as scalable markers of conceptual disorganization. The findings warrant further investigation into the use of recorded interviews and passive sensing technologies to assist in the characterization and tracking of psychotic illness.

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Document 17

## **Acoustic **speech** features in social comparison: how stress impacts the way you sound**

**Author:** Kappen, Mitchel 1 ; van der Donckt, Jonas 2 ; Vanhollebeke, Gert 3 ; Allaert, Jens 1 ; Degraeve, Vic 2 ; Madhu, Nilesh 2 ; Van Hoecke, Sofie 2 ; Vanderhasselt, Marie-Anne 4

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**Abstract (summary):** The use of **speech** as a **digital biomarker** to detect stress levels is increasingly gaining attention. Yet, heterogeneous effects of stress on specific acoustic **speech** features have been observed, possibly due to previous studies' use of different stress labels/categories and the lack

of solid stress induction paradigms or validation of experienced stress. Here, we deployed a controlled, within-subject psychosocial stress induction experiment in which participants received both neutral (control condition) and negative (negative condition) comparative feedback after solving a challenging cognitive task. This study is the first to use a (non-actor) within-participant design that verifies a successful stress induction using both self-report (i.e., decreased reported valence) and physiological measures (i.e., increased heart rate acceleration using event-related cardiac responses during feedback exposure). Analyses of acoustic **speech** features showed a significant increase in Fundamental Frequency (F0) and Harmonics-to-Noise Ratio (HNR), and a significant decrease in shimmer during the negative feedback condition. Our results using read-out-loud **speech** comply with earlier research, yet we are the first to validate these results in a well-controlled but ecologically-valid setting to guarantee the generalization of our findings to real-life settings. Further research should aim to replicate these results in a free **speech** setting to test the robustness of our findings for real-world settings and should include semantics to also take into account what you say and not only how you say it.

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Document 18

## **A prospective observational study for a Federated **Artificial Intelligence** solution for monitoring mental Health status after cancer treatment (FAITH): study protocol**

**Author:** Lemos, Raquel 1 ; Areias-Marques, Sofia 2 ; Ferreira, Pedro 3 ; O'Brien, Philip 4 ; Beltrán-Jaunsarás, María Eugenia 5 ; Ribeiro, Gabriela 6 ; Martín, Miguel 7 ; Del Monte-Millán, María 8 ; López-Tarruella, Sara 7 ; Massarrah, Tatiana 8 ; Luís-Ferreira, Fernando 9 ; Frau, Giuseppe 10 ; Venios, Stefanos 11 ; McManus, Gary 4 ; Oliveira-Maia, Albino J 6

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**Publication info:** BMC psychiatry 22.1: 817. (Dec 21, 2022)

**Abstract (summary):** BACKGROUND

Depression is a common condition among cancer patients, across several points in the disease trajectory. Although presenting higher prevalence rates than the general population, it is often not reported or remains unnoticed. Moreover, somatic symptoms of depression are common in the oncological context and should not be dismissed as a general symptom of cancer. It becomes even more challenging to track psychological distress in the period after the treatment, where connection with the healthcare system typically becomes sporadic. The main goal of the FAITH project is to remotely identify and predict depressive symptoms in cancer survivors, based on a federated **machine learning** (ML) approach, towards optimization of privacy.

## METHODS

FAITH will remotely analyse depression **markers**, predicting their negative trends. These **markers** will be treated in distinct categories, namely nutrition, sleep, activity and **voice**, assessed in part through wearable technologies. The study will include 300 patients who have had a previous diagnosis of breast or lung cancer and will be recruited 1 to 5 years after the end of primary cancer. The study will be organized as a 12-month longitudinal prospective observational cohort study, with monthly assessments to evaluate depression symptoms and quality of life among cancer survivors. The primary endpoint is the severity of depressive symptoms as measured by the Hamilton Depression Rating Scale (Ham-D) at months 3, 6, 9 and 12. Secondary outcomes include self-reported anxiety and depression symptoms (HADS scale), and perceived quality of life (EORTC questionnaires), at baseline and monthly. Based on the predictive models gathered during the study, FAITH will also aim at further developing a conceptual federated learning framework, enabling to build **machine learning** models for the prediction and monitoring of depression without direct access to user's personal data.

## DISCUSSION

Improvements in the objectivity of psychiatric assessment are necessary. Wearable technologies can provide potential indicators of depression and anxiety and be used for biofeedback. If the FAITH application is effective, it will provide healthcare systems with a novel and innovative method to screen depressive symptoms in oncological settings.

## TRIAL REGISTRATION

Trial ID: ISRCTN10423782 . Date registered: 21/03/2022.

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Document 19

## Using **Vocal** Characteristics To Classify Psychological Distress in Adult Helpline Callers: Retrospective Observational Study

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**Publication info:** JMIR formative research 6.12: e42249. (Dec 19, 2022)

## **Abstract (summary): BACKGROUND**

Elevated psychological distress has demonstrated impacts on individuals' health. Reliable and efficient ways to detect distress are key to early intervention. **Artificial intelligence** has the potential to detect states of emotional distress in an accurate, efficient, and timely manner.

## **OBJECTIVE**

The aim of this study was to automatically classify short segments of **speech** obtained from callers to national suicide prevention helpline services according to high versus low psychological distress and using a range of **vocal** characteristics in combination with **machine learning** approaches.

## **METHODS**

A total of 120 telephone call recordings were initially converted to 16-bit pulse code modulation format. Short variable-length segments of each call were rated on psychological distress using the distress thermometer by the responding counselor and a second team of psychologists (n=6) blinded to the initial ratings. Following this, 24 **vocal** characteristics were initially extracted from 40-ms **speech** frames nested within segments within calls. After highly correlated variables were eliminated, 19 remained. Of 19 **vocal** characteristics, 7 were identified and validated as predictors of psychological distress using a penalized generalized additive mixed effects regression model, accounting for nonlinearity, autocorrelation, and moderation by sex. **Speech** frames were then grouped using k-means clustering based on the selected **vocal** characteristics. Finally, component-wise gradient boosting incorporating these clusters was used to classify each **speech** frame according to high versus low psychological distress. Classification accuracy was confirmed via leave-one-caller-out cross-validation, ensuring that **speech** segments from individual callers were not used in both the training and test data.

## **RESULTS**

The sample comprised 87 female and 33 male callers. From an initial pool of 19 characteristics, 7 **vocal** characteristics were identified. After grouping **speech** frames into 2 separate clusters (correlation with sex of caller, Cramer's  $V = 0.02$ ), the component-wise gradient boosting algorithm successfully classified psychological distress to a high level of accuracy, with an area under the receiver operating characteristic curve of 97.39% (95% CI 96.20-98.45) and an area under the precision-recall curve of 97.52 (95% CI 95.71-99.12). Thus, 39,282 of 41,883 (93.39%) **speech** frames nested within 728 of 754 segments (96.6%) were classified as exhibiting low psychological distress, and 71455 of 75503 (94.64%) **speech** frames nested within 382 of 423 (90.3%) segments were classified as exhibiting high psychological distress. As the probability of high psychological distress increases, male callers spoke louder, with greater vowel articulation but with greater

roughness (subharmonic depth). In contrast, female callers exhibited decreased **vocal** clarity (entropy), greater proportion of signal noise, higher frequencies, increased breathiness (spectral slope), and increased roughness of **speech** with increasing psychological distress. Individual caller random effects contributed 68% to risk reduction in the classification algorithm, followed by cluster configuration (23.4%), spectral slope (4.4%), and the 50th percentile frequency (4.2%).

## CONCLUSIONS

The high level of accuracy achieved suggests possibilities for real-time detection of psychological distress in helpline settings and has potential uses in pre-emptive triage and evaluations of counseling outcomes.

## TRIAL REGISTRATION

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**Identifier (keyword):** **artificial intelligence**, **biomarker**, digital health intervention, distress, emotional distress, **machine learning**, mental distress, mental health, mental health intervention, psychological stress, psychological well being, **speech** analysis, **voice**, **voicebiomarker**

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Document 20

## **Towards Fair ML-based Language Assessment Methods for Detecting Alzheimer's Disease**

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**Publication info:** Alzheimer's & dementia : the journal of the Alzheimer's Association, suppl. Supplement 2 18 : e063426. NLM (Medline). (Dec 1, 2022)

**Abstract (summary):** BACKGROUND: Alzheimer's disease (AD) tends to affect the parietal lobe, which is responsible for language functions in the patient's brain. Thus, one significant impairment associated with AD is language impairment which is the cause that patients with AD have deficits at the word level (vocabulary size in **speech** can be an early sign of cognitive impairment [1]), sentence-level, and discourse-level of their languages. Thus, language disorders can be considered as **markers** to diagnose AD in a patient at its earliest stage [2]. The recent progress in the **machine learning** (ML) domain has revolutionized the early detection of AD in particular developing and deploying ML-based language assessment (MLLA) methods for detecting AD at its mild cognitive impairment stage [3]. The ML community needs to develop fair MLLA methods for detecting individuals with AD. METHOD: To develop a fair MLLA first we should consider how we can formulate the fairness for developing a MLLA method and how potential bias in language data can be identified and quantified, how text preprocessing, data augmentation and word embedding techniques can be applied without adding biases to MLLA, how can we identify protected and unprotected linguistic features? and finally how can we protect underserved groups in the deployment process of MLLA methods? RESULT: We suggest a fair ML pipeline includes 1) preprocessing (i.e., eliminating sources of bias in data collection and data sharing, text augmentation and text preprocessing, defining unknown sensitive features including linguistic diversity, which are highly correlated with sensitive attributes such as races and genders. Note that sensitive attributes can be used to alleviate the bias). 2) In-processing (i.e., adjusting **machine learning** process, e.g., using a regularization approach). 3) Post-processing (i.e., adjusting trained model). CONCLUSION: The development of fair MLLA methods is crucial to ensure all groups are treated fairly and there are no results that unfairly harm any subgroups of our population. Using our suggested pipeline, we can foster the confidence of clinical services to use MLLA methods and motivate patients to accept the results.

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**Language:** English

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**Publisher:** NLM (Medline)

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**Subject:** MEDLINE;Alzheimer disease -- diagnosis (major);complication;female;human;language;language disability (major);**machine learning**;male;**speech**

**Updates:** 2022-12-232022-12-27

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Document 21

## **Understanding psychiatric illness through natural language processing (UNDERPIN): Rationale, design, and methodology**

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**Publication info:** Frontiers in Psychiatry 13 Frontiers Media S.A. (Dec 1, 2022)

**Abstract (summary):** Introduction: Psychiatric disorders are diagnosed through observations of psychiatrists according to diagnostic criteria such as the DSM-5. Such observations, however, are mainly based on each psychiatrist's level of experience and often lack objectivity, potentially leading to disagreements among psychiatrists. In contrast, specific linguistic features can be observed in some psychiatric disorders, such as a loosening of associations in schizophrenia. Some studies explored **biomarkers**, but **biomarkers** have yet to be used in clinical practice. Aim: The purposes of this study are to create a large dataset of Japanese **speech** data labeled with detailed information on psychiatric disorders and neurocognitive disorders to quantify the linguistic features of those disorders using natural language processing and, finally, to develop objective and easy-to-use **biomarkers** for diagnosing and assessing the severity of them. Methods: This study will have a multi-center prospective design. The DSM-5 or ICD-11 criteria for major depressive disorder, bipolar disorder, schizophrenia, and anxiety disorder and for major and minor neurocognitive disorders will be regarded as the inclusion criteria for the psychiatric disorder samples. For the healthy subjects, the absence of a history of psychiatric disorders will be confirmed using the Mini-International Neuropsychiatric Interview (M.I.N.I.). The absence of current cognitive decline will be confirmed using the Mini-Mental State Examination (MMSE). A psychiatrist or psychologist will conduct 30-to-60-min interviews with each participant; these interviews will include free conversation, picture-description task, and story-telling task, all of which will be recorded using a microphone headset. In addition, the severity of disorders will be assessed using clinical rating scales. Data will be collected from each participant at least twice during the study period and up to a maximum of five times at an interval of at least one month. Discussion: This study is unique in its large sample size and the novelty of its method, and has potential for applications in many fields. We have some challenges regarding inter-rater reliability and the linguistic peculiarities of Japanese. As of September 2022, we have collected a total of >1000 records from >400 participants. To the best of our knowledge, this data sample is one of the largest in this field. Clinical Trial Registration: Identifier: UMIN000032141.

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**Identifier (keyword):** biomarker, language, machine learning, natural language processing (computer science), neurocognitive disorders, psychiatric disorders

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**Subject:** Embase;biological marker (major);adult;anxiety disorder;article;bipolar disorder;clinical practice;cognitive defect;computer (major);controlled study;conversation;disorders of higher cerebral function (major);DSM-5;female;human;ICD-11;interrater reliability;machine learning (major);major clinical study;major depression;male;mental disease (major);microphone;mini international neuropsychiatric interview;Mini Mental State Examination;natural language processing (major);prospective study;psychiatrist;psychologist;quantitative analysis;rating scale;sample size;schizophrenia;speech

**Updates:** 2022-12-20

## **PREDICTING TAU PET SIGNAL in PRODROMAL-TO MILD ALZHEIMER'S DISEASE from **SPEECH BIOMARKERS** and **MACHINE LEARNING****

**Author:** Mina, M.M.M. 1 ; Troeger, J.T. 1 ; Schwed, L.S. 1 ; Linz, N.L. 1 ; Bohórquez, S.S. 2 ; Hashemifar, S.H. 2 ; Boggiano, T.B. 3 ; Teng, E.T. 2

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**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 9 : S184. Springer. (Dec 2022)

**Abstract (summary):** Background: In alzheimer's Disease (AD), the amount and extent of deposition of tau protein correlates with the severity of cognitive and functional impairment, and behavioral symptomatology. However, assessing cerebral tau levels currently requires PET imaging or lumbar punctures, which may be costly, inaccessible, and/or less acceptable for AD patients. Therefore, alternative approaches to estimating brain tau levels may have utility for facilitating decentralized trial designs, higher frequency intra-trial monitoring, or accelerated screening funnels at scale. In this context, **speech**-based digital measures have great potential as they offer remote assessment, pose lower participant burden, and can be collected frequently at low cost. Objectives: To examine whether cerebral tau pathology measured with tau PET can be modeled through **speech biomarkers**. Methods: We performed cross-sectional analyses of baseline assessments from the Phase 2 Tauriel study of semorinemab (an anti-tau antibody) in prodromal-to-mild AD (NCT03289143) in a subset of right-handed English-speaking participants recruited from sites in the United States (N=86, 59% female). **Speech** data were collected from recordings of the semi-structured Clinical Dementia Rating (CDR) interview with study participants, then processed by the ki:e **speech** pipeline, which extracts features that have construct validity with cognitive subdomains such as memory and language. Several **machine learning** models, including Support Vector Regressor, Random Forest Regressor, and Extra Trees Regressor, were trained on those features to predict [18F]GTP1 standardized uptake value ratio (SUVR) in left-hemisphere domain-specific brain regions of interest (ROIs) from the Hammers atlas for language (parahippocampal gyrus, inferior middle temporal gyrus, anteromedial temporal lobe, inferior frontal lobe, lateral inferior parietal lobe, posterior temporal), bilateral ROIs for memory (caudate nucleus, hippocampus, middle frontal gyrus, parahippocampal gyrus, inferior middle temporal gyrus, anteromedial temporal lobe), and whole cortical gray matter. For each model, we used feature selection based on mutual information to optimize performance with the most relevant features. Furthermore, we trained the same models using cognitive scores (including Repeatable Battery for the Assessment of Neuropsychological Status [RBANS] and alzheimer's Disease Assessment Scale-Cognitive subscale [ADAS-Cog13]) as input to predict [18F]GTP1 SUVR. We used a leave-one-out cross validation to maximize training data while still maintaining testing on the whole



population. **Speech** features were also checked for correlation with cognitive scores, including ADAS-Cog13 and CDR-sum of boxes (SB). Results: **Speech biomarkers** consistently showed better performance relative to cognitive scores in predicting [18F]GTP1 SUVR in ROIs that correspond to language and memory function. Our model on **speech** features achieved a R2 equal to 0.22, 0.17, and 0.17 for the middle frontal gyrus, inferior frontal lobe, and whole cortical gray ROIs, respectively. Models derived from **speech** features yielded R2 values that are on average 41% larger than those achieved with the same models derived from cognitive scores. Importantly, incorporating **speech** features with cognitive scores improves model performance by increasing R2 up to 0.38. **Speech biomarkers** also moderately correlated with scores on the ADAS-Cog13 ( $r=-0.22$ ) and CDR-SB ( $r=-0.39$ ). Conclusion: The results show that **speech biomarkers** have the potential to predict cerebral [18F]GTP1 SUVR related to severity of cognitive impairment in prodromal-to-mild AD. Potential future applications include more rapid population-wide screening for trial inclusion, more frequent estimates of underlying cerebral tau burden during trials, and diagnostic screening to facilitate appropriate use of approved disease modifying therapeutics.

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**Conference end date:** 2022-12-02

**Conference location:** San Francisco, CA

**Conference start date:** 2022-11-29

**Conference title:** 15th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** Mina, M.M.M. Ki:elements, Saarbruecken, Germany.

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**Subject:** Embase;biological marker (major);semorinemab;adult;Alzheimer disease (major);Alzheimer Disease Assessment Scale;brain region;caudate nucleus;clinical dementia rating scale;cognitive defect;conference abstract;construct validity;controlled study;cross-sectional study;feature selection;female;frontal lobe;genetic marker;gray matter;hippocampus;human;interview;language;leave one out cross validation;left hemisphere;machine learning (major);major clinical study;male;memory;middle frontal gyrus;middle temporal gyrus;parahippocampal gyrus;parietal lobe;phase 2 clinical trial;pipeline;random forest;speech (major);standardized uptake value ratio;support vector machine;temporal lobe;United States

**Substance:** Substance Substance: semorinemab; CAS: 2159141-27-0;

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Document 23

## **INTUITION: A BRAIN HEALTH STUDY USING MULTIMODAL DIGITAL BIOMARKERS to DECIPHER COGNITIVE PROFILES of INDIVIDUALS AT-RISK for ALZHEIMER'S and RELATED DEMENTIAS**

**Author:** Butler, M. 1 ; Porsteinsson, A. 2 ; Kenny, S. 1 ; Lenyoun, H. 3 ; Hobbs, M. 1 ; Brown, R. 1 ; Bianchi, M. 3 ; Williams, J. 1 ; Gabelle, A. 1 ; Belachew, S. 1

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**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 9 : S242. Springer. (Dec 2022)

**Abstract (summary):** Background: Identifying individuals at-risk for alzheimer's disease (AD) and related dementias is critical for early diagnosis, monitoring, and treatment. Emerging digital health technologies offer unique opportunities to describe and decipher cognitive trajectories in at-risk populations. Consumer-grade digital devices can unobtrusively trace real-world behaviors and generate digital signatures of everyday cognition. Passive and active data collection with digital tools may open new avenues for early detection in non-clinical settings and expand the scope and scale of screening for cognitive decline. Remote and frequent cognitive sampling allows for increased spatiotemporal resolution at an individual level and has the potential to optimize prediction of clinical progression in a robust, dynamic fashion. Development and validation of personalized digital tools may equip and empower patients to track cognitive wellness and promote societal awareness of brain health. Objectives: The co-primary objectives of the INTUITION study are to (1) develop real-world high-accuracy classifier models that distinguish cognitive impairments from healthy aging to promote

screening and monitoring of people at-risk to develop AD and related dementias, and (2) to construct a trackable cognitive health score. The secondary aims are to predict cognitive decline and risk of conversion to mild cognitive impairment (MCI) in healthy and subjective cognitive complaint (SCC) populations. In a subset of participants, AD-biomarkers define the at-risk populations and will be used to assess classifier selectivity for suspected underlying pathology. Methods: The INTUITION study (NCT 05058950) is a two-year observational digital study enrolling 23,000 U.S.-based participants aged 21 to 86 years of age inclusive, including healthy controls, SCC, and MCI. The study launched in September of 2021 and continues recruitment in 2022. This virtual app-based study uses multimodal sensor devices, including an iPhone and Apple Watch, for longitudinal data collection from consenting participants. The study has been designed with privacy, control, and transparency in mind as well as data security. Device use is coupled with passive sensor-based monitoring in conjunction with validated cognitive tests and behavioral surveys. The sources of passive data collected from the study specific app using Apple Watch and iPhone cover multiple domains, including motor and autonomic function, diurnal rhythms, speech and language, social function, and everyday cognition. We aim to demonstrate the utility of using data from features derived from sensor streams to distinguish cognitive status between cognitively intact participants and those with MCI. Those features which drive model outputs will be mapped to cognitive outcome measures with the purpose of deriving a trackable cognitive health score. There are two study arms with a design to support the development of a classifier model which is both accurate and generalizable. In one study arm, model accuracy will be appraised in subjects with recently established cognitive status based on expert clinical evaluation, phenotyping, and AD-biomarkers. In the second study arm, a larger population-based cohort will provide data to understand classifier model generalizability. In this arm cognitive status is established by self-report and the confidence in cognitive status labeling is adjudicated by tele-research evaluation. Cognitive assessments are deployed at monthly and quarterly intervals using neuropsychological methods adapted for virtual research and with a high-frequency, repeated measurement approach. Cognitive test selection was designed to probe the integrity of learning and memory, processing speed, attention, executive and visuospatial function. App-based administration of validated surveys occurs at regular intervals and covers multiple domains, including mood, sleep, diet, substance use, exercise, quality-of-life, stress and discrimination, self-efficacy, medical history, medications, risk-factors for dementia, global cognitive health, and instrumental activities of daily living. Results: The INTUITION study is currently enrolling and is proceeding along expected timelines with full enrollment expected before the end of 2022. Baseline characteristics and cognitive profiles of the whole population and subgroups of interest (e.g., SCC, MCI) will be presented at the conference. We will provide preliminary results of the normative cognitive data of the population both with and without cognitive complaints across the aging spectrum from the third to ninth decades of life. Conclusions: The INTUITION study is the first digital health and medicine study of this scope and will provide a large and comprehensive dataset of passive and active digital biomarker assessments on participants with and without vulnerability to cognitive decline due to AD or other underlying disease processes.

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**Conference title:** 15th Conference Clinical Trials Alzheimer's Disease  
**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.  
**Correspondence author:** Butler, M. Biogen, Cambridge, United States.

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**Subject:** Embase;biological marker (major);adult;aged;aging;Alzheimer disease (major);apple;attention;brain (major);circadian rhythm;classifier;clinical evaluation;cognition;cognitive defect;conference abstract;daily life activity;dementia (major);diet;exercise;healthy aging;human;information security;intuition;language;learning;medical history;memory;mild cognitive impairment;mood;motor performance;nonhuman;outcome assessment;phenotype;physiological stress;prediction;preliminary data;privacy;processing speed;quality of life;risk assessment;risk factor;self concept;self report;sensor;sleep;social status;speech;substance use;validation process;very elderly

**Updates:** 2022-12-31

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Document 24

## Natural Language Processing of Movie Recall and Drug Fluency, and Associated Brain Function, in Cocaine and Heroin Addiction

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**Publication info:** Neuropsychopharmacology, suppl. Supplement 1 47 : 10. Springer Science+Business Media B.V. (Dec 2022)

**Abstract (summary):** Background: Individuals with addiction attribute excessive salience to drug/drug-related cues, which could enhance performance on neuropsychological probes. For example, individuals with cocaine addiction outperform healthy controls (HC) when prompted to generate drug-related words. Here we tested this effect in individuals with heroin use disorder (iHUD), in addition testing for verbal recall following watching of a heroin-related movie, before and after 14-weeks of treatment. We aimed to test for group differences and the potential reduction in drug-related verbal fluency and recall biases following inpatient treatment. Methods: The drug fluency task was performed by 32 inpatients with iHUD (age=40.8 ± 9.2, 6 women) and 16 HC (age=43.8 ± 10.3, 6 women). Participants watched the first 17 min of the movie *Trainspotting*, containing drug and nondrug scenes. After watching the movie, participants verbally recalled it. Fourteen iHUD performed the tasks again following 14 weeks of treatment, when adherence was tracked by daily EMAs. Results: The iHUD named more drug-related words than HC on the verbal fluency task (18.4 ± 5.8 vs. 15.6 ± 3.3 p = .02). In the recall task, iHUD proportionally recalled more drug>nondrug scenes (recall frequency: .7 ± .2 vs. .6 ± .2, p = .045) with a similar pattern for recall duration (p = .024). While fluency, recall frequency or duration did not change with treatment (ps >.60), there was a trend for less decrease in drug over nondrug recall frequency between the sessions to be associated with longer lifetime heroin use (r = .5, p = .051). Also, longer drug over nondrug recall duration at the post-treatment session was associated with worse treatment adherence in the iHUD (r = .6, p = .018). Conclusions: Here we identify simple and naturalistic, ecologically-valid, **speech**-based neuropsychological measures that tap language, memory/retrieval and higher order executive functions, revealing a drug bias in drug addiction. Associations with addiction severity and treatment adherence suggest these contextually-biased measures may be **biomarkers** of clinical endpoints. Current efforts are geared towards the use of **machine learning** (e.g., natural language processing) for the exploration of these **speech**-based **biomarkers** vis-à-vis brain function.

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**Conference country:** United States

**Conference end date:** 2022-12-07

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**Correspondence author:** Goldstein, Rita Icahn School of Medicine at Mount Sinai, New York, NY, United States.

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**Subject:** Embase;biological marker;cocaine (major);diamorphine;Addiction Severity Index;adult;brain function (major);clinical article;cocaine dependence (major);conference abstract;controlled study;drug dependence;drug therapy;executive function;female;heroin dependence (major);hospital patient;human;information retrieval;machine learning;memory;movie (major);natural language processing (major);recall (major);recall bias;speech;word recognition

**Substance:** Substance Substance: cocaine; CAS: 50-36-253-21-45937-29-1; Substance: diamorphine; CAS: 1502-95-0561-27-3;

**Updates:** 2022-12-29

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Document 25

## **Speech Biomarkers for Delirium and Cognitive Impairment in Hospitalized Older Adults**

**Author:** Tang, Sunny 1 ; Cong, Yan 1 ; Mercep, Gwenyth 1 ; Bhatti, Mutahira 1 ; Serpe, Grace 1 ; Gromova, Valeria 1 ; John, Majnu 1 ; Liberman, Mark 1 ; Sinvani, Liron 1

**Abstract (summary):** Background: Up to 50% of hospitalized older adults (75+) experience delirium, which is associated with increased morbidity, mortality, and resource utilization, as well as a 12-fold increased risk for new-onset dementia. Yet, 75% of delirium remains undiagnosed. Few studies have systematically studied **speech** and language disturbances in hospitalized older adults with delirium, and to our knowledge, no previous study has attempted to objectively quantify these phenomena with computational methods. The objectives of this study were to 1) systematically evaluate and describe **speech** and language disturbance in hospitalized older adults with and without delirium, 2) evaluate whether automated **speech** analysis could be feasibly implemented for acutely ill hospitalized patients, and 3) explore whether computational **speech** and language features could be used to diagnose patients with delirium. Methods: Hospitalized older adults aged 75 years and older (n=33) were recruited across three medicine units at an academic hospital. Patients with documented diagnosis of dementia were excluded. Delirium assessment was completed by trained research assistants and verified by a delirium expert (LS), and included: Orientation, 3-item recall, confusion assessment method (CAM) long form; and Richmond Agitation and Sedation Scale (RASS). Diagnosis was based on these datapoints and the DSM-5 criteria for delirium. Clinical ratings for language disturbance were completed using the Scale for the Assessment of Thought Language and Communication (TLC). Audio recordings were collected for open-ended prompts, a paragraph reading, and fluency tasks, then transcribed verbatim. Recordings and transcripts were processed separately for each task using an automated pipeline to extract acoustic (prosody and **voice** quality, speaking tempo and pauses) and textual features (semantic coherence, dysfluencies and **speech** errors, lexical characteristics, parts-of-**speech**, **speech** quantity). To reduce the feature space, we first selected only the features which showed a trend-level correlation with the total CAM score ( $p < 0.10$ ), then visually inspected correlation plots to remove redundancy. The final feature set included 26 measures. Group effects were compared using ANOVA and chi-squared tests, correlations were measured with Pearson coefficients, and category fluency totals were compared to normative data using one-sided t-tests. We used binomial elastic net regression models to predict delirium status (delirium(-) vs. delirium(+)), training on the full dataset with 10-fold internal crossvalidation. Results: Of the 33 participants, 10 met criteria for delirium (Delirium(+)) and 23 did not (Delirium(-)). The Delirium(+) group scored significantly higher on total TLC score ( $p = 0.05$ ,  $d = 0.81$ ) and incoherence ( $p = 0.001$ ,  $d = 1.41$ ). Participants with delirium scored lower on category fluency compared to those without delirium ( $p = 0.02$ ,  $d = -0.97$ ), and both groups scored lower than the normative population (Delirium(-):  $p < 0.001$ ,  $d = -1.22$ ; Delirium(+):  $p < 0.001$ ,  $d = -2.20$ ). Higher CAM score was correlated with total TLC score ( $r = 0.41$ ,  $p = 0.02$ ), incoherence ( $r = 0.58$ ,  $p < 0.001$ ), loss of goal ( $r = 0.36$ ,  $p = 0.04$ ) and lower category fluency ( $r = -0.41$ ,  $p = 0.02$ ). Delirium status was predicted with demographics alone, demographics and clinical **speech** ratings, demographics and computational **speech**/language features, or all of these. The model with demographics and computational **speech**/language features performed best, classifying delirium status with accuracy of 78%, kappa of 0.4, and area under the curve of 0.90. All 23 Delirium(-) participants were correctly identified, in addition to 8/10 Delirium(+) participants. In this model, presence of delirium was most highly predicted

by **speech** errors during paragraph reading, transcribed symbols (including punctuation, restarts, and incomplete words) in the open-ended narratives, use of determiners in the family narrative task, and semantic diversity (lexical ambiguity) of words given during the fluency tasks. Absence of delirium was most highly predicted by filled pauses during the family narrative task (e.g., “um,” “uh”), use of adverbs in open-ended narratives, use of adjectives during the picture description, and variance in jitter (fluctuations in **voice** amplitude) during fluency tasks. Conclusions: Hospitalized older adults with delirium demonstrate significant impairments in **speech** and language. In particular, delirium is associated with incoherence, loss of goal, and decreased category fluency scores. Hospitalized older adults without delirium may also demonstrate a subtle cognitive impairment relative to the normative population, as reflected in lower category fluency scores. Automated **speech** and language analysis was feasibly completed in the acute care setting, and computational features were highly informative for predicting delirium status, providing a proof of concept for this approach.

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**Correspondence author:** Tang, Sunny Feinstein Institutes for Medical Research, Glen Oaks, NY, United States.

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**Identifier (keyword):** Automated Natural **Speech** Analysis, Cognitive Impairment, Delirium, Natural Language Processing (NLP), Older Adults

**Language:** English

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**Subject:** Embase;biological marker (major);acutely ill patient;aged;analysis of variance;area under the curve (major);audio recording;clinical article;cognitive defect (major);conference abstract;controlled study;cross validation;delirium (major);delirium assessment;dementia;demographics;diagnosis;DSM-5;elastic tissue;emergency care;female;fluency disorder;genetic transcription;human;language disability;male;memory;narrative;natural language processing (major);pipeline;proof of concept;prosody;regression model;Richmond Agitation Sedation Scale;speech (major);speech analysis (major);speech disorder;university hospital;voice

**Updates:** 2022-12-29

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Document 26

## **An explainable COVID-19 detection system based on human sounds**

**Author:** Li, Huining 1 ; Chen, Xingyu 2 ; Qian, Xiaoye 3 ; Chen, Huan 3 ; Li, Zhengxiong 2 ; Bhattacharjee, Soumyadeep 1 ; Zhang, Hanbin 1 ; Huang, Ming-Chun 4 ; Xu, Wenyao 1

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**Publication info:** Smart Health 26 Elsevier B.V. (Dec 2022)

**Abstract (summary):** Acoustic signals generated by the human body have often been used as biomarkers to diagnose and monitor diseases. As the pathogenesis of COVID-19 indicates impairments in the respiratory system, digital acoustic biomarkers of COVID-19 are under investigation. In this paper, we explore an accurate and explainable COVID-19 diagnosis approach based on human speech, cough, and breath data using the power of machine learning. We first analyze our design space considerations from the data aspect and model aspect. Then, we perform data augmentation, Mel-spectrogram transformation, and develop a deep residual architecture-based model for prediction. Experimental results show that our system outperforms the baseline, with the

ROC-AUC result increased by 5.47%. Finally, we perform an interpretation analysis based on the visualization of the activation map to further validate the model.

**Accession number:** 2021019653

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**Correspondence author:** Xu, Wenyao Department of Computer Science and Engineering, University at Buffalo, United States.

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**Document type:** Article

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**Grant:** CNS-2050910. , NSF. National Science Foundation.

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**Identifier (keyword):** Accurate, Acoustic, COVID-19, Explainable

**Language:** English

**Language of abstract:** English

**Number of references:** 15

**Publication date:** Dec 2022

**Publication type:** Journal

**Publisher:** Elsevier B.V.

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**Subject:** Embase;biomedical software;abnormal respiratory sound (major);adolescent;adult;Article;audio recording;breathing (major);classifier;comparative study;controlled study;convolutional neural network;coronavirus disease 2019 -- diagnosis (major);coughing (major);data analysis;deep learning;diagnostic accuracy;diagnostic test accuracy study;feature extraction;female;human;machine learning;major clinical study;male;model;noise;pitch;short time Fourier transform;sound analysis (major);speech (major);speech analysis

**Updates:** 2022-11-102022-11-16

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Document 27

## Detecting Parkinson's disease and its cognitive phenotypes via automated semantic analyses of action stories

**Author:** García, Adolfo M. 1 ; Escobar-Grisales, Daniel 2 ; Vásquez Correa, Juan Camilo 3 ; Bocanegra, Yamile 4 ; Moreno, Leonardo 5 ; Carmona, Jairo 6 ; Orozco-Arroyave, Juan Rafael 7

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**Publication info:** npj Parkinson's Disease 8.1 Nature Research. (Dec 2022)

**Abstract (summary):** Action-concept outcomes are useful targets to identify Parkinson's disease (PD) patients and differentiate between those with and without mild cognitive impairment (PD-MCI, PD-nMCI). Yet, most approaches employ burdensome examiner-dependent tasks, limiting their utility. We introduce a framework capturing action-concept markers automatically in natural speech. Patients from both subgroups and controls retold an action-laden and a non-action-laden text (AT, nAT). In each retelling, we weighed action and non-action concepts through our automated Proximity-to-Reference-Semantic-Field (P-RSF) metric, for analysis via ANCOVAs (controlling for cognitive dysfunction) and support vector machines. Patients were differentiated from controls based on AT

(but not nAT) P-RSF scores. The same occurred in PD-nMCI patients. Conversely, PD-MCI patients exhibited reduced P-RSF scores for both texts. Direct discrimination between patient subgroups was not systematic, but it yielded best outcomes via AT scores. Our approach outperformed classifiers based on corpus-derived embeddings. This framework opens scalable avenues to support PD diagnosis and phenotyping.

**Accession number:** 2020249205

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**Publication date:** Dec 2022

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**Publisher:** Nature Research

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**Subject:** Embase;microphone;accuracy;adult;Article;cognition (major);controlled study;diagnostic test accuracy study;exploratory factor analysis;female;Hoehn and Yahr scale;human;human experiment;language;machine learning;male;middle aged;mild cognitive impairment;Montreal cognitive assessment;Parkinson disease (major);phenotype (major);receiver operating characteristic;semantic memory (major);sensitivity and specificity;support vector machine;Unified Parkinson Disease Rating Scale

**Updates:** 2022-11-282022-12-20

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Document 28

## Interpreting acoustic features for the assessment of Alzheimer's disease using ForestNet

**Author:** Pérez-Toro, Paula Andrea 1 ; Rodríguez-Salas, Dalia 2 ; Arias-Vergara, Tomás 3 ; Klumpp, Philipp 2 ; Schuster, Maria 4 ; Nöth, Elmar 2 ; Orozco-Aroyave, Juan Rafael 1 ; Maier, Andreas K. 2

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**Publication info:** Smart Health 26 Elsevier B.V. (Dec 2022)

**Abstract (summary):** Nowadays, interpretable machine learning models are one of the most critical topics in the medical domain. The lack of interpretation leads to blind and unreliable models for clinicians, despite the fact that the aim is to support diagnosis through these tools. This problem has been increasing since the creation of large models such as those based on deep learning, which, despite providing good performance in prediction and classification tasks, are not transparent to human understanding. One of the increasingly prevalent clinical problems related to acoustic and linguistic disorders is Alzheimer's disease (AD), where one important challenge is to provide speech

**markers** that help in supporting, understanding, and facilitating the diagnosis and monitoring of the disease. It motivates this study which proposes a methodology focused on analyzing acoustic features in AD and at the same time providing interpretation from the results. The proposed approach consists of using decision tree-based methods together with neural networks (ForestNet) for analyzing the classification results. Only features that can give interpretation were considered. Unweighted average recalls of up to 79% were achieved for discriminating AD patients. Then, we looked at the relevant features that provided most of the information for assessing AD, which were those related to rhythm, voiced rates, duration, and phone rates. This confirms that this kind of approach can be suitable for the discrimination of AD while maintaining a good performance.

**Accession number:** 2020718347

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**Identifier (keyword):** Acoustic analysis, Alzheimer's disease, ForestNets, Interpretability

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**Language of abstract:** English

**Number of references:** 28

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**Subject:** Embase;acoustic analysis (major);aged;Alzheimer disease (major);Article;artificial neural network (major);classification;classifier;controlled study;decision tree;emotion;female;human;major clinical study;male;medical assessment (major);phoneme;rhythm;voice

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Document 29

## Exploring the digital footprint of depression: a PRISMA systematic literature review of the empirical evidence

**Author:** Zarate, Daniel 1 ; Stavropoulos, Vasileios 2 ; Ball, Michelle 1 ; de Sena Collier, Gabriel 1 ; Jacobson, Nicholas C. 3

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**Publication info:** BMC Psychiatry 22.1 BioMed Central Ltd. (Dec 2022)

**Abstract (summary):** Background: This PRISMA systematic literature review examined the use of digital data collection methods (including ecological momentary assessment [EMA], experience sampling method [ESM], digital biomarkers, passive sensing, mobile sensing, ambulatory assessment, and time-series analysis), emphasizing on digital phenotyping (DP) to study depression. DP is defined as the use of digital data to profile health information objectively. Aims: Four distinct yet interrelated goals underpin this study: (a) to identify empirical research examining the use of DP to study depression; (b) to describe the different methods and technology employed; (c) to integrate the evidence regarding the efficacy of digital data in the examination, diagnosis, and monitoring of depression and (d) to clarify DP definitions and digital mental health records terminology. Results: Overall, 118 studies were assessed as eligible. Considering the terms employed, “EMA”, “ESM”, and “DP” were the most predominant. A variety of DP data sources were reported, including voice, language, keyboard typing kinematics, mobile phone calls and texts, geocoded activity, actigraphy

sensor-related recordings (i.e., steps, sleep, circadian rhythm), and self-reported apps' information. Reviewed studies employed subjectively and objectively recorded **digital** data in combination with interviews and psychometric scales. Conclusions: Findings suggest links between a person's **digital** records and depression. Future research recommendations include (a) deriving consensus regarding the DP definition and (b) expanding the literature to consider a person's broader contextual and developmental circumstances in relation to their **digital** data/records.

**Accession number:** 2017996789

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The authors would like to acknowledge the fantastic work of this wonderful team. Additionally, Figures presented here were produced by Casandra graphics (casugp@gmail.com).

**Identifier (keyword):** Ambulatory assessment, Depression, **Digital** phenotype, Ecological momentary assessment, Experience sampling, Passive sensing, PRISMA, Systematic literature review

**Language:** English

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**Number of references:** 200

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**Publisher:** BioMed Central Ltd

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**Subject:** Embase;MEDLINE;biological marker;bioinformatics software;biosensor;actimetry;ambulatory care;Article;cell phone use;circadian rhythm;consensus;depression -- diagnosis (major);diagnostic test (major);digital phenotyping + (major);digital technology (major);ecological momentary assessment;electronic health record (major);empirical research;evidence based medicine (major);human;information processing;interview;kinematics;nomenclature (major);patient monitoring (major);phenotype (major);psychologic test (major);psychometry;sampling;self report;systematic review

**Updates:** 2022-06-272022-06-282022-07-052022-08-18

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Document 30

## **BRINGING MEANING to PERSONALISED BRAIN HEALTH: A TOOL THAT EMPOWERS INDIVIDUALS to DEFINE and MONITOR PERSONALLY MEANINGFUL CHANGE**

**Author:** Saunders, S. 1 ; Bates, D. 2 ; Bharija, A. 3 ; Gomes-Osman, J. 4 ; Luz, S. 1 ; Muniz-Terrera, G. 1 ; Pascual-Leone, Á. 5 ; Ritchie, C. 1

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**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 9 : S182-S183. Springer. (Dec 2022)

**Abstract (summary):** Background: In the early stages of alzheimer's disease (AD), the aim is to maintain brain health by preventing entirely, or delaying significantly, the development of symptoms. However, it is essential to demonstrate an intervention delivers a meaningful outcome for the patient. Therefore, it is critical to associate most commonly used outcome measures in clinical trials (i.e., biomarkers and symptoms) with outcomes that are relevant for the individual patient and account for the change in treatment priorities over time. To fill this knowledge gap, researchers at the University of Edinburgh have partnered with Linus Health to create a tool for capturing personally meaningful outcomes to monitor functional trajectory, and importantly, treatment effects over time. Objectives: Our aim is to create a tool to easily capture what aspects are most important for individuals to retain should their brain health deteriorate through conditions like AD. The presentation aims to (1) to update on the latest results of the electronic Person Specific Outcome Measure (ePSOM) programme, reporting findings from a large UK-wide survey on what outcomes matter to people when

developing new treatments for AD and (2) outline a development plan to validate a new **digital** tool to capture and monitor personally meaningful outcomes in Brain Health. Method: The UK-wide survey (conducted Aug 2019 - Nov 2019) probed individuals to define most important individual priorities in five domains of Brain Health (Everyday functioning; Enjoying life; Thinking abilities; Relationships and Social interactions; Sense of identity). These data were collected using primarily free text responses, alongside relevant clinical and demographic data. We used natural language processing (NLP) techniques to analyse the data. We report findings from a subgroup analysis which includes individuals with a self-reported neurodegenerative disease diagnosis (primarily Mild Cognitive Impairment (MCI) or AD) whereby we conducted comparisons with an age and gender matched control group. We also describe the development and validation plan for a tool aimed at capturing personally meaningful outcomes for use in clinical trials as adjunct to **biomarker**, cognitive and functional endpoints. Importantly, this tool has the potential to create a critical anchor for personalised interventions by allowing individuals to define 'what does treatment success look like for them? Results: The ePSOM survey was filled in by n=5808 respondents across the UK, with over 80,000 free text responses of what outcomes matter to individuals. The automated NLP analysis resulted in 184 unique themes of importance about Brain Health across the whole data set. A sub-set of n=167 respondents (2.9%) (women n = 91, men n = 69, other n = 7) had received one of our pre-defined neurodegenerative disease diagnoses: most commonly MCI n = 52, 1.1%; or alzheimer's disease n = 48, 1.0%. Several thematic clusters were significantly more important for the target diagnostic group, e.g.: Expressing opinions; and less important, e.g., Cognitive Games. Conclusion: The person specific **digital** tool developed by our team invites each person using the tool to first define their brain health priorities. While deriving a numeric score is less central in clinical practice than in regulatory trials where a change of score indicates improvement/decline/no change over time, this 'personal outcomes tool- allows patients to define the most important outcomes against which we should measure treatment success. It also informs the most appropriate interventions so that the person can 'be the best version of themselves-, i.e., a truly personalised medicine approach. For instance, if a patient defines driving as the key outcome, then as well as personalised interventions to maintain brain health and risk factor modification, the person may also be directed to 'coaching- for driving to build resilience with driving, maintain confidence and develop new skills that helps keep them driving for as long as possible. By employing NLP of either **speech** or text, we ensure every outcome recorded is unique to that individual and immune to cultural/language biases inherent with tools using pre-defined items. In clinical trials, there is much value for such a tool in parallel with biological measures of AD and provide a secondary endpoint to offer further proof of drug effectiveness, from the study participant's point of view. The ePSOM programme results to date suggest that outcomes that matter shift along the preclinical, prodromal and dementia continuum. This has important implications for the development of outcome measures that may be used in long-term clinical monitoring and interventional studies that may last several years. Our personalised medicine approach could have value more broadly in other diseases which affect brain health.

**Accession number:** 639873321

**Conference country:** United States

**Conference end date:** 2022-12-02

**Conference location:** San Francisco, CA

**Conference start date:** 2022-11-29

**Conference title:** 15th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** Saunders, S. Centre for Clinical Brain Sciences, University of Edinburgh, UK, Edinburgh, United Kingdom.

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**Date created:** 2022-12-30

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**Document type:** Conference Abstract

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**Publication date:** Dec 2022

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**Subject:** Embase;biological marker;adult;Alzheimer disease;brain (major);clinical monitoring;clinical practice;conference abstract;controlled study;degenerative disease;dementia;demographics;diagnosis;diagnosis related group;female;gender;health care planning;human;intervention study;major clinical study;male;mild cognitive impairment;natural language processing;outcome assessment;personalized medicine;preclinical study;risk factor;skill;social interaction;speech;thinking;validation process

**Updates:** 2022-12-31

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Document 31

## **INCREASING STUDY POWER VIA FREQUENT **SPEECH**-BASED ASSESSMENTS of COGNITION**

**Author:** Stegmann, G. 1 ; Hahn, S. 1 ; Liss, J. 1 ; Berisha, V. 1 ; Mueller, K. 2

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**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 9 : S236-S237. Springer. (Dec 2022)

**Abstract (summary):** Background: With an increase in clinical trials targeting patients early in their disease course comes challenges in trial design. Powering a trial focused on traditional **biomarkers** in early-stage patients requires large sample sizes and lengthy trials, with significant consequences for recruitment and retention. To address these problems, there is interest in novel **biomarkers** that are more sensitive than traditional **biomarkers** and can be measured frequently, at low cost to patient and trial sponsor. One way to increase the power, and therefore decrease the sample size requirement for a clinical trial, is by collecting data at more frequent time intervals. Rutkove et al (2020) demonstrated how frequent sampling of both traditional and **digital biomarkers** improved the ability to detect small changes in disease progression. Frequent data collection is made feasible if the participants are measured remotely. Stegmann et al. (2022) demonstrated that **speech** samples could be collected outside of the clinic, without clinical supervision, and that it was possible to use it to measure cognitive function. The authors used transcripts from healthy and cognitively impaired participants performing the Cookie Theft picture description to automatically extract a **speech**-based measure of communicative efficiency, Semantic Relevance, and showed that it correlated with the Mini Mental State Exam. **Speech** is therefore a promising candidate **biomarker** for measuring clinically-relevant changes to cognition in a low-burden manner. Objective: In our study, we used Semantic Relevance as the cognitive outcome of interest, and the model described in Stegmann et al. (2022), to show the relationship between power and **speech** sampling frequency in participants with mild cognitive impairment. Methods: A power analysis was conducted using the longitudinal parameter estimates from Stegmann et al. (2022). In the published article, a growth curve model (longitudinal mixed-effects model) was estimated such that the longitudinal change in a Semantic Relevance was modeled for participants from different levels of cognitive impairment. The parameter estimates from the mild cognitive impairment participants- longitudinal model were used as the basis for the power analysis. The power analysis was performed through a simulation study. In the simulation study, a treatment and a control group were generated. The control group followed the longitudinal decline according to the parameter estimates obtained from the article, and the treatment group declined 10%, 30%, 50%, and 75% slower than the control group. Sample sizes of N = 100, 125, and 150 participants per group were generated for a hypothetical 2-year study. Finally, sampling frequencies of 15 (every 15 days), 30, 60, 90, 180, and 365 were generated. For each combination of simulation conditions, the slopes were estimated for each participant, and a two-sample t-test was used to estimate the mean difference in slopes between the two groups. 200 replicates were performed for each simulation condition, and the proportion of replicates where the t-test was significant was used to compute the power to detect the treatment effect. Results: The power (proportion of replicates with significant differences between the two groups) was calculated for each simulation condition. The power increased as the differences between the hypothesized treatment and control group increased, but more importantly, the power increased substantially as the sampling frequency increased. For example, for an effect size of 50% difference in mean slope between a treatment and control group of

100 participants per group, the power to detect a significant effect was 14% when sampling every 365 days, and it increased to 71% when sampling every 15 days. Conclusion: This study highlights the value of frequent sampling in clinical trials as a way to increase the power to detect significant treatment effects. An added benefit of this approach is that participants do not need a clinic visit for data to be obtained, and this also reduces participant burden and attrition.

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**Conference country:** United States

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**Conference location:** San Francisco, CA

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**Conference title:** 15th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** Stegmann, G. Arizona State University and Aural Analytics, Scottsdale, AZ, United States.

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**Subject:** Embase;biological marker;adult;clinical supervision;cognition;cognition assessment (major);cognitive defect;conference abstract;controlled study;cookie;effect size;female;genetic transcription;growth curve;human;human tissue;major clinical study;male;mild cognitive impairment;Mini Mental State Examination;outcome assessment;power analysis;sample size;simulation;speech (major);speech analysis;theft

## Quantifying **Speech** and Language Disturbance in Schizophrenia With Neural Language Models

**Author:** Cong, Yan 1 ; Nikzad, Amir 1 ; Pradhan, Sameer 1 ; Cho, Sunghye 1 ; Hänsel, Katrin 1 ; Mehta, Aarush 1 ; Berretta, Sarah 1 ; Behbehani, Leily 1 ; Liberman, Mark 1 ; Tang, Sunny 1

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**Publication info:** Neuropsychopharmacology, suppl. Supplement 1 47 : 359-360. Springer Science+Business Media B.V. (Dec 2022)

**Abstract (summary):** Background: Disorganized **speech** is a hallmark of schizophrenia spectrum disorders (SSD) and related psychotic disorders and represents complex language disturbances which cannot be easily captured on a semantic or syntactic level. Since their introduction in 2017, pre-trained neural language models (nLMs) continue achieving state-of-the-art results on a variety of natural language processing tasks. We hypothesized that nLMs are promising tools for automatically quantifying disorganized **speech** in SSD because nLMs are effective at encoding contextual content and more complex referential information. We tested multiple validated semantic similarity strategies to examine the extent to which nLMs can improve accuracy of detecting and characterizing different types of **speech** and language disturbances, especially incoherent and inefficient disorganized **speech** among people with SSD. Methods: Healthy volunteers (HV) and participants with SSD were recruited from inpatient and outpatient facilities (SSD = 74, HV = 37). They were rated on the Scale for the Assessment of Thought Language and Communication (TLC) and two items from the Scale for the Assessment of Negative Symptoms (SANS; decreased **vocal** inflection and increased latency). Open-ended **speech** (162 ± 121 words) was recorded and underwent transcription and processing for cosine similarity of word- and sentencelevel embeddings. Three levels of pre-processing were conducted incrementally. Level 1 included verbatim transcripts excluding non-**speech** verbalizations like laughter. Level 2 excluded disfluencies such as repetitions and filled pauses. Level 3 additionally excluded NLTK stop words. We adopted 3 primary strategies to measure semantic similarity, sometimes referred to as “semantic coherence” in other studies: (1) the word-to-word variability at K inter-word distances, with K ranging from 2 to 10 (K2:10); (2) average semantic similarity of each word in 5- or 10-words window (W5/10); (3) First Order similarity of consecutive phrase vectors and Second Order similarity between phrase separated by another intervening phrase (FO/SO). Vector embeddings were generated from a static model GloVe and 3 nLMs (BERT, T5, GPT3) to compute similarity. Median, inter-quartile range (IQR), 5th percentile (Q5), and 95th percentile (Q95) values were then derived. Welch's t-test were used to examine group diagnosis (SSD vs. HV). Significance was two-tailed with alpha=0.05. Results: Using the K2:10 semantic similarity strategies, across all levels of pre-processing, GloVe showed statistically significant lower similarity in SSD than in HV for 7

measures with medium effect size (Cohen's  $d$  0.5-0.8) in median, Q5, and Q95 similarity. BERT showed lower similarity in SSD for 9 measures with medium effect size, and for 46 measures with large effect size (Cohen's  $d \geq 0.8$ ) in median, Q95, and IQR values. T5 showed lower similarity in SSD for 43 measures with medium effect size, and for 37 measures with large effect size in median, Q95, and IQR values. In contrast, GPT3 showed higher similarity in SSD for 39 measures but lower IQR in SSD for 2 measures (Cohen's  $d \geq 0.5$ ). For each of the models, more extensive data pre-processing generally resulted in fewer significant results. Using the W5/10 semantic similarity strategies, GloVe showed statistically significant higher similarity in SSD for 1 measure (Cohen's  $d$  0.41) with Level 1 preprocessing, and no significant results with more pre-processing. BERT showed lower similarity in SSD for 18 measures (Cohen's  $d \geq 0.5$ ), including 13 measures with large effect size. The results were consistent across pre-processing levels. T5 showed lower similarity in SSD for 15 measures (Cohen's  $d \geq 0.5$ ), including 6 measures with large effect size. In contrast, GPT3 showed higher similarity in SSD for 8 measures of median, Q5 and Q95 values but lower IQR in SSD for 3 measures (Cohen's  $d \geq 0.5$ ). For both T5 and GPT3, Level 3 pre-processing resulted in fewer significant effects. Using the FO/SO strategies, GloVe showed statistically significant lower similarity in SSD for SO Q95 (Cohen's  $d$  -0.77) and FO Q95 (Cohen's  $d$  -0.81) with Level 1 pre-processing, but higher similarity in SSD for FO Q5 (Cohen's  $d$  0.43) with Level 2, and null results for Level 3. BERT showed higher similarity in SSD for 4 measures (Cohen's  $d$  0.2-0.5), and T5 for 2 measures with medium effects. The results improved with more extensive pre-processing for both BERT and T5. GPT3 showed higher similarity in SSD for 6 measures (Cohen's  $d$  0.5-0.8), including 2 measures with large effect size. The results were mostly consistent across levels of preprocessing. Conclusions: We evaluated three different types of nLMs to quantify **speech** and language disturbances in SSD, using static embeddings from GloVe as baseline. nLMs were, in general, more sensitive than GloVe in identifying language disturbances in SSD, reflecting that nLMs are better tools for studying SSD. Preprocessing by removing disfluencies did not greatly alter the results but removing stop words masked the SSD group difference in some cases, particularly for GPT3. GloVe, BERT and T5 all generally show lower similarity in SSD, across analysis frameworks, while GPT3 mostly shows higher similarity in similar tests. We hypothesized that the differences can be explained by how nLMs are pre-trained and what data they are trained on. Future directions include evaluating the robustness of language measures generated from nLMs across **speech** tasks and samples, and finetuning nLMs with domain specific data.

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**Correspondence author:** Cong, Yan Feinstein Institute for Medical Research, Glen Oaks, NY, United States.

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**Subject:** Embase;biological marker (major);adult;conference abstract;controlled study;effect size;embedding;genetic transcription;glove;hospital patient;human;laughter;natural language processing (major);negative syndrome>null result;outpatient;phenotype (major);psychiatry (major);quantitative analysis;schizophrenia (major);schizophrenia spectrum disorder (major);speech (major);speech disorder (major);speech test;verbalization

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Document 33

### **Vocal biomarker predicts fatigue in people with COVID-19: results from the prospective Predi-COVID cohort study**

**Author:** Elbéji, Abir 1 ; Zhang, Lu 1 ; Higa, Eduardo 1 ; Fischer, Aurélie 1 ; Despotovic, Vladimir 2 ; Nazarov, Petr V 2 ; Aguayo, Gloria 1 ; Fagherazzi, Guy 1



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**Publication info:** BMJ Open 12.11 BMJ Publishing Group. (Nov 22, 2022)

**Abstract (summary):** Objective To develop a **vocal biomarker** for fatigue monitoring in people with COVID-19. Design Prospective cohort study. Setting Predi-COVID data between May 2020 and May 2021. Participants A total of 1772 **voice** recordings were used to train an **AI**-based algorithm to predict fatigue, stratified by gender and smartphone's operating system (Android/iOS). The recordings were collected from 296 participants tracked for 2 weeks following SARS-CoV-2 infection. Primary and secondary outcome measures Four **machine learning** algorithms (logistic regression, k-nearest neighbours, **support vector machine** and soft voting classifier) were used to train and derive the fatigue **vocal biomarker**. The models were evaluated based on the following metrics: area under the curve (AUC), accuracy, F1-score, precision and recall. The Brier score was also used to evaluate the models' calibrations. Results The final study population included 56% of women and had a mean ( $\pm$ SD) age of 40 ( $\pm$ 13) years. Women were more likely to report fatigue ( $p < 0.001$ ). We developed four models for Android female, Android male, iOS female and iOS male users with a weighted AUC of 86%, 82%, 79%, 85% and a mean Brier Score of 0.15, 0.12, 0.17, 0.12, respectively. The **vocal biomarker** derived from the prediction models successfully discriminated COVID-19 participants with and without fatigue. Conclusions This study demonstrates the feasibility of identifying and remotely monitoring fatigue thanks to **voice**. **Vocal biomarkers**, digitally integrated into telemedicine technologies, are expected to improve the monitoring of people with COVID-19 or Long-COVID. Trial registration number NCT04380987.

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**Correspondence author:** Fagherazzi, Guy Department of Precision Health, Luxembourg Institute of Health, 1A-B, rue Thomas Edison, Strassen, L-1445, Luxembourg.

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**Subject:** Embase;MEDLINE;biological marker (major);smartphone;adult;area under the curve;Article;artificial intelligence;audio recording;classifier;cohort analysis;controlled clinical trial;controlled study;convolutional neural network;coronavirus disease 2019 (major);diagnostic test accuracy study;fatigue -- diagnosis (major);feature extraction;female;human;k nearest neighbor;logistic regression analysis;machine learning (major);major clinical study;male;prediction;prospective study;soft voting classifier +;support vector machine;telemedicine (major);voice

**Updates:** 2022-12-132022-12-19

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Document 34

### **Artificial intelligence assisted tools for the detection of anxiety and depression leading to suicidal ideation in adolescents: a review**

**Author:** Barua, Prabal Datta 1 ; Vinesh, Jahmunah 2 ; Lih, Oh Shu 2 ; Palmer, Elizabeth Emma 3 ; Yamakawa, Toshitaka 4 ; Kobayashi, Makiko 4 ; Acharya, Udyavara Rajendra 5

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**Publication info:** Cognitive neurodynamics : 1-22. (Nov 22, 2022)

**Abstract (summary):** Epidemiological studies report high levels of anxiety and depression amongst adolescents. These psychiatric conditions and complex interplays of biological, social and

environmental factors are important risk factors for suicidal behaviours and suicide, which show a peak in late adolescence and early adulthood. Although deaths by suicide have fallen globally in recent years, suicide deaths are increasing in some countries, such as the US. Suicide prevention is a challenging global public health problem. Currently, there aren't any validated clinical **biomarkers** for suicidal diagnosis, and traditional methods exhibit limitations. **Artificial intelligence (AI)** is budding in many fields, including in the diagnosis of medical conditions. This review paper summarizes recent studies (past 8 years) that employed **AI** tools for the automated detection of depression and/or anxiety disorder and discusses the limitations and effects of some modalities. The studies assert that **AI** tools produce promising results and could overcome the limitations of traditional diagnostic methods. Although using **AI** tools for suicidal ideation exhibits limitations, these are outweighed by the advantages. Thus, this review article also proposes extracting a fusion of features such as facial images, **speech** signals, and visual and clinical history features from deep models for the automated detection of depression and/or anxiety disorder in individuals, for future work. This may pave the way for the identification of individuals with suicidal thoughts.

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**Correspondence author:** Barua, Prabal Datta School of Management and Enterprise, University of Southern Queensland, Springfield, Australia.

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**Document type:** Journal Article, Review

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**Language:** English

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Document 35

## **Recommendations for Successful Implementation of the Use of Vocal Biomarkers for Remote Monitoring of COVID-19 and Long COVID in Clinical Practice and Research**

**Author:** Fischer, Aurelie 1 ; Elbeji, Abir 1 ; Aguayo, Gloria 1 ; Fagherazzi, Guy 1

1 Deep Digital Phenotyping Research Unit, Department of Precision Health, Luxembourg Institute of Health, Strassen, Luxembourg, Luxembourg

**Publication info:** Interactive journal of medical research 11.2: e40655. (Nov 15, 2022)

**Abstract (summary):** The COVID-19 pandemic accelerated the use of remote patient monitoring in clinical practice or research for safety and emergency reasons, justifying the need for innovative digital health solutions to monitor key parameters or symptoms related to COVID-19 or Long COVID. The use of voice-based technologies, and in particular vocal biomarkers, is a promising approach, voice being a rich, easy-to-collect medium with numerous potential applications for health care, from diagnosis to monitoring. In this viewpoint, we provide an overview of the potential benefits and limitations of using voice to monitor COVID-19, Long COVID, and related symptoms. We then describe an optimal pipeline to bring a vocal biomarker candidate from research to clinical practice and discuss recommendations to achieve such a clinical implementation successfully.

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**Copyright:** ©Aurelie Fischer, Abir Elbeji, Gloria Aguayo, Guy Fagherazzi. Originally published in the Interactive Journal of Medical Research (<https://www.i-jmr.org/>), 15.11.2022.

**Correspondence author:** Fischer, Aurelie Deep Digital Phenotyping Research Unit, Department of Precision Health, Luxembourg Institute of Health, Strassen, Luxembourg.

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**Identifier (keyword):** COVID-19, COVID-19 symptoms, Long COVID, artificial intelligence, digital health, digital health monitoring, digital health solution, health care application, health monitoring, health technology, remote monitoring, remote patient monitoring, vocalbiomarker, voice, voice-based technology

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Document 36

## **Discovery and Analytical Validation of a Vocal Biomarker to Monitor Anosmia and Ageusia in Patients With COVID-19: Cross-sectional Study**

**Author:** Higa, Eduardo 1 ; Elbéji, Abir 1 ; Zhang, Lu 2 ; Fischer, Aurélie 1 ; Aguayo, Gloria A 1 ; Nazarov, Petr V 2 ; Fagherazzi, Guy 1

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**Publication info:** JMIR medical informatics 10.11: e35622. (Nov 8, 2022)

### **Abstract (summary): BACKGROUND**

The COVID-19 disease has multiple symptoms, with anosmia and ageusia being the most prevalent, varying from 75% to 95% and from 50% to 80% of infected patients, respectively. An automatic assessment tool for these symptoms will help monitor the disease in a fast and noninvasive manner.

### **OBJECTIVE**

We hypothesized that people with COVID-19 experiencing anosmia and ageusia had different **voice** features than those without such symptoms. Our objective was to develop an **artificial intelligence** pipeline to identify and internally validate a **vocal biomarker** of these symptoms for remotely monitoring them.

## METHODS

This study used population-based data. Participants were assessed daily through a web-based questionnaire and asked to register 2 different types of **voice** recordings. They were adults (aged >18 years) who were confirmed by a polymerase chain reaction test to be positive for COVID-19 in Luxembourg and met the inclusion criteria. Statistical methods such as recursive feature elimination for dimensionality reduction, multiple statistical learning methods, and hypothesis tests were used throughout this study. The TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) Prediction Model Development checklist was used to structure the research.

## RESULTS

This study included 259 participants. Younger (aged <35 years) and female participants showed higher rates of ageusia and anosmia. Participants were aged 41 (SD 13) years on average, and the data set was balanced for sex (female: 134/259, 51.7%; male: 125/259, 48.3%). The analyzed symptom was present in 94 (36.3%) out of 259 participants and in 450 (27.5%) out of 1636 audio recordings. In all, 2 **machine learning** models were built, one for Android and one for iOS devices, and both had high accuracy-88% for Android and 85% for iOS. The final **biomarker** was then calculated using these models and internally validated.

## CONCLUSIONS

This study demonstrates that people with COVID-19 who have anosmia and ageusia have different **voice** features from those without these symptoms. Upon further validation, these **vocal biomarkers** could be nested in digital devices to improve symptom assessment in clinical practice and enhance the telemonitoring of COVID-19-related symptoms.

## TRIAL REGISTRATION

Clinicaltrials.gov NCT04380987; <https://clinicaltrials.gov/ct2/show/NCT04380987>.

**Accession number:** 36265042

**Clinical trial ID:** NCT04380987 (ClinicalTrials.gov)

**Copyright:** ©Eduardo Higa, Abir Elbéji, Lu Zhang, Aurélie Fischer, Gloria A Aguayo, Petr V Nazarov, Guy Fagherazzi. Originally published in JMIR Medical Informatics (<https://medinform.jmir.org>), 08.11.2022.

**Correspondence author:** Higa, Eduardo Deep Digital Phenotyping Research Unit, Department of Population Health, Luxembourg Institute of Health, Strassen, Luxembourg.

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Document 37

## **A deep learning-based model for detecting depression in senior population**

**Author:** Lin, Yunhan 1 ; Liyanage, Biman Najika 2 ; Sun, Yutao 3 ; Lu, Tianlan 1 ; Zhu, Zhengwen 2 ; Liao, Yundan 1 ; Wang, Qiushi 2 ; Shi, Chuan 1 ; Yue, Weihua 4

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**Publication info:** Frontiers in Psychiatry 13 Frontiers Media S.A. (Nov 7, 2022)

**Abstract (summary):** Objectives: With the attention paid to the early diagnosis of depression, this study tries to use the biological information of **speech**, combined with **deep learning** to build a rapid binary-classification model of depression in the elderly who use Mandarin and test its effectiveness. Methods: Demographic information and acoustic data of 56 Mandarin-speaking older adults with major depressive disorder (MDD), diagnosed with the Mini-International Neuropsychiatric Interview (MINI) and the fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5), and 47 controls was collected. Acoustic data were recorded using different smart phones and analyzed by **deep learning** model which is developed and tested on independent validation set. The accuracy of the model is shown by the ROC curve. Results: The quality of the collected **speech** affected the accuracy of the model. The initial sensitivity and specificity of the model were respectively 82.14% [95%CI, (70.16–90.00)] and 80.85% [95%CI, (67.64–89.58)]. Conclusion: This study provides a new method for rapid identification and diagnosis of depression utilizing **deep learning** technology. **Vocal biomarkers** extracted from raw **speech** signals have high potential for the early diagnosis of depression in older adults.

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**Author e-mail address:** dryue@bjmu.edu.cn

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**Correspondence author:** Yue, Weihua Institute of Mental Health, Peking University Sixth Hospital, Beijing, China.

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**Identifier (keyword):** acoustic information, deep learning, major depressive disorder, screening test, senior population

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Document 38

## **A remote speech-based AI system to screen for early Alzheimer's disease via smartphones**

**Author:** Fristed, Emil 1 ; Skirrow, Caroline 1 ; Meszaros, Marton 1 ; Lenain, Raphael 1 ; Meepegama, Udeepa 1 ; Cappa, Stefano 2 ; Aarsland, Dag 3 ; Weston, Jack 1

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**Publication info:** Alzheimer's & dementia (Amsterdam, Netherlands) 14.1: e12366. (Nov 3, 2022)

**Abstract (summary):** Introduction

Artificial intelligence (AI) systems leveraging speech and language changes could support timely detection of Alzheimer's disease (AD).

## Methods

The AMYPRED study (NCT04828122) recruited 133 subjects with an established amyloid beta (A $\beta$ ) biomarker (66 A $\beta$ +, 67 A $\beta$ -) and clinical status (71 cognitively unimpaired [CU], 62 mild cognitive impairment [MCI] or mild AD). Daily story recall tasks were administered via smartphones and analyzed with an AI system to predict MCI/mild AD and A $\beta$  positivity.

## Results

Eighty-six percent of participants (115/133) completed remote assessments. The AI system predicted MCI/mild AD (area under the curve [AUC] = 0.85,  $\pm$ 0.07) but not A $\beta$  (AUC = 0.62  $\pm$ 0.11) in the full sample, and predicted A $\beta$  in clinical subsamples (MCI/mild AD: AUC = 0.78  $\pm$ 0.14; CU: AUC = 0.74  $\pm$ 0.13) on short story variants (immediate recall). Long stories and delayed retellings delivered broadly similar results.

## Discussion

Speech-based testing offers simple and accessible screening for early-stage AD.

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**Correspondence author:** Fristed, Emil Novoic Ltd London UK.

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**Identifier (keyword):** Alzheimer's disease, artificial intelligence, clinical assessment, clinical screening, deep learning, diagnostics, digital health, episodic memory, language, machine learning, mild cognitive impairment, remote, speech

**Language:** English

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Document 39

## **Evaluation of **Speech** and Pause Alterations in Patients With Acute and Chronic Heart Failure**

**Author:** Schöbi, Dario 1 ; Zhang, Yan-Ping 1 ; Kehl, Joelle 2 ; Aissani, Meriam 2 ; Pfister, Otmar 2 ; Strahm, Martin 1 ; van Haelst, Paul 3 ; Zhou, Qian 4

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**Publication info:** Journal of the American Heart Association 11.21 American Heart Association Inc. (Nov 1, 2022)

**Abstract (summary):** BACKGROUND: Acute heart failure is the most frequent cause of unplanned hospital admission in elderly patients. Various **biomarkers** have been evaluated to better assess the status of these patients and prevent decompensation. Recently, **voice** has been suggested as a cost-effective and noninvasive way to monitor disease progression. This study evaluates **speech** and pause alterations in patients with acute decompensated and stable heart failure. Specifically, we aim

to identify a **vocal biomarker** that could be used to monitor patients with heart failure and to prevent decompensation. **METHODS AND RESULTS:** **Speech** and pause patterns were evaluated in 68 patients with acute and 36 patients with stable heart failure. **Voice** recordings were performed using a web-browser based application that consisted of 5 tasks. **Speech** and pause patterns were automatically extracted and compared between acute and stable patients and with clinical markers. Compared with stable patients, pause ratio was up to 14.9% increased in patients with acute heart failure. This increase was largely independent of sex, age, and ejection fraction and persisted in patients with lower degrees of edema or dyspnea. Furthermore, pause ratio was positively correlated with NT-proBNP (N-terminal pro-B-type natriuretic peptide) after controlling for acute versus stable heart failure. Collectively, our findings indicate that the pause ratio could be useful in identifying acute heart failure, particularly in patients who do not display traditional indicators of decompensation. **CONCLUSIONS:** **Speech** and pause patterns are altered in patients with acute heart failure. Particularly, we identified pause ratio as an easily interpretable **vocal biomarker** to support the monitoring of heart failure decompensation.

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**Subject:** Embase;MEDLINE;amino terminal pro brain natriuretic peptide -- endogenous compound;biological marker -- endogenous compound (major);furosemide -- drug dose;furosemide -- drug therapy -- acute heart failure;furosemide -- intravenous drug administration;furosemide -- oral drug administration;furosemide -- special situation for pharmacovigilance -- aged;metolazone -- drug dose;metolazone -- drug therapy -- acute heart failure;metolazone -- oral drug administration;metolazone -- special situation for pharmacovigilance -- aged;torasemide -- drug dose;torasemide -- drug therapy -- acute heart failure;torasemide -- oral drug administration;torasemide -- special situation for pharmacovigilance -- aged;web browser;acute heart failure -- drug therapy -- furosemide (major);acute heart failure -- drug therapy -- metolazone (major);acute heart failure -- drug therapy -- torasemide (major);acute heart failure -- prevention (major);adult;age;aged;altered pause pattern + -- diagnosis (major);Article;cohort analysis;controlled study;digital technology;disease control;disease severity;drug dose increase;dyspnea;female;heart ejection fraction;heart failure (major);human;major clinical study;male;mental task;patient assessment;patient monitoring;peripheral edema;sex;speech analysis;speech disorder -- diagnosis (major);voice analysis

**Substance:** Substance Substance: furosemide; CAS: 54-31-9; Substance: metolazone; CAS: 17560-51-956436-31-856436-32-9; Substance: torasemide; CAS: 56211-40-6;

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Document 40

## Clinical Utility of Machine Learning-Derived Vocal-Biomarker in the Management of Heart Failure

**Author:** Okada, Kozo; Omiya, Yasuhiro; Mizuguchi, Daisuke; Endo, Koji; Kobayashi, Yusuke; Matsuzawa, Yasushi; Iwahashi, Noriaki; Kosuge, Masami; Ebina, Toshiaki; Tamura, Kouichi; Hibi, Kiyoshi

**Publication info:** Circulation, suppl. Supplement 1 146 Lippincott Williams and Wilkins. (Nov 2022)

**Abstract (summary):** Introduction: Previous studies have suggested that early therapeutic intervention could prevent heart failure (HF) worsening, while early detection of signs and symptoms of cardiac decompensation remains challenging. For the first time, this study focused on voice symptoms and aimed to explore its potential utility in the management of heart failure. Methods: This single-center, prospective, observational study included 38 patients admitted due to worsening HF. A total of 726 voice data were recorded during the therapeutic time course at the hospital. Changes in clinical symptoms (New York Heart Association [NYHA]) evaluated by an experienced cardiologist and B-type natriuretic peptide (BNP, pg/ml) during the time course were also evaluated. Here we

tested if the acoustic features of the patient **voice** could predict the NYHA class and BNP levels, using the **machine learning** (ML) models trained with a gradient boosting algorithm. A 5-fold cross-validation was applied to evaluate the model performance. Results: There were significant correlations of some acoustic features with clinical symptoms and BNP levels (data not shown). We created the prototype of the ML model on the acoustic features extracted from the data set. Receiver operating characteristic (ROC) analysis revealed a good diagnostic accuracy of our ML model to predict NYHA class  $\geq 2$  (sensitivity 0.78, specificity 0.75, area under the curve (AUC) 0.79, and accuracy 0.77). There was also a significant correlation between **voice**-derived BNP and actual BNP levels (Figure). AUC of ROC analysis for predicting NYHA class  $\geq 2$  from BNP was 0.688. Conclusions: The prototype of the ML model was related to clinical symptoms of HF decompensation and BNP levels, demonstrating greater diagnostic accuracy for NYHA prediction than actual BNP levels. Further studies are warranted to investigate the possible contributions of our ML model to the early detection of worsening HF as ML-derived **vocal-biomarkers**. (Figure Presented).

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**Correspondence author:** Okada, Kozo

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**Substance:** Substance Substance: brain natriuretic peptide; CAS: 114471-18-0;

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Document 41

## Computerized analysis of speech and voice for Parkinson's disease: A systematic review

**Author:** Ngo, Quoc Cuong 1 ; Motin, Mohammad Abdul 2 ; Pah, Nemuel Daniel 3 ; Drotár, Peter 4 ; Kempster, Peter 5 ; Kumar, Dinesh 1

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**Publication info:** Computer Methods and Programs in Biomedicine 226 Elsevier Ireland Ltd. (Nov 2022)

**Abstract (summary):** Background and objective: Speech impairment is an early symptom of Parkinson's disease (PD). This study has summarized the literature related to speech and voice in detecting PD and assessing its severity. Methods: A systematic review of the literature from 2010 to 2021 to investigate analysis methods and signal features. The keywords "Automatic analysis" in conjunction with "PD speech" or "PD voice" were used, and the PubMed and ScienceDirect databases were searched. A total of 838 papers were found on the first run, of which 189 were selected. One hundred and forty-seven were found to be suitable for the review. The different datasets, recording protocols, signal analysis methods and features that were reported are listed. Values of the features that separate PD patients from healthy controls were tabulated. Finally, the barriers that limit the wide use of computerized speech analysis are discussed. Results: Speech and voice may be valuable markers for PD. However, large differences between the datasets make it

difficult to compare different studies. In addition, **speech** analytic methods that are not informed by physiological understanding may alienate clinicians. Conclusions: The potential usefulness of **speech** and **voice** for the detection and assessment of PD is confirmed by evidence from the classification and correlation results.

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**Subject:** Embase;MEDLINE;adult;dimensionality reduction;disease severity;effect size;**feature selection**;female;human;male;Parkinson disease (major);**phonation**;Review;signal processing;**speech analysis** (major);**speech articulation**;speech test;systematic review;**voice analysis** (major)

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Document 42



## Semantic and Acoustic Markers in Schizophrenia-Spectrum Disorders; a Combinatory Machine Learning Approach

**Author:** Voppel, Alban E. 1 ; de Boer, Janna N. 2 ; Brederoo, Sanne G. 1 ; Schnack, Hugo G. 3 ; Sommer, Iris E C 1

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**Publication info:** Schizophrenia bulletin NLM (Medline). (Oct 28, 2022)

**Abstract (summary):** BACKGROUND AND HYPOTHESIS: Speech is a promising marker to aid diagnosis of schizophrenia-spectrum disorders, as it reflects symptoms like thought disorder and negative symptoms. Previous approaches made use of different domains of speech for diagnostic classification, including features like coherence (semantic) and form (acoustic). However, an examination of the added value of each domain when combined is lacking as of yet. Here, we investigate the acoustic and semantic domains separately and combined. STUDY DESIGN: Using semi-structured interviews, speech of 94 subjects with schizophrenia-spectrum disorders (SSD) and 73 healthy controls (HC) was recorded. Acoustic features were extracted using a standardized feature-set, and transcribed interviews were used to calculate semantic word similarity using word2vec. Random forest classifiers were trained for each domain. A third classifier was used to combine features from both domains; 10-fold cross-validation was used for each model. RESULTS: The acoustic random forest classifier achieved 81% accuracy classifying SSD and HC, while the semantic domain classifier reached an accuracy of 80%. Joining features from the two domains, the combined classifier reached 85% accuracy, significantly improving on separate domain classifiers. For the combined classifier, top features were fragmented speech from the acoustic domain and variance of similarity from the semantic domain. CONCLUSIONS: Both semantic and acoustic analyses of speech achieved ~80% accuracy in classifying SSD from HC. We replicate earlier findings per domain, additionally showing that combining these features significantly improves classification performance. Feature importance and accuracy in combined classification indicate that the domains measure different, complementing aspects of speech.

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Document 43

## **A **voice**-based **biomarker** for monitoring symptom resolution in adults with COVID-19: Findings from the prospective Predi-COVID cohort study**

**Author:** Fagherazzi, Guy 1 ; Zhang, Lu 2 ; Elbéji, Abir 1 ; Higa, Eduardo 1 ; Despotovic, Vladimir 3 ; Ollert, Markus 4 ; Aguayo, Gloria A 1 ; Nazarov, Petr V 5 ; Fischer, Aurélie 1

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**Publication info:** PLOS digital health 1.10: e0000112. (Oct 20, 2022)

**Abstract (summary):** People with COVID-19 can experience impairing symptoms that require enhanced surveillance. Our objective was to train an **artificial intelligence**-based model to predict the presence of COVID-19 symptoms and derive a digital **vocal biomarker** for easily and quantitatively monitoring symptom resolution. We used data from 272 participants in the prospective Predi-COVID cohort study recruited between May 2020 and May 2021. A total of 6473 **voice** features were derived from recordings of participants reading a standardized pre-specified text. Models were trained separately for Android devices and iOS devices. A binary outcome (symptomatic versus asymptomatic) was considered, based on a list of 14 frequent COVID-19 related symptoms. A total of 1775 audio recordings were analyzed (6.5 recordings per participant on average), including 1049 corresponding to symptomatic cases and 726 to asymptomatic ones. The best performances were obtained from **Support Vector Machine** models for both audio formats. We observed an elevated predictive capacity for both Android (AUC = 0.92, balanced accuracy = 0.83) and iOS (AUC = 0.85, balanced accuracy = 0.77) as well as low Brier scores (0.11 and 0.16 respectively for Android and iOS when assessing calibration). The **vocal biomarker** derived from the predictive models accurately discriminated asymptomatic from symptomatic individuals with COVID-19 (t-test P-values < 0.001). In this prospective cohort study, we have demonstrated that using a simple, reproducible task of reading a standardized pre-specified text of 25 seconds enabled us to derive a **vocal biomarker** for monitoring the resolution of COVID-19 related symptoms with high accuracy and calibration.

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Document 44

### Utilizing digital predictive biomarkers to identify Veteran suicide risk

**Author:** Holmgren, Jackson G 1 ; Morrow, Adelene 1 ; Coffee, Ali K 1 ; Nahod, Paige M 2 ; Santora, Samantha H 2 ; Schwartz, Brian 3 ; Stiegmann, Regan A 4 ; Zanetti, Cole A 5

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**Publication info:** Frontiers in digital health 4 : 913590. (Oct 18, 2022)

**Abstract (summary):** Veteran suicide is one of the most complex and pressing health issues in the United States. According to the 2020 National Veteran Suicide Prevention Annual Report, since 2018 an average of 17.2 Veterans died by suicide each day. Veteran suicide risk screening is currently limited to suicide hotlines, patient reporting, patient visits, and family or friend reporting. As a result of these limitations, innovative approaches in suicide screening are increasingly garnering attention. An essential feature of these innovative methods includes better incorporation of risk factors that might indicate higher risk for tracking suicidal ideation based on personal behavior. Digital technologies create a means through which measuring these risk factors more reliably, with higher fidelity, and more frequently throughout daily life is possible, with the capacity to identify potentially telling behavior patterns. In this review, digital predictive biomarkers are discussed as they pertain to suicide risk, such as sleep vital signs, sleep disturbance, sleep quality, and speech pattern recognition. Various digital predictive biomarkers are reviewed and evaluated as well as their potential utility in predicting and diagnosing Veteran suicidal ideation in real time. In the future, these digital biomarkers

could be combined to generate further suicide screening for diagnosis and severity assessments, allowing healthcare providers and healthcare teams to intervene more optimally.

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**Copyright:** © 2022 Holmgren, Morrow, Coffee, Nahod, Santora, Schwartz, Stiegmann and Zanetti.

**Correspondence author:** Holmgren, Jackson G Rocky Vista University College of Osteopathic Medicine, Ivins, UT, United States.

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Document 45

**Robust, Generalizable, and Interpretable Artificial Intelligence-Derived Brain Fingerprints of Autism and Social Communication Symptom Severity**

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**Publication info:** Biological psychiatry 92.8: 643-653. (Oct 15, 2022)

### **Abstract (summary): BACKGROUND**

Autism spectrum disorder (ASD) is among the most pervasive neurodevelopmental disorders, yet the neurobiology of ASD is still poorly understood because inconsistent findings from underpowered individual studies preclude the identification of robust and interpretable neurobiological markers and predictors of clinical symptoms.

## **METHODS**

We leverage multiple brain imaging cohorts and exciting recent advances in explainable **artificial intelligence** to develop a novel spatiotemporal **deep neural network** (stDNN) model, which identifies robust and interpretable dynamic brain markers that distinguish ASD from neurotypical control subjects and predict clinical symptom severity.

## **RESULTS**

stDNN achieved consistently high classification accuracies in cross-validation analysis of data from the multisite ABIDE (Autism Brain Imaging Data Exchange) cohort (n = 834). Crucially, stDNN also accurately classified data from independent Stanford (n = 202) and GENDAAR (Gender Exploration of Neurogenetics and Development to Advanced Autism Research) (n = 90) cohorts without additional training. stDNN could not distinguish attention-deficit/hyperactivity disorder from neurotypical control subjects, highlighting the model's specificity. Explainable **artificial intelligence** revealed that brain features associated with the posterior cingulate cortex and precuneus, dorsolateral and ventrolateral prefrontal cortex, and superior temporal sulcus, which anchor the default mode network, cognitive control, and human **voice** processing systems, respectively, most clearly distinguished ASD from neurotypical control subjects in the three cohorts. Furthermore, features associated with the posterior cingulate cortex and precuneus nodes of the default mode network emerged as robust predictors of the severity of core social and communication deficits but not restricted/repetitive behaviors in ASD.

## **CONCLUSIONS**

Our findings, replicated across independent cohorts, reveal robust individualized functional brain fingerprints of ASD psychopathology, which could lead to more objective and precise phenotypic characterization and targeted treatments.

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**Identifier (keyword):** Autism, Biomarkers, Clinical heterogeneity, Default mode network, Explainable artificial intelligence, Reproducible science

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Document 46

## **Deep learning and machine learning-based voice analysis for the detection of COVID-19: A proposal and comparison of architectures**

**Author:** Costantini, Giovanni 1 ; Dr, Valerio Cesarini 1 ; Robotti, Carlo 2 ; Benazzo, Marco 2 ; Pietrantonio, Filomena 3 ; Di Girolamo, Stefano 4 ; Pisani, Antonio 5 ; Canzi, Pietro 6 ; Mauramati, Simone 6 ; Bertino, Giulia 6 ; Cassaniti, Irene 7 ; Baldanti, Fausto 8 ; Saggio, Giovanni 1

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**Publication info:** Knowledge-based systems 253 : 109539. (Oct 11, 2022)

**Abstract (summary):** Alongside the currently used nasal swab testing, the COVID-19 pandemic situation would gain noticeable advantages from low-cost tests that are available at any-time, anywhere, at a large-scale, and with real time answers. A novel approach for COVID-19 assessment is adopted here, discriminating negative subjects versus positive or recovered subjects. The scope is to identify potential discriminating features, highlight mid and short-term effects of COVID on the **voice** and compare two custom algorithms. A pool of 310 subjects took part in the study; recordings were collected in a low-noise, controlled setting employing three different **vocal** tasks. Binary classifications followed, using two different custom algorithms. The first was based on the coupling of boosting and bagging, with an AdaBoost classifier using Random Forest learners. A feature selection process was



employed for the training, identifying a subset of features acting as clinically relevant **biomarkers**. The other approach was centered on two custom **CNN** architectures applied to mel-Spectrograms, with a custom knowledge-based data augmentation. Performances, evaluated on an independent test set, were comparable: Adaboost and **CNN** differentiated COVID-19 positive from negative with accuracies of 100% and 95% respectively, and recovered from negative individuals with accuracies of 86.1% and 75% respectively. This study highlights the possibility to identify COVID-19 positive subjects, foreseeing a tool for on-site screening, while also considering recovered subjects and the effects of COVID-19 on the **voice**. The two proposed novel architectures allow for the identification of **biomarkers** and demonstrate the ongoing relevance of traditional ML versus **deep learning** in **speech** analysis.

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**Correspondence author:** Costantini, Giovanni Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy.

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**Language:** English

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Document 47

## **Brain age predicts long-term recovery in post-stroke aphasia**

**Author:** Kristinsson, Sigfus 1 ; Busby, Natalie 1 ; Rorden, Christopher 2 ; Newman-Norlund, Roger 2 ; den Ouden, Dirk B 3 ; Magnúsdóttir, Sigríður 4 ; Hjaltason, Haukur 5 ; Thors, Helga 4 ; Hillis, Argye E 6 ; Kjartansson, Ólafur 7 ; Bonilha, Leonardo 8 ; Fridriksson, Julius 3

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**Publication info:** Brain communications 4.5: fcac252. (Oct 6, 2022)

**Abstract (summary):** The association between age and language recovery in stroke remains unclear. Here, we used neuroimaging data to estimate brain age, a measure of structural integrity, and examined the extent to which brain age at stroke onset is associated with (i) cross-sectional language performance, and (ii) longitudinal recovery of language function, beyond chronological age alone. A total of 49 participants (age:  $65.2 \pm 12.2$  years, 25 female) underwent routine clinical neuroimaging (T1) and a bedside evaluation of language performance (Bedside Evaluation Screening Test-2) at onset of left hemisphere stroke. Brain age was estimated from enantiomorphically

reconstructed brain scans using a **machine learning** algorithm trained on a large sample of healthy adults. A subsample of 30 participants returned for follow-up language assessments at least 2 years after stroke onset. To account for variability in age at stroke, we calculated proportional brain age difference, i.e. the proportional difference between brain age and chronological age. Multiple regression models were constructed to test the effects of proportional brain age difference on language outcomes. Lesion volume and chronological age were included as covariates in all models. Accelerated brain age compared with age was associated with worse overall aphasia severity ( $F(1, 48) = 5.65, P = 0.022$ ), naming ( $F(1, 48) = 5.13, P = 0.028$ ), and **speech** repetition ( $F(1, 48) = 8.49, P = 0.006$ ) at stroke onset. Follow-up assessments were carried out  $\geq 2$  years after onset; decelerated brain age relative to age was significantly associated with reduced overall aphasia severity ( $F(1, 26) = 5.45, P = 0.028$ ) and marginally failed to reach statistical significance for auditory comprehension ( $F(1, 26) = 2.87, P = 0.103$ ). Proportional brain age difference was not found to be associated with changes in naming ( $F(1, 26) = 0.23, P = 0.880$ ) and **speech** repetition ( $F(1, 26) = 0.00, P = 0.978$ ). Chronological age was only associated with naming performance at stroke onset ( $F(1, 48) = 4.18, P = 0.047$ ). These results indicate that brain age as estimated based on routine clinical brain scans may be a strong **biomarker** for language function and recovery after stroke.

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**Correspondence author:** Kristinsson, Sigfus Center for the Study of Aphasia Recovery, University of South Carolina, Columbia, SC 29208, USA.

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Document 48

## **Post-stroke respiratory complications using machine learning with voice features from mobile devices**

**Author:** Park, Hae-Yeon 1 ; Park, DoGyeom 2 ; Kang, Hye Seon 3 ; Kim, HyunBum 4 ; Lee, Seungchul 5 ; Im, Sun 6

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**Publication info:** Scientific reports 12.1: 16682. NLM (Medline). (Oct 6, 2022)

**Abstract (summary):** Abnormal voice may identify those at risk of post-stroke aspiration. This study was aimed to determine whether machine learning algorithms with voice recorded via a mobile device can accurately classify those with dysphagia at risk of tube feeding and post-stroke aspiration pneumonia and be used as digital biomarkers. Voice samples from patients referred for swallowing disturbance in a university-affiliated hospital were collected prospectively using a mobile device. Subjects that required tube feeding were further classified to high risk of respiratory complication, based on the voluntary cough strength and abnormal chest x-ray images. A total of 449 samples were obtained, with 234 requiring tube feeding and 113 showing high risk of respiratory complications. The eXtreme gradient boosting multimodal models that included abnormal acoustic features and clinical variables showed high sensitivity levels of 88.7% (95% CI 82.6-94.7) and 84.5% (95% CI 76.9-92.1)

in the classification of those at risk of tube feeding and at high risk of respiratory complications; respectively. In both cases, **voice** features proved to be the strongest contributing factors in these models. **Voice** features may be considered as viable digital **biomarkers** in those at risk of respiratory complications related to post-stroke dysphagia.

**Accession number:** 639214578

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**Subject:** MEDLINE;**biological marker**;breathing disorder (major);cerebrovascular accident (major);complication;dysphagia -- etiology (major);human;**machine learning**;personal digital assistant;swallowing

**Updates:** 2022-10-122022-10-17

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Document 49

## HEPATIC ENCEPHALOPATHY DETECTION VIA ARTIFICIAL INTELLIGENCE-ENABLED VOICE ANALYTICS

**Author:** Penrice, Daniel 1 ; Yerrapragada, Gayathri 1 ; Hara, Kamalpreet 1 ; Arunachalam, Shivaram Poigai 1 ; Simonetto, Douglas A. 1

1 Division of Gastroenterology and Hepatology, Mayo Clinic, United States

**Publication info:** Hepatology, suppl. Supplement 1 76 : S1184-S1185. John Wiley and Sons Inc. (Oct 2022)

**Abstract (summary):** Background: Development of hepatic encephalopathy (HE) is associated with 50% one-year mortality, and it is one of the most common causes of hospital (re) admission in patients with cirrhosis. Early recognition of HE relies on neuropsychometric testing, and simple, low effort and widely available diagnostic tests are lacking. We hypothesize that HE-specific **voice biomarkers** exist and may be identified through a **deep learning** approach for the development of a novel **voice-enabled** HE recognition test. Methods: We prospectively enrolled eight participants hospitalized with overt HE. Baseline laboratory, clinical history, encephalopathy grade (West-Haven criteria and CHES) and **voice** samples were obtained daily while subjects were hospitalized until return to baseline mental status. **Voice** samples included breathing, counting, coughing, vowels and reading a short text. The **voice** samples were converted into 3 second spectrograms. A total of 344 spectrogram images were labeled HE (CHES $\geq$ 2) and another 547 images were labeled non-HE (CHES $\leq$  1). A **deep learning** model, HePatic EncepHalopathy Detection via **VOice** ANalytICs (PHONIC model) was developed using these images and was validated on a distinct set of 88 images. Results: **Voice** samples were collected for an average of 3.2 days. Mean age was 52 and the average Child-Pugh score was 9.4. Median time to HE resolution was 2 days. All participants were prescribed lactulose at baseline and had lactulose dose increased while in the hospital. Three subjects were also chronically taking Rifaximin. Four subjects had some degree of ascites present at the time of enrollment. The training dataset consisted of 803 spectrogram images and had an overall accuracy of 99% for distinguishing between HE and non-HE. The validation dataset consisted of 88 images and had an overall accuracy of 90.9%. The AUC of the PHONIC model was 0.93 (Figure 1A). A consistent trend of higher **voice** frequencies was observed during episodes of HE compared to non-HE (Figure 1B). Conclusion: This proof-of- concept study suggests the presence of HE-specific **voice** signals identified using a **machine learning** approach. A larger prospective study is underway for further optimization and validation of the PHONIC model. (Figure Presented).

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**Correspondence author:** Penrice, Daniel Division of Gastroenterology and Hepatology, Mayo Clinic, United States.

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**Subject:** Embase;biological marker;lactulose;rifaximin;adult;artificial intelligence (major);ascites;brain disease;breathing;Child Pugh score;clinical article;conference abstract;controlled study;coughing;deep learning;drug therapy;hepatic encephalopathy (major);human;machine learning;male;mental health;middle aged;proof of concept;prospective study;voice (major);vowel

**Substance:** Substance: lactulose; CAS: 4618-18-258166-24-8; Substance: rifaximin; CAS: 80621-81-488747-56-2;

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Document 50

## **REDUCING SAMPLE SIZES BY UP TO 30% IN CLINICAL TRIALS FOR MOOD DISORDERS VIA ENHANCED PRIMARY ENDPOINT RELIABILITY USING AUDIOVISUAL MULTIMODAL MACHINE LEARNING**

**Author:** Jones, Jeremy 1 ; Cicconet, Marcelo 1 ; Barone, Ben 1 ; Aafjes-van Doorn, Katie 2 ; Cohn, Jeff 3 ; Aafjes, Marc 1

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**Publication info:** Innovations in Clinical Neuroscience, suppl. Supplement 19.10-12: S7. Matrix  
Medical Communications. (Oct 2022 - Dec 2022)

**Abstract (summary):** Background/Objective: Suboptimal interrater reliability of clinician-reported outcome assessments (ClinROs) in central nervous system (CNS) clinical trials attenuates signal detection and statistical power and contributes to comparatively high failure rates. Much effort is put into developing digital **biomarkers**-for instance, using **speech** or oculometrics-that could act as surrogate endpoints. However, most only weakly and nonlinearly correlate to outcomes and struggle with clinical validation. Our objective was to develop multimodal **machine learning** (ML) models that combined a comprehensive set of behavioral and peripheral physiological **biomarkers** that directly predict United States (US) Food and Drug Administration (FDA)-preferred primary endpoints for mood disorders, Hamilton Depression Rating Scale (HAM-D), and Hamilton Anxiety Rating Scale (HAM-A). By pairing ML with human raters, we aimed to improve the effective reliability of endpoints and increase statistical power, thus reducing the necessary size of cohorts. Design: Over 100 HAM-D and HAM-A clinical interviews were conducted, across multiple settings, with a full range of mood disorder severity. An extensive set of facial expressions, face and head dynamics, vital signs, oculometrics, **voice**, linguistics, and physiological features were extracted from interview audio-video recordings. ML models were developed to predict HAM-D and HAM-A scores. Analytical validation was accomplished by testing on an independent test set. Results: The HAM-D model achieved an intraclass correlation coefficient (ICC) of 0.882 (root-mean-square error [RMSE]: 2.89 and mean absolute error [MAE]: 2.35). The HAM-A model achieved an ICC of 0.874 (RMSE: 3.36 and MAE: 2.57). Conclusion: The models outperformed typical observed rater reliability. By combining human raters with ML models, effective reliability of endpoints can be increased and result in sample size reduction of 10 to 30 percent.

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**Copyright:** Copyright 2023 Elsevier B.V., All rights reserved.

**Correspondence author:** Jones, Jeremy Deliberate AI, United States.

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**Subject:** Embase;biological marker;audiovisual recording;conference abstract;controlled study;correlation coefficient;depression (major);facial expression;Food and Drug Administration;Hamilton Anxiety Scale;Hamilton Depression Rating Scale;human;interview;linguistics;machine learning (major);mean absolute error;mood disorder (major);reliability (major);root mean squared error;sample size (major);vital sign;voice

**Updates:** 2023-01-24

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Document 51

## **Cognitive Digital Biomarkers from Automated Transcription of Spoken Language**

**Author:** Tavabi, N. 1 ; Stück, D. 2 ; Signorini, A. 2 ; Karjadi, C. 3 ; Al Hanai, T. 4 ; Sandoval, M. 2 ; Lemke, C. 2 ; Glass, J. 4 ; Hardy, S. 3 ; Lavalley, M. 5 ; Wasserman, B. 5 ; Ang, T.F.A. 6 ; Nowak, C.M. 5 ; Kainkaryam, R. 2 ; Foschini, L. 2 ; Au, Rhoda 7

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**Publication info:** Journal of Prevention of Alzheimer's Disease 9.4: 791-800. Serdi-Editions. (Oct 2022)

**Abstract (summary):** Background: Although patients with Alzheimer's disease and other cognitive-related neurodegenerative disorders may benefit from early detection, development of a reliable diagnostic test has remained elusive. The penetration of digital voice-recording technologies and multiple cognitive processes deployed when constructing spoken responses might offer an opportunity to predict cognitive status. Objective: To determine whether cognitive status might be predicted from voice recordings of neuropsychological testing Design: Comparison of acoustic and (para)linguistic variables from low-quality automated transcriptions of neuropsychological testing (n = 200) versus variables from high-quality manual transcriptions (n = 127). We trained a logistic regression classifier to predict cognitive status, which was tested against actual diagnoses. Setting: Observational cohort study. Participants: 146 participants in the Framingham Heart Study. Measurements: Acoustic and either paralinguistic variables (e.g., speaking time) from automated transcriptions or linguistic variables (e.g., phrase complexity) from manual transcriptions. Results: Models based on demographic features alone were not robust (area under the receiver-operator characteristic curve [AUROC] 0.60). Addition of clinical and standard acoustic features boosted the AUROC to 0.81. Additional inclusion of transcription-related features yielded an AUROC of 0.90. Conclusions: The use of voice-based digital biomarkers derived from automated processing methods, combined with standard patient screening, might constitute a scalable way to enable early detection of dementia.

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**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

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**Subject:** Embase;MEDLINE;biological marker (major);acoustic analysis;adolescent;adult;area under the curve;Article;audio recording;automated transcription + (major);automation (major);clinical article;cognition (major);cohort analysis;consensus;controlled study;dementia;demography;female;human;language processing (major);linguistics;Logical Memory test +;male;memory test;mild cognitive impairment;Mini Mental State Examination;natural language processing;observational study;paralanguage;phrase complexity +;receiver operating characteristic;speaking time +;task performance;Wechsler memory scale

**Updates:** 2022-07-222022-10-272022-10-312022-11-03

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Document 52

### **Validation of the Remote Automated ki:e **Speech Biomarker** for Cognition in Mild Cognitive Impairment: Verification and Validation following DiME V3 Framework**

**Author:** Tröger, Johannes 1 ; Baykara, Ebru 1 ; Zhao, Jian 1 ; Ter Huurne, Daphne 2 ; Possemis, Nina 2 ; Mallick, Elisa 1 ; Schäfer, Simona 1 ; Schwed, Louisa 1 ; Mina, Mario 1 ; Linz, Nicklas 1 ; Ramakers, Inez 2 ; Ritchie, Craig 3

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**Publication info:** Digital Biomarkers 6.3: 107-116. S. Karger AG. (Sep 30, 2022)

**Abstract (summary):** Introduction: Progressive cognitive decline is the cardinal behavioral symptom in most dementia-causing diseases such as Alzheimer's disease. While most well-established measures for cognition might not fit tomorrow's decentralized remote clinical trials, digital cognitive assessments will gain importance. We present the evaluation of a novel digital **speech biomarker** for cognition (SB-C) following the Digital Medicine Society's V3 framework: verification, analytical validation, and clinical validation. Methods: Evaluation was done in two independent clinical samples: the Dutch DeepSpA (N = 69 subjective cognitive impairment [SCI], N = 52 mild cognitive impairment [MCI], and N = 13 dementia) and the Scottish SPeAk datasets (N = 25, healthy controls). For validation, two anchor scores were used: the Mini-Mental State Examination (MMSE) and the Clinical

Dementia Rating (CDR) scale. Results: Verification: The SB-C could be reliably extracted for both languages using an automatic **speech** processing pipeline. Analytical Validation: In both languages, the SB-C was strongly correlated with MMSE scores. Clinical Validation: The SB-C significantly differed between clinical groups (including MCI and dementia), was strongly correlated with the CDR, and could track the clinically meaningful decline. Conclusion: Our results suggest that the **ki:e SB-C** is an objective, scalable, and reliable indicator of cognitive decline, fit for purpose as a remote assessment in clinical early dementia trials.

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**Author e-mail address:** johannes.troeger@ki-elements.de

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Tröger, Johannes Ki elements, Saarbrücken, Germany.

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**Identifier (keyword):** Clinical trials, Dementia, Digital **biomarker**, Mild cognitive impairment, **Speech** analysis, **Speechbiomarker**

**Language:** English

**Language of abstract:** English

**Number of references:** 30

**Publication date:** Sep 30, 2022

**Publication type:** Journal

**Publisher:** S. Karger AG

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**Subject:** Embase;**biological marker** -- endogenous compound (major);adult;aged;Article;**automatic speech recognition**;birth cohort;clinical dementia rating scale;cognition (major);cohort analysis;conceptual framework (major);controlled study;dementia;DSM-5;evaluation study;**feature extraction**;female;follow up;human;language;learning;major clinical study;male;mild cognitive impairment (major);Mini Mental State Examination;neuropsychological test;performance;Rey auditory

verbal learning test; speech (major); speech analysis (major); speech discrimination; test retest reliability; validation process (major); verbal learning

**Updates:** 2022-11-09 2022-12-12 2022-12-16

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Document 53

## **Voice Features of Sustained Phoneme as COVID-19 Biomarker**

**Author:** Pah, Nemuel D 1 ; Indrawati, Veronica 1 ; Kumar, Dinesh K 2

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**Publication info:** IEEE journal of translational engineering in health and medicine 10 : 4901309. (Sep 20, 2022)

### **Abstract (summary): BACKGROUND**

The COVID-19 pandemic has resulted in enormous costs to our society. Besides finding medicines to treat those infected by the virus, it is important to find effective and efficient strategies to prevent the spreading of the disease. One key factor to prevent transmission is to identify COVID-19 biomarkers that can be used to develop an efficient, accurate, noninvasive, and self-administered screening procedure. Several COVID-19 variants cause significant respiratory symptoms, and thus a voice signal may be a potential biomarker for COVID-19 infection.

### **AIM**

This study investigated the effectiveness of different phonemes and a range of voice features in differentiating people infected by COVID-19 with respiratory tract symptoms.

### **METHOD**

This cross-sectional, longitudinal study recorded six phonemes (i.e., /a/, /e/, /i/, /o/, /u/, and /m/) from 40 COVID-19 patients and 48 healthy subjects for 22 days. The signal features were obtained for the recordings, which were statistically analyzed and classified using Support Vector Machine (SVM).

### **RESULTS**

The statistical analysis and SVM classification show that the voice features related to the vocal tract filtering (e.g., MFCC, VTL, and formants) and the stability of the respiratory muscles and lung volume (Intensity-SD) were the most sensitive to voice change due to COVID-19. The result also shows that the features extracted from the vowel /i/ during the first 3 days after admittance to the hospital were

the most effective. The SVM classification accuracy with 18 ranked features extracted from /i/ was 93.5% (with F1 score of 94.3%).

## CONCLUSION

A measurable difference exists between the voices of people with COVID-19 and healthy people, and the phoneme /i/ shows the most pronounced difference. This supports the potential for using computerized voice analysis to detect the disease and consider it a biomarker.

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**Correspondence author:** Pah, Nemuel D Department of Electrical Engineering Universitas Surabaya Surabaya 60293 Indonesia.

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**MeSH:** Humans; COVID-19 (major); Cross-Sectional Studies; Longitudinal Studies; Pandemics; SARS-CoV-2; Biomarkers

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**Updates:** 2022-10-29 2022-10-29 2022-10-31 2022-11-22

## **Classification of Parkinson's disease from smartphone recording data using time-frequency analysis and convolutional neural network**

**Author:** Worasawate, Denchai 1 ; Asawaponwiput, Warisara 1 ; Yoshimura, Natsue 2 ; Intarapanich, Apichart 3 ; Surangsrirat, Decho 4

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**Publication info:** Technology and health care : official journal of the European Society for Engineering and Medicine (Sep 16, 2022)

### **Abstract (summary): BACKGROUND**

Parkinson's disease (PD) is a long-term neurodegenerative disease of the central nervous system. The current diagnosis is dependent on clinical observation and the abilities and experience of a trained specialist. One of the symptoms that affects most patients is voice impairment.

### **OBJECTIVE**

Voice samples are non-invasive data that can be collected remotely for diagnosis and disease progression monitoring. In this study, we analyzed voice recording data from a smartphone as a possible medical self-diagnosis tool by using only one-second voice recording. The data from one of the largest mobile PD studies, the mPower study, was used.

### **METHODS**

A total of 29,798 ten-second voice recordings on smartphone from 4,051 participants were used for the analysis. The voice recordings were from sustained phonation by participants saying /aa/ for ten seconds into an iPhone microphone. A dataset comprising 385,143 short one-second audio samples was generated from the original ten-second voice recordings. The samples were converted to a spectrogram using a short-time Fourier transform. CNN models were then applied to classify the samples.

### **RESULTS**

Classification accuracies of the proposed method with LeNet-5, ResNet-50, and VGGNet-16 are  $97.7 \pm 0.1\%$ ,  $98.6 \pm 0.2\%$ , and  $99.3 \pm 0.1\%$ , respectively.

## CONCLUSIONS

We achieve a respectable classification performance using a generalized approach on a dataset with a large number of samples. The result emphasizes that an analysis based on one-second clip recorded on a smartphone could be a promising non-invasive and remotely available PD **biomarker**.

**Accession number:** 36155539

**Correspondence author:** Worasawate, Denchai Department of Electrical Engineering, Kasetsart University, Bangkok, Thailand.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2022-09-26

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**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.3233/THC-220386>

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**Identifier (keyword):** PD **voice**, audio classification, **convolutionalneural network**, mPower study

**Language:** English

**Language of abstract:** English

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**Notes:** Publication model: Print-Electronic;; Cited medium:Internet

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**Publication type:** Journal

**Publisher location:** NETHERLANDS

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Document 55

**A rapid, non-invasive method for fatigue detection based on **voice** information**



**Author:** Gao, Xiujie 1 ; Ma, Kefeng 1 ; Yang, Honglian 1 ; Wang, Kun 1 ; Fu, Bo 1 ; Zhu, Yingwen 1 ; She, Xiaojun 1 ; Cui, Bo 1

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**Publication info:** Frontiers in Cell and Developmental Biology 10 Frontiers Media S.A. (Sep 13, 2022)

**Abstract (summary):** Fatigue results from a series of physiological and psychological changes due to continuous energy consumption. It can affect the physiological states of operators, thereby reducing their labor capacity. Fatigue can also reduce efficiency and, in serious cases, cause severe accidents. In addition, it can trigger pathological-related changes. By establishing appropriate methods to closely monitor the fatigue status of personnel and relieve the fatigue on time, operation-related injuries can be reduced. Existing fatigue detection methods mostly include subjective methods, such as fatigue scales, or those involving the use of professional instruments, which are more demanding for operators and cannot detect fatigue levels in real time. **Speech** contains information that can be used as acoustic **biomarkers** to monitor physiological and psychological statuses. In this study, we constructed a fatigue model based on the method of sleep deprivation by collecting various physiological indexes, such as P300 and glucocorticoid level in saliva, as well as fatigue questionnaires filled by 15 participants under different fatigue procedures and graded the fatigue levels accordingly. We then extracted the **speech** features at different instances and constructed a model to match the **speech** features and the degree of fatigue using a **machine learning** algorithm. Thus, we established a method to rapidly judge the degree of fatigue based on **speech**. The accuracy of the judgment based on unitary **voice** could reach 94%, whereas that based on long **speech** could reach 81%. Our fatigue detection method based on acoustic information can easily and rapidly determine the fatigue levels of the participants. This method can operate in real time and is non-invasive and efficient. Moreover, it can be combined with the advantages of information technology and big data to expand its applicability.

**Accession number:** 2019287719

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**Correspondence author:** She, Xiaojun Tianjin Institute of Environmental and Operational Medicine, Tianjin, China.

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**Embase document status:** Embase

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**Identifier (keyword):** acoustic **biomarkers**, fatigue detection, fatigue scale, **speech** features, **vocal** print

**Language:** English

**Language of abstract:** English

**Number of references:** 71

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**Publisher:** Frontiers Media S.A.

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**Subject:** Embase;glucocorticoid;adult;algorithm;Article;**artificial neural network**;Bayesian **learning**;body weight;controlled study;**cross validation**;diagnostic accuracy;fatigue -- diagnosis (major);human;**machine learning**;male;**multilayer perceptron**;non invasive procedure (major);normal human;questionnaire;sleep deprivation;**speech**;**speech analysis**;**support vector machine**;**voice**;vowel;wakefulness;young adult

**Updates:** 2022-10-032022-10-10

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Document 56

### **Automatic Parkinson's disease detection based on the combination of long-term acoustic features and Mel frequency cepstral coefficients (MFCC)**

**Author:** Hawi, Sara 1 ; Alhozami, Jana 1 ; AlQahtani, Raneem 1 ; AlSafran, Dannah 1 ; Alqarni, Maram 1 ; Sahmarany, Lola El 1

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**Publication info:** Biomedical Signal Processing and Control 78 Elsevier Ltd. (Sep 2022)

**Abstract (summary):** In recent years, acoustic signals have found increasing popularity among the scientific community as **biomarkers** for detecting Parkinson's disease. Literature highlights that 90% of people with Parkinson's disease have **vocal** impairment symptoms at earlier stages of the disease. Standard Parkinson's disease diagnosis depends on medical imaging or observation of motor symptoms such as gait disturbance and muscle rigidity which may appear at later stages. Several acoustic feature extraction algorithms, such as long-term and short-term features, were developed to train **machine learning** models to detect Parkinson's disease using a single algorithm. Although the literature demonstrates promising results, there has not been any exploitation of the potential of combining solely long-term and short-term algorithms to the best of the authors' knowledge. This paper presents a novel method to investigate the effect of a dataset incorporating long-term and short-term features known as Mel frequency cepstral coefficients (MFCC) on the performance of random forest model for Parkinson's disease detection. The performance of random forest has been compared between three feature sets: MFCC features, long-term features, and a combination of MFCC with long-term features. The combined features improved the detection accuracy to 88.84%, while independent sets of MFCC and long-term features, were 84.12% and 84.00%, respectively. The findings of the proposed method indicates the effectiveness of the long-term features and MFCC combination in improving the overall performance of Parkinson's disease detection model.

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**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Sahmarany, Lola El Biomedical Engineering Department, College of Engineering, Imam Abdulrahman Bin Faisal University, Dammam, 31441, Saudi Arabia.

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**Date created:** 2022-08-15

**Document status:** Revised

**Document type:** Article

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**Grant:** The authors want to express their acknowledgment to C. Okan Şakar of Bahcesehir University, who has created the database in collaboration with Bahcesehir university's department of neurology, where voice signal recording and feature extraction took place. This research has been supported by the deanship of scientific research of Imam Abdulrahman Bin Faisal University, Kingdom of Saudi Arabia (Project 2020-109).

**Identifier (keyword):** Long-term features, Machine Learning, MFCC, Parkinson's disease detection, Random Forest, Vocal impairment

**Language:** English

**Language of abstract:** English

**Number of references:** 33

**Publication date:** Sep 2022

**Publication type:** Journal

**Publisher:** Elsevier Ltd

**Publisher location:** United Kingdom

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**Subject:** Embase;acoustic analysis (major);adult;aged;Article;autocorrelation;automatic speech recognition;automation (major);binary classification;controlled study;decision tree;diagnostic accuracy;discrete cosine transform;feature selection algorithm;female;Fourier transform;human;k nearest neighbor;major clinical study;male;mathematical parameters (major);mel frequency cepstral coefficient + (major);multilayer perceptron;Parkinson disease -- diagnosis (major);phonation;radial basis function;random forest;sensitivity and specificity;support vector machine;vocal cord

**Updates:** 2022-07-292022-08-15

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Document 57

## **Assessing clinical utility of machine learning and artificial intelligence approaches to analyze speech recordings in multiple sclerosis: A pilot study**

**Author:** Svoboda, E. 1 ; Bořil, T. 2 ; Rusz, J. 3 ; Tykalová, T. 4 ; Horáková, D. 5 ; Guttman, C.R.G. 6 ; Blagojev, K.B. 7 ; Hatabu, H. 8 ; Valtchinov, V.I. 9

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**Publication info:** Computers in Biology and Medicine 148 Elsevier Ltd. (Sep 2022)

**Abstract (summary):** Background: An early diagnosis together with an accurate disease progression monitoring of multiple sclerosis is an important component of successful disease management. Prior studies have established that multiple sclerosis is correlated with **speech** discrepancies. Early research using objective acoustic measurements has discovered measurable **dysarthria**. Method: The objective was to determine the potential clinical utility of **machine learning** and **deep learning/AI** approaches for the aiding of diagnosis, **biomarker** extraction and progression monitoring of multiple sclerosis using **speech** recordings. A corpus of 65 MS-positive and 66 healthy individuals reading the same text aloud was used for targeted acoustic feature extraction utilizing automatic phoneme segmentation. A series of binary classification models was trained, tuned, and evaluated regarding their Accuracy and area-under-the-curve. Results: The Random Forest model performed best, achieving an Accuracy of 0.82 on the validation dataset and an area-under-the-curve of 0.76 across 5 k-fold cycles on the training dataset. 5 out of 7 acoustic features were statistically significant. Conclusion: **Machine learning** and **artificial intelligence** in automatic analyses of **voice** recordings for aiding multiple sclerosis diagnosis and progression tracking seems promising. Further clinical validation of these methods and their mapping onto multiple sclerosis progression is needed, as well as a validating utility for English-speaking populations.

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**Correspondence author:** Valtchinov, V.I. Center for Evidence Based Imaging (CEBI), One Brigham Circle, 1620 Tremont Street, 3rd Floor, Suite 3010, Boston, MA, 02120, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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European Union – Next Generation EU, and by the Cooperatio Program, research area Neuroscience.

**Identifier (keyword):** Biomedical, Dysarthria, Machine learning, Multiple sclerosis, Phonetics, Speech acoustics, Technology assessment

**Language:** English

**Language of abstract:** English

**Number of references:** 40

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**Subject:** Embase;MEDLINE;biological marker;microphone;acoustic analysis;acoustics;adult;Article;artificial intelligence (major);binary classification;clinical monitoring;controlled study;data accuracy;deep learning;disease exacerbation;feature extraction;female;human;machine learning (major);major clinical study;male;multiple sclerosis (major);neurologic disease;phoneme (major);pilot study;random forest;reading;recording (major);speech analysis (major)

**Updates:** 2022-07-272022-07-292022-08-23

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Document 58

### **WATCH-PD: Detecting Early-Stage PD using Feature Engineering and Machine Learning in Remote Sensor-Based Assessments**

**Author:** Anderson, D. 1 ; Merickel, M. 1 ; Severson, B. 1 ; Amato, D. 1 ; Kangarloo, T. 1 ; Edgerton, J. 1 ; Dorsey, R. 1 ; Adams, J. 1 ; Jezewski, S. 1 ; Keil, A. 1 ; Johnson, S. 1 ; Kantartjis, M. 1 ; Polyak, S. 1 ; Severson, J. 1 ; Cosman, J. 1

1 , Horsham, PA, United States

**Publication info:** Movement Disorders, suppl. Supplement 2 37 : S183-S184. John Wiley and Sons Inc. (Sep 2022)

**Abstract (summary):** Objective: Use feature engineering and machine learning to evaluate digital biomarkers of early-stage Parkinson's disease (PD) in the WATCH-PD study. Background: WATCH-PD - a one-year longitudinal study -aims to relate remote sensor-based assessments to clinician-rated

early-stage PD. Here, we used a combination of feature engineering and machine learning to evaluate the sensitivity of digital endpoints to detect early-stage PD status. Methods: 17 study sites enrolled PD (n=82) and healthy control (HC; n=50) participants into a one-year longitudinal study. BrainBaseline assessments of cognition, psychomotor performance, speech, and mobility were administered both on-site and at-home during the study. Continuous data were collected actively and passively on study provisioned Apple iPhones and Watches. Feature engineering routines estimated distributional properties of time-and frequency-dependent features derived from signal processing routines performed on continuous voice and accelerometry data sources. Machine learning algorithms were performed iteratively using Monte Carlo simulation (n=100). Each iteration randomly sorted features into independent training (90% of participants) and test sets. Feature selection was performed using linear regression to identify the most groupselective features. Logistic regression models of PD status were trained on independent features. Accuracy, sensitivity, and specificity were calculated from model predictions in the test set. Results: At the time of analysis, participants completed 551 and 1,642 clinic and home sessions, respectively. Feature engineering yielded 3,622 features, 39.5% of which were selective for PD status. Features consistently selected across each Monte Carlo simulation (n=52) were associated with tremor-related activity during postural stability and at standing rest, wrist-to-trunk movement synchronization and tremor-related activity during active walking, and finger tapping efficiency. Model predictions yielded 85% accuracy, 83% sensitivity, and 86% specificity. Conclusions: Remotely monitored sensor-based WATCH-PD assessments produced digital endpoints that predicted early-stage PD status with good accuracy, sensitivity, and specificity. Digital endpoints of primary interest were associated with tremor-and gait-related metrics. Further work is necessary to determine how well these digital endpoints track PD severity and progression.

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**Conference country:** Spain

**Conference end date:** 2022-09-18

**Conference location:** Madrid

**Conference start date:** 2022-09-15

**Conference title:** 2022 MDS International Congress

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**Correspondence author:** Anderson, D. , Horsham, PA, United States.

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**Subject:** Embase;accelerometry;adult;algorithm (major);apple;cognition assessment;conference abstract;controlled study;disease assessment;feature selection;female;finger;gait;human;linear regression analysis;longitudinal study;machine learning (major);major clinical study;male;Monte Carlo method;nonhuman;Parkinson disease;prediction;psychomotor performance;sensitivity and specificity;sensor (major);signal processing;speech;tremor;trunk;voice;walking;wrist

**Updates:** 2022-10-27

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Document 59

## **DystoniaBoTXNet: A Deep Learning Platform for Predictive Outcome of Botulinum Toxin Treatment in Isolated Dystonia**

**Author:** Yao, D. 1 ; O'Flynn, L. 1 ; Simonyan, K. 1

1 , Boston, MA, United States

**Publication info:** Movement Disorders, suppl. Supplement 2 37 : S281. John Wiley and Sons Inc. (Sep 2022)

**Abstract (summary):** Objective: To develop and validate an objective measure of the botulinum toxin treatment outcome in isolated dystonia. Background: Dystonia is characterized by abnormal, often painful, postures and repetitive movements due to involuntary sustained or intermittent muscle contractions. Despite its debilitating impact on patients' quality of life, clinical management of dystonia represents a significant challenge, with about one-third of patients not receiving any treatment. Botulinum neurotoxin (BoTX) injections into the affected muscles are considered the gold standard therapy for patients with focal and segmental dystonias. However, the variable effectiveness of BoTX therapy necessitates a repeated series of injections to refine the injection location, dosage, and administration regimen before the final treatment efficacy is established. An estimated 40% of patients with dystonia fail to benefit from BoTX treatment. One of the major factors limiting the efficient use of BoTX in dystonia patients is the absence of an objective predictive marker of treatment response. Methods: We developed and tested a deep learning platform, DystoniaBoTXNet, to predict the BoTX



treatment outcome in 285 patients with focal dystonia (cervical dystonia, blepharospasm, laryngeal dystonia, writer's cramp) based on their structural brain MRI and demographic information. Results: The training model of DystoniaBoTXNet achieved an area under the curve (AUC) of 100% in discriminating 165 patients with or without BoTX treatment benefits based on a fully automated, data-driven identification of a neural **biomarker** of BoTX efficacy. In the independent testing sets, DystoniaBoTXNet achieved high accuracy in predicting the BoTX treatment outcome, including 92.9% accuracy in blepharospasm, 88.9% accuracy in cervical dystonia, 85% accuracy in laryngeal dystonia, and 76.9% accuracy in writer's cramp. Conclusions: The DystoniaBoTXNet **deep learning** platform is feasible for the objective and accurate algorithmic assessment of the BoTX treatment outcome prior to injection administration.

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**Conference start date:** 2022-09-15

**Conference title:** 2022 MDS International Congress

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Yao, D. , Boston, MA, United States.

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**Subject:** Embase;biological marker;botulinum toxin (major);adult;algorithm (major);area under the curve (major);blepharospasm;brain;cervical dystonia;conference abstract;deep learning (major);demographics;drug efficacy;dystonia (major);female;focal dystonia;gold standard;human;major clinical study;male;neuroimaging;nuclear magnetic resonance imaging;outcome assessment;segmental dystonia;spasmodic dysphonia;treatment failure;treatment response;writer's cramp

**Updates:** 2022-10-27

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Document 60

### **Loss of speech and functional impairment in Alzheimer's disease-related primary progressive aphasia: predictive factors of decline**

**Author:** Mazzeo, Salvatore 1 ; Polito, Cristina 2 ; Lassi, Michael 3 ; Bagnoli, Silvia 4 ; Mattei, Marta 4 ; Padiglioni, Sonia 5 ; Berti, Valentina 6 ; Lombardi, Gemma 2 ; Giacomucci, Giulia 4 ; De Cristofaro, Maria Teresa 7 ; Passeri, Alessandro 8 ; Ferrari, Camilla 4 ; Nacmias, Benedetta 1 ; Mazzoni, Alberto 3 ; Sorbi, Sandro 1 ; Bessi, Valentina 4

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**Publication info:** Neurobiology of Aging 117 : 59-70. Elsevier Inc. (Sep 2022)

**Abstract (summary):** We aimed to identify features associated with different disease trajectories in Alzheimer's disease (AD)-related primary progressive aphasia (PPA). We considered 23 patients diagnosed with AD-related PPA. All patients underwent neuropsychological evaluation, <sup>18</sup>F-Fluorodeoxyglucose-PET brain scan, CSF biomarkers measurement and APOE genotype analysis at baseline and underwent neurological follow-up for a mean time of 3 years. Patients who progressed to total loss of speech (TLoS<sup>-</sup>) had greater impairment in writing and higher t-tau concentration as compared to TLoS<sup>+</sup> patients. Patients who progressed to loss of functional autonomy (LoFA<sup>-</sup>) had greater impairment in single-word comprehension as compared to patients who maintained autonomy in self-care. Furthermore, <sup>18</sup>F-FDG-PET SPM analyses revealed different brain metabolic patterns

between TLoS<sup>+</sup> and TLoS<sup>-</sup> and between LoFA<sup>+</sup> and LoFA<sup>-</sup>. In conclusion, linguistic profile, CSF t-tau and brain metabolic pattern might be useful tools to predict progression to total loss of **speech** and loss of functional autonomy in AD-related PPA patients.

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**Author e-mail address:** valentina.bessi@unifi.it

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**Correspondence author:** Bessi, Valentina Department of Neuroscience, Psychology, Drug Research and Child Health, University of Florence, Azienda Ospedaliero-Universitaria Careggi, Largo Brambilla, 3, Florence, 50134, Italy.

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**Date created:** 2022-11-13

**Device trade name:** Device trade name Name: LUMIPULSE; Manufacturer: Fujirebio;

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**Identifier (keyword):** Alzheimer's disease, Amyloid **biomarkers**, Brain metabolism, Disease progression, Neuropsychology, Primary progressive aphasia

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**Subject:** Embase;MEDLINE;amyloid precursor protein -- endogenous compound;apolipoprotein E -- endogenous compound;**biological marker** -- endogenous compound;cholinesterase inhibitor -- drug therapy -- Alzheimer disease;cholinesterase inhibitor -- special situation for pharmacovigilance --

aged;fluorodeoxyglucose f 18;flutemetamol f 18;granulin -- endogenous compound;guanine nucleotide exchange C9orf72 -- endogenous compound;memantine -- drug therapy -- Alzheimer disease;memantine -- special situation for pharmacovigilance -- aged;presenilin 1 -- endogenous compound;presenilin 2 -- endogenous compound;tau protein -- endogenous compound;immunoassay analyzer;LUMIPULSE +;PET-CT scanner;aged;Alzheimer disease -- diagnosis (major);Alzheimer disease -- drug therapy -- cholinesterase inhibitor (major);Alzheimer disease -- drug therapy -- memantine (major);Article;brain metabolism;brain scintiscanning;cerebrospinal fluid;clinical article;cohort analysis;computer assisted tomography;controlled study;cross validation;daily life activity;degenerative disease;diagnostic accuracy;diagnostic test accuracy study;disease duration;disease exacerbation;DNA sequencing;female;follow up;functional anatomy;functional disease (major);gene mutation;genotype;human;male;middle temporal gyrus;Mini Mental State Examination;Montreal cognitive assessment;neuropsychological test;neuropsychology;nuclear magnetic resonance imaging;positron emission tomography;predictive value;primary progressive aphasia (major);receiver operating characteristic;Rey auditory verbal learning test;sensitivity and specificity;speech disorder -- diagnosis (major);task performance;token test;trail making test;Unified Parkinson Disease Rating Scale;working memory

**Substance:** Substance Substance: fluorodeoxyglucose f 18; CAS: 63503-12-8; Substance: flutemetamol f 18; CAS: 765922-62-1; Substance: memantine; CAS: 19982-08-241100-52-151052-62-1; Substance: presenilin 1; CAS: 186986-30-1; Substance: presenilin 2; CAS: 172593-10-1;

**Updates:** 2022-06-132022-11-14

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Document 61

## **Predicting clinical scores in Huntington's disease: a lightweight speech test**

**Author:** Riad, Rachid 1 ; Lunven, Marine 2 ; Titeux, Hadrien 3 ; Cao, Xuan-Nga 3 ; Hamet Bagnou, Jennifer 2 ; Lemoine, Laurie 2 ; Montillot, Justine 2 ; Sliwinski, Agnes 2 ; Youssouf, Katia 4 ; Cleret de Langavant, Laurent 2 ; Dupoux, Emmanuel 3 ; Bachoud-Lévi, Anne-Catherine 2

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**Publication info:** Journal of Neurology 269.9: 5008-5021. Springer Science and Business Media Deutschland GmbH. (Sep 2022)

**Abstract (summary):** Objectives: Using brief samples of **speech** recordings, we aimed at predicting, through **machine learning**, the clinical performance in Huntington's Disease (HD), an inherited Neurodegenerative disease (NDD). Methods: We collected and analyzed 126 samples of audio recordings of both forward and backward counting from 103 Huntington's disease gene carriers [87 manifest and 16 premanifest; mean age 50.6 (SD 11.2), range (27–88) years] from three multicenter prospective studies in France and Belgium (MIG-HD (ClinicalTrials.gov NCT00190450); BIO-HD (ClinicalTrials.gov NCT00190450) and Repair-HD (ClinicalTrials.gov NCT00190450)). We pre-registered all of our methods before running any analyses, in order to avoid inflated results. We automatically extracted 60 **speech** features from blindly annotated samples. We used **machine learning** models to combine multiple **speech** features in order to make predictions at individual levels of the clinical **markers**. We trained **machine learning** models on 86% of the samples, the remaining 14% constituted the independent test set. We combined **speech** features with demographics variables (age, sex, CAG repeats, and burden score) to predict cognitive, motor, and functional scores of the Unified Huntington's disease rating scale. We provided correlation between **speech** variables and striatal volumes. Results: **Speech** features combined with demographics allowed the prediction of the individual cognitive, motor, and functional scores with a relative error from 12.7 to 20.0% which is better than predictions using demographics and genetic information. Both mean and standard deviation of pause durations during backward recitation and clinical scores correlated with striatal atrophy (Spearman 0.6 and 0.5–0.6, respectively). Interpretation: Brief and examiner-free **speech** recording and analysis may become in the future an efficient method for remote evaluation of the individual condition in HD and likely in other NDD.

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We are very thankful to the patients that participated in our study. We thank Marvin Lavechin, Alex Cristia for the multiple helpful discussions and we thank the speech pathologists for the annotations of the speech data.

**Identifier (keyword):** Huntington's disease, Machine learning, Speech

**Language:** English

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**Number of references:** 58

**Publication date:** Sep 2022

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**Publisher:** Springer Science and Business Media Deutschland GmbH

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**Subject:** Embase; huntingtin (major); imaging software; adult; aged; Article; atrophy; audio recording; Belgium; clinical evaluation; cohort analysis; controlled study; correlation coefficient; disease burden; female; France; functional status; human; Huntington chorea (major); machine learning; major clinical study; male; multicenter study; perseveration; prospective study; speech; speech analysis; speech and language; speech test (major); statistical significance; Stroop test; Unified Huntington Disease Rating Scale; vocalization

**Updates:** 2022-05-23 2022-08-15 2022-09-02

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Document 62

## Natural language signatures of psilocybin microdosing

**Author:** Sanz, Camila 1 ; Cavanna, Federico 2 ; Muller, Stephanie 1 ; de la Fuente, Laura 3 ; Zamberlan, Federico 4 ; Palmucci, Matías 1 ; Janeckova, Lucie 5 ; Kuchar, Martin 6 ; Carrillo, Facundo 7 ; García, Adolfo M. 8 ; Pallavicini, Carla 2 ; Tagliacruzchi, Enzo 9

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**Publication info:** Psychopharmacology 239.9: 2841-2852. Springer Science and Business Media Deutschland GmbH. (Sep 2022)

**Abstract (summary):** Rationale: Serotonergic psychedelics are being studied as novel treatments for mental health disorders and as facilitators of improved well-being, mental function, and creativity. Recent studies have found mixed results concerning the effects of low doses of psychedelics (“microdosing”) on these domains. However, microdosing is generally investigated using instruments designed to assess larger doses of psychedelics, which might lack sensitivity and specificity for this purpose. Objectives: Determine whether unconstrained speech contains signatures capable of identifying the acute effects of psilocybin microdoses. Methods: Natural speech under psilocybin

microdoses (0.5 g of psilocybin mushrooms) was acquired from thirty-four healthy adult volunteers (11 females:  $32.09 \pm 3.53$  years; 23 males:  $30.87 \pm 4.64$  years) following a double-blind and placebo-controlled experimental design with two measurement weeks per participant. On Wednesdays and Fridays of each week, participants consumed either the active dose (psilocybin) or the placebo (edible mushrooms). Features of interest were defined based on variables known to be affected by higher doses: verbosity, semantic variability, and sentiment scores. **Machine learning** models were used to discriminate between conditions. Classifiers were trained and tested using stratified cross-validation to compute the AUC and p-values. Results: Except for semantic variability, these metrics presented significant differences between a typical active microdose and the inactive placebo condition. **Machine learning** classifiers were capable of distinguishing between conditions with high accuracy (AUC  $\approx 0.8$ ). Conclusions: These results constitute first evidence that low doses of serotonergic psychedelics can be identified from unconstrained natural **speech**, with potential for widely applicable, affordable, and ecologically valid monitoring of microdosing schedules.

**Accession number:** 2017814606

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**Identifier (keyword):** Language, **Machine learning**, Microdosing, Psilocybin, Psychedelics

**Language:** English

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**Publication date:** Sep 2022



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**Subject:** Embase;MEDLINE;psilocybine -- pharmacology (major);psychedelic agent;Article;classifier;controlled study;cross validation;double blind procedure;drug mechanism;drug microdose;edible mushroom;experimental design;female;human;machine learning;male;metric system;randomized controlled trial;serotonergic system;speech

**Substance:** Substance Substance: psilocybine; CAS: 520-52-5;

**Updates:** 2022-06-132022-06-142022-08-232022-09-14

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Document 63

## **Natural speech markers of Alzheimer's disease co-pathology in Lewy body dementias**

**Author:** Shellikeri, Sanjana 1 ; Cho, Sunghye 2 ; Cousins, Katheryn A Q 1 ; Liberman, Mark 3 ; Howard, Erica 4 ; Balganorth, Yvonne 1 ; Weintraub, Daniel 5 ; Spindler, Meredith 6 ; Deik, Andres 6 ; Lee, Edward B 7 ; Trojanowski, John Q 7 ; Irwin, David 1 ; Wolk, David 1 ; Grossman, Murray 1 ; Nevler, Naomi 1

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**Publication info:** Parkinsonism & related disorders 102 : 94-100. (Sep 2022)

### **Abstract (summary): INTRODUCTION**

An estimated 50% of patients with Lewy body dementias (LBD), including Parkinson's disease dementia (PDD) and Dementia with Lewy bodies (DLB), have co-occurring Alzheimer's disease (AD) that is associated with worse prognosis. This study tests an automated analysis of natural speech as an inexpensive, non-invasive screening tool for AD co-pathology in biologically-confirmed cohorts of LBD patients with AD co-pathology (SYN + AD) and without (SYN-AD).

## METHODS

We analyzed lexical-semantic and acoustic features of picture descriptions using automated methods in 22 SYN + AD and 38 SYN-AD patients stratified using AD CSF **biomarkers** or autopsy diagnosis. **Speech** markers of AD co-pathology were identified using best subset regression, and their diagnostic discrimination was tested using receiver operating characteristic. ANCOVAs compared measures between groups covarying for demographic differences and cognitive disease severity. We tested relations with CSF tau levels, and compared **speech** measures between PDD and DLB clinical disorders in the same cohort.

## RESULTS

Age of acquisition of nouns ( $p = 0.034$ ,  $|d| = 0.77$ ) and lexical density ( $p = 0.0064$ ,  $|d| = 0.72$ ) were reduced in SYN + AD, and together showed excellent discrimination for SYN + AD vs. SYN-AD (95% sensitivity, 66% specificity; AUC = 0.82). Lower lexical density was related to higher CSF t-Tau levels ( $R = -0.41$ ,  $p = 0.0021$ ). Clinically-diagnosed PDD vs. DLB did not differ on any **speech** features.

## CONCLUSION

AD co-pathology may result in a deviant natural **speech** profile in LBD characterized by specific lexical-semantic impairments, not detectable by clinical disorder diagnosis. Our study demonstrates the potential of automated **digital speech** analytics as a screening tool for underlying AD co-pathology in LBD.

**Accession number:** 35985146

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**Identifier (keyword):** Alzheimer's disease, Automatic speech processing, Digitalbiomarker, Lewy body dementia, Natural language processing, Parkinson disease dementia, Speech analysis

**Language:** English

**Language of abstract:** English

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**MeSH:** Alzheimer Disease (major) -- pathology; Amyloid beta-Peptides; Biomarkers; Dementia (major) - complications; Humans; Lewy Body Disease (major) -- complications; Parkinson Disease (major) -- psychology; Speech; alpha-Synuclein; tau Proteins

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Document 64

## **Imperative Role of Machine Learning Algorithm for Detection of Parkinson's Disease: Review, Challenges and Recommendations**

**Author:** Rana, Arti 1 ; Dumka, Ankur 2 ; Singh, Rajesh 3 ; Panda, Manoj Kumar 4 ; Priyadarshi, Neeraj 5 ; Twala, Bhesisipho 6

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**Publication info:** Diagnostics (Basel, Switzerland) 12.8 (Aug 19, 2022)

**Abstract (summary):** Parkinson's disease (PD) is a neurodegenerative disease that affects the neural, behavioral, and physiological systems of the brain. This disease is also known as tremor. The common symptoms of this disease are a slowness of movement known as 'bradykinesia', loss of automatic movements, speech/writing changes, and difficulty with walking at early stages. To solve these issues and to enhance the diagnostic process of PD, machine learning (ML) algorithms have been implemented for the categorization of subjective disease and healthy controls (HC) with comparable medical appearances. To provide a far-reaching outline of data modalities and artificial intelligence techniques that have been utilized in the analysis and diagnosis of PD, we conducted a literature analysis of research papers published up until 2022. A total of 112 research papers were included in this study, with an examination of their targets, data sources and different types of datasets, ML algorithms, and associated outcomes. The results showed that ML approaches and new biomarkers have a lot of promise for being used in clinical decision-making, resulting in a more systematic and informed diagnosis of PD. In this study, some major challenges were addressed along with a future recommendation.

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**Correspondence author:** Rana, Arti Computer Science & Engineering, Veer Madho Singh Bhandari Uttarakhand Technical University, Dehradun 248007, Uttarakhand, India.

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**Language:** English

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Document 65

## **Using Voice Biomarkers to Classify Suicide Risk in Adult Telehealth Callers: Retrospective Observational Study**

**Author:** Iyer, Ravi 1 ; Nedeljkovic, Maja 1 ; Meyer, Denny 1

1 Centre for Mental Health, Swinburne University of Technology, Hawthorn, Australia, Australia

**Publication info:** JMIR mental health 9.8: e39807. (Aug 15, 2022)

### **Abstract (summary): BACKGROUND**

Artificial intelligence has the potential to innovate current practices used to detect the imminent risk of suicide and to address shortcomings in traditional assessment methods.

### **OBJECTIVE**

In this paper, we sought to automatically classify short segments (40 milliseconds) of speech according to low versus imminent risk of suicide in a large number (n=281) of telephone calls made to 2 telehealth counselling services in Australia.

### **METHODS**

A total of 281 help line telephone call recordings sourced from On The Line, Australia (n=266, 94.7%) and 000 Emergency services, Canberra (n=15, 5.3%) were included in this study. Imminent risk of suicide was coded for when callers affirmed intent, plan, and the availability of means; level of risk was assessed by the responding counsellor and reassessed by a team of clinical researchers using the Columbia Suicide Severity Rating Scale (=5/6). Low risk of suicide was coded for in an absence of intent, plan, and means and via Columbia suicide Severity Scale Ratings (=1/2). Preprocessing involved normalization and pre-emphasis of voice signals, while voice biometrics were extracted using the statistical language r. Candidate predictors were identified using Lasso regression. Each voice biomarker was assessed as a predictor of suicide risk using a generalized additive mixed effects

model with splines to account for nonlinearity. Finally, a component-wise gradient boosting model was used to classify each call recording based on precoded suicide risk ratings.

## RESULTS

A total of 77 imminent-risk calls were compared with 204 low-risk calls. Moreover, 36 **voice biomarkers** were extracted from each **speech** frame. Caller sex was a significant moderating factor ( $\beta = -.84$ , 95% CI -0.85, -0.84;  $t = 6.59$ ,  $P < .001$ ). Candidate **biomarkers** were reduced to 11 primary markers, with distinct models developed for men and women. Using leave-one-out cross-validation, ensuring that the **speech** frames of no single caller featured in both training and test data sets simultaneously, an area under the precision or recall curve of 0.985 was achieved (95% CI 0.97, 1.0). The gamboost classification model correctly classified 469,332/470,032 (99.85%) **speech** frames.

## CONCLUSIONS

This study demonstrates an objective, efficient, and economical assessment of imminent suicide risk in an ecologically valid setting with potential applications to real-time assessment and response.

## TRIAL REGISTRATION

Australian New Zealand Clinical Trials Registry ACTRN12622000486729;  
<https://www.anzctr.org.au/ACTRN12622000486729.aspx>.

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**Copyright:** ©Ravi Iyer, Maja Nedeljkovic, Denny Meyer. Originally published in JMIR Mental Health (<https://mental.jmir.org>), 15.08.2022.

**Correspondence author:** Iyer, Ravi Centre for Mental Health, Swinburne University of Technology, Hawthorn, Australia.

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**Identifier (keyword):** **machine learning**, mental health, prediction model, risk prediction, suicide, suicide prevention, telehealth, **voicebiomarker**, **voice** biometrics

**Language:** English

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Document 66

## **The applicability of the Beck Depression Inventory and Hamilton Depression Scale in the automatic recognition of depression based on **speech** signal processing**

**Author:** Hajduska-Dér, Bálint 1 ; Kiss, Gábor 2 ; Sztahó, Dávid 2 ; Vicsi, Klára 2 ; Simon, Lajos 1

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**Publication info:** Frontiers in Psychiatry 13 Frontiers Media S.A. (Aug 4, 2022)

**Abstract (summary):** Depression is a growing problem worldwide, impacting on an increasing number of patients, and also affecting health systems and the global economy. The most common diagnostic rating scales of depression are self-reported or clinician-administered, which differ in the symptoms that they are sampling. **Speech** is a promising **biomarker** in the diagnostic assessment of depression, due to non-invasiveness and cost and time efficiency. In our study, we try to achieve a more accurate, sensitive model for determining depression based on **speech** processing. Regression and classification models were also developed using a **machine learning** method. During the research, we had access to a large **speech** database that includes **speech** samples from depressed and healthy subjects. The database contains the Beck Depression Inventory (BDI) score of each subject and the Hamilton Rating Scale for Depression (HAMD) score of 20% of the subjects. This fact provided an opportunity to compare the usefulness of BDI and HAMD for training models of automatic recognition of depression based on **speech** signal processing. We found that the estimated values of the acoustic model trained on BDI scores are closer to HAMD assessment than to the BDI scores, and the partial application of HAMD scores instead of BDI scores in training improves the accuracy of automatic recognition of depression.

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**Correspondence author:** Hajduska-Dér, Bálint Department of Psychiatry and Psychotherapy, Semmelweis University, Budapest, Hungary.

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**Identifier (keyword):** depression, diagnosis, machine learning, speech, Support Vector Regression

**Language:** English

**Language of abstract:** English

**Number of references:** 36

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**Subject:** Embase;acoustics;adult;article;Beck Depression Inventory (major);controlled study;female;Hamilton Depression Rating Scale (major);human;human experiment;machine learning (major);male;signal processing (major);speech (major);speech analysis;support vector machine (major)

**Updates:** 2022-08-25

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Document 67



## **Speech disturbances in schizophrenia: Assessing cross-linguistic generalizability of NLP automated measures of coherence**

**Author:** Parola, Alberto 1 ; Lin, Jessica Mary 1 ; Simonsen, Arndis 2 ; Bliksted, Vibeke 2 ; Zhou, Yuan 3 ; Wang, Huiling 4 ; Inoue, Lana 5 ; Koelkebeck, Katja 5 ; Fusaroli, Riccardo 6

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**Publication info:** Schizophrenia research (Aug 1, 2022)

### **Abstract (summary): INTRODUCTION**

Language disorders - disorganized and incoherent **speech** in particular - are distinctive features of schizophrenia. Natural language processing (NLP) offers automated measures of incoherent **speech** as promising markers for schizophrenia. However, the scientific and clinical impact of NLP markers depends on their generalizability across contexts, samples, and languages, which we systematically assessed in the present study relying on a large, novel, cross-linguistic corpus.

### **METHODS**

We collected a Danish (DK), German (GE), and Chinese (CH) cross-linguistic dataset involving transcripts from 187 participants with schizophrenia (111DK, 25GE, 51CH) and 200 matched controls (129DK, 29GE, 42CH) performing the Animated Triangles Task. Fourteen previously published NLP coherence measures were calculated, and between-groups differences and association with symptoms were tested for cross-linguistic generalizability.

### **RESULTS**

One coherence measure, i.e. second-order coherence, robustly generalized across samples and languages. We found several language-specific effects, some of which partially replicated previous findings (lower coherence in German and Chinese patients), while others did not (higher coherence in Danish patients). We found several associations between symptoms and measures of coherence, but the effects were generally inconsistent across languages and rating scales.

## CONCLUSIONS

Using a cumulative approach, we have shown that NLP findings of reduced semantic coherence in schizophrenia have limited generalizability across different languages, samples, and measures. We argue that several factors such as sociodemographic and clinical heterogeneity, cross-linguistic variation, and the different NLP measures reflecting different clinical aspects may be responsible for this variability. Future studies should take this variability into account in order to develop effective clinical applications targeting different patient populations.

**Accession number:** 35927097

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**Identifier (keyword):** Biomarker, Communication disorders, Digital phenotyping, Natural language processing, Schizophrenia spectrum disorder, Semantic coherence, Thought disorder

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## **A cross-linguistic perspective to classification of healthiness of speech in Parkinson's disease**

**Author:** Verkhodanova, Vass 1 ; Coler, Matt 2 ; Jonkers, Roel 3 ; Timmermans, Sanne 4 ; Maurits, Natasha 4 ; de Jong, Bauke 4 ; Lowie, Wander 3

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**Publication info:** Journal of Neurolinguistics 63 Elsevier Ltd. (Aug 2022)

**Abstract (summary):** People with Parkinson's disease often experience communication problems. The current cross-linguistic study investigates how listeners' perceptual judgements of speech healthiness are related to the acoustic changes appearing in the speech of people with Parkinson's disease. Accordingly, we report on an online experiment targeting perceived healthiness of speech. We studied the relations between healthiness perceptual judgements and a set of acoustic characteristics of speech in a cross-sectional design. We recruited 169 participants, who performed a classification task judging speech recordings of Dutch speakers with Parkinson's disease and of Dutch control speakers as 'healthy' or 'unhealthy'. The groups of listeners differed in their training and expertise in speech language therapy as well as in their native languages. Such group separation allowed us to investigate the acoustic correlates of speech healthiness without influence of the content of the recordings. We used a Random Forest method to predict listeners' responses. Our findings demonstrate that, independently of expertise and language background, when classifying speech as healthy or unhealthy listeners are more sensitive to speech rate, presence of phonation deficiency reflected by maximum phonation time measurement, and centralization of the vowels. The results indicate that both specifics of the expertise and language background may lead to listeners relying more on the features from either prosody or phonation domains. Our findings demonstrate that more global perceptual judgements of different listeners classifying speech of people with Parkinson's disease may be predicted with sufficient reliability from conventional acoustic features. This suggests universality of acoustic change in speech of people with Parkinson's disease. Therefore, we concluded that certain aspects of phonation and prosody serve as prominent markers of speech healthiness for listeners independent of their first language or expertise. Our findings have outcomes

for the clinical practice and real-life implications for subjective perception of **speech** of people with Parkinson's disease, while information about particular acoustic changes that trigger listeners to classify **speech** as 'unhealthy' can provide specific therapeutic targets in addition to the existing **dysarthria** treatment in people with Parkinson's disease.

**Accession number:** 2017018500

**Author e-mail address:** v.verkhodanova@rug.nl

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**Subject:** Embase;acoustics;adult;Article;clinical practice;controlled study;cross-sectional study;demography;**dysarthria**;female;human;linguistics (major);major clinical study;male;middle aged;Parkinson disease -- diagnosis (major);patient

participation;phonation;prediction;prosody;random forest;speech and language rehabilitation;speech perception (major)

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Document 69

## **Digital phenotype of mood disorders: A conceptual and critical review**

**Author:** Maatoug, Redwan 1 ; Oudin, Antoine 1 ; Adrien, Vladimir 2 ; Saudreau, Bertrand 3 ; Bonnot, Olivier 4 ; Millet, Bruno 1 ; Ferreri, Florian 2 ; Mouchabac, Stephane 2 ; Bourla, Alexis 5

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**Publication info:** Frontiers in Psychiatry 13 Frontiers Media S.A. (Jul 26, 2022)

**Abstract (summary):** Background: Mood disorders are commonly diagnosed and staged using clinical features that rely merely on subjective data. The concept of digital phenotyping is based on the idea that collecting real-time **markers** of human behavior allows us to determine the digital **signature** of a pathology. This strategy assumes that behaviors are quantifiable from data extracted and analyzed through digital sensors, wearable devices, or smartphones. That concept could bring a shift in the diagnosis of mood disorders, introducing for the first time additional examinations on psychiatric routine care. Objective: The main objective of this review was to propose a conceptual and critical review of the literature regarding the theoretical and technical principles of the digital phenotypes applied to mood disorders. Methods: We conducted a review of the literature by updating a previous article and querying the PubMed database between February 2017 and November 2021 on titles with relevant keywords regarding digital phenotyping, mood disorders and **artificial intelligence**. Results: Out of 884 articles included for evaluation, 45 articles were taken into account and classified by data source (multimodal, actigraphy, ECG, smartphone use, **voice** analysis, or body temperature). For depressive episodes, the main finding is a decrease in terms of functional and

biological parameters [decrease in activities and walking, decrease in the number of calls and SMS messages, decrease in temperature and heart rate variability (HRV)], while the manic phase produces the reverse phenomenon (increase in activities, number of calls and HRV). Conclusion: The various studies presented support the potential interest in digital phenotyping to computerize the clinical characteristics of mood disorders.

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**Identifier (keyword):** artificial intelligence, bipolar disorder, depressive disorder, digital phenotyping, machine learning, mood disorders

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**Updates:** 2022-08-162022-08-19

## Reliability of Automatic Computer Vision-Based Assessment of Orofacial Kinematics for Telehealth Applications

**Author:** Simmatis, Leif 1 ; Barnett, Carolina 2 ; Marzouqah, Reeman 3 ; Taati, Babak 4 ; Boulos, Mark 5 ; Yunusova, Yana 6

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**Publication info:** Digital Biomarkers 6.2: 71-82. S. Karger AG. (Jul 21, 2022)

**Abstract (summary):** Introduction: Telehealth/remote assessment using readily available 2D mobile cameras and **deep learning**-based analyses is rapidly becoming a viable option for detecting orofacial and **speech** impairments associated with neurological and neurodegenerative disease during telehealth practice. However, the psychometric properties (e.g., internal consistency and reliability) of kinematics obtained from these systems have not been established, which is a crucial next step before their clinical usability is established. Methods: Participants were assessed in lab using a 3 dimensional (3D)-capable camera and at home using a readily-available 2D camera in a tablet. Orofacial kinematics was estimated from videos using a deep facial landmark tracking model. Kinematic features quantified the clinically relevant constructs of velocity, range of motion, and lateralization. In lab, all participants performed the same oromotor task. At home, participants were split into two groups that each performed a variant of the in-lab task. We quantified within-assessment consistency (Cronbach's  $\alpha$ ), reliability (intraclass correlation coefficient [ICC]), and fitted linear mixed-effects models to at-home data to capture individual-/task-dependent longitudinal trajectories. Results: Both in lab and at home, Cronbach's  $\alpha$  was typically high ( $>0.80$ ) and ICCs were often good ( $>0.70$ ). The linear mixed-effect models that best fit the longitudinal data were those that accounted for individual- or task-dependent effects. Discussion: Remotely gathered orofacial kinematics were as internally consistent and reliable as those gathered in a controlled laboratory setting using a high-

performance 3D-capable camera and could additionally capture individual- or task-dependent changes over time. These results highlight the potential of remote assessment tools as digital **biomarkers** of disease status and progression and demonstrate their suitability for novel telehealth applications.

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**Updates:** 2022-08-16 2022-08-22 2022-09-02



## **Multimodal Assessment of Schizophrenia and Depression Utilizing Video, Acoustic, Locomotor, Electroencephalographic, and Heart Rate Technology: Protocol for an Observational Study**

**Author:** Cotes, Robert O 1 ; Boazak, Mina 2 ; Griner, Emily 1 ; Jiang, Zifan 3 ; Kim, Bona 4 ; Bremer, Whitney 5 ; Seyedi, Salman 5 ; Bahrami Rad, Ali 5 ; Clifford, Gari D 3

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**Publication info:** JMIR research protocols 11.7: e36417. (Jul 13, 2022)

### **Abstract (summary): BACKGROUND**

Current standards of psychiatric assessment and diagnostic evaluation rely primarily on the clinical subjective interpretation of a patient's outward manifestations of their internal state. While psychometric tools can help to evaluate these behaviors more systematically, the tools still rely on the clinician's interpretation of what are frequently nuanced **speech** and behavior patterns. With advances in computing power, increased availability of clinical data, and improving resolution of recording and sensor hardware (including acoustic, video, accelerometer, infrared, and other modalities), researchers have begun to demonstrate the feasibility of cutting-edge technologies in aiding the assessment of psychiatric disorders.

### **OBJECTIVE**

We present a research protocol that utilizes facial expression, eye gaze, **voice** and **speech**, locomotor, heart rate, and electroencephalography monitoring to assess schizophrenia symptoms and to distinguish patients with schizophrenia from those with other psychiatric disorders and control subjects.

### **METHODS**

We plan to recruit three outpatient groups: (1) 50 patients with schizophrenia, (2) 50 patients with unipolar major depressive disorder, and (3) 50 individuals with no psychiatric history. Using an internally developed semistructured interview, psychometrically validated clinical outcome measures, and a multimodal sensing system utilizing video, acoustic, actigraphic, heart rate, and electroencephalographic sensors, we aim to evaluate the system's capacity in classifying subjects

(schizophrenia, depression, or control), to evaluate the system's sensitivity to within-group symptom severity, and to determine if such a system can further classify variations in disorder subtypes.

## RESULTS

Data collection began in July 2020 and is expected to continue through December 2022.

## CONCLUSIONS

If successful, this study will help advance current progress in developing state-of-the-art technology to aid clinical psychiatric assessment and treatment. If our findings suggest that these technologies are capable of resolving diagnoses and symptoms to the level of current psychometric testing and clinician judgment, we would be among the first to develop a system that can eventually be used by clinicians to more objectively diagnose and assess schizophrenia and depression with the possibility of less risk of bias. Such a tool has the potential to improve accessibility to care; to aid clinicians in objectively evaluating diagnoses, severity of symptoms, and treatment efficacy through time; and to reduce treatment-related morbidity.

## INTERNATIONAL REGISTERED REPORT IDENTIFIER (IRRID)

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**Correspondence author:** Cotes, Robert O Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, United States.

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Document 72

## **Evaluating the COVID-19 Identification ResNet (CIdER) on the INTERSPEECH COVID-19 From Audio Challenges**

**Author:** Akman, Alican 1 ; Coppock, Harry 1 ; Gaskell, Alexander 1 ; Tzirakis, Panagiotis 1 ; Jones, Lyn 2 ; Schuller, Björn W 3

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**Publication info:** Frontiers in digital health 4 : 789980. (Jul 7, 2022)

**Abstract (summary):** Several machine learning-based COVID-19 classifiers exploiting vocal biomarkers of COVID-19 has been proposed recently as digital mass testing methods. Although these classifiers have shown strong performances on the datasets on which they are trained, their methodological adaptation to new datasets with different modalities has not been explored. We report on cross-running the modified version of recent COVID-19 Identification ResNet (CIdER) on the two Interspeech 2021 COVID-19 diagnosis from cough and speech audio challenges: ComParE and DiCOVA. CIdER is an end-to-end deep learning neural network originally designed to classify whether an individual is COVID-19-positive or COVID-19-negative based on coughing and breathing audio recordings from a published crowdsourced dataset. In the current study, we demonstrate the potential of CIdER at binary COVID-19 diagnosis from both the COVID-19 Cough and Speech Sub-Challenges of INTERSPEECH 2021, ComParE and DiCOVA. CIdER achieves significant improvements over

several baselines. We also present the results of the cross dataset experiments with CIdER that show the limitations of using the current COVID-19 datasets jointly to build a collective COVID-19 classifier.

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**Copyright:** Copyright © 2022 Akman, Coppock, Gaskell, Tzirakis, Jones and Schuller.

**Correspondence author:** Akman, Alican GLAM-Group on Language, Audio, and Music, Imperial College London, London, United Kingdom.

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Document 73

## **Artificial Intelligence and Laryngeal Cancer: From Screening to Prognosis: A State of the Art Review**

**Author:** Bensoussan, Yael 1 ; Vanstrum, Erik B 2 ; Johns, Michael M, 3rd 3 ; Rameau, Anaïs 4

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**Publication info:** Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery : 1945998221110839. (Jul 5, 2022)

### **Abstract (summary): OBJECTIVE**

This state of the art review aims to examine contemporary advances in applications of **artificial intelligence (AI)** to the screening, detection, management, and prognostication of laryngeal cancer (LC).

## DATA SOURCES

Four bibliographic databases were searched: PubMed, EMBASE, Cochrane, and IEEE.

## REVIEW METHODS

A structured review of the current literature (up to January 2022) was performed. Search terms related to topics of **AI** in LC were identified and queried by 2 independent reviewers. Citations of selected studies and review articles were also evaluated to ensure comprehensiveness.

## CONCLUSIONS

**AI** applications in LC have encompassed a variety of data modalities, including radiomics, genomics, acoustics, clinical data, and videomics, to support screening, diagnosis, therapeutic decision making, and prognosis. However, most studies remain at the proof-of-concept level, as **AI** algorithms are trained on single-institution databases with limited data sets and a single data modality.

## IMPLICATIONS FOR PRACTICE

**AI** algorithms in LC will need to be trained on large multi-institutional data sets and integrate multimodal data for optimal performance and clinical utility from screening to prognosis. Out of the data types reviewed, genomics has the most potential to provide generalizable models thanks to available large multi-institutional open access genomic data sets. **Voice** acoustic data represent an inexpensive and accurate **biomarker**, which is easy and noninvasive to capture, offering a unique opportunity for screening and monitoring of LA, especially in low-resource settings.

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**Correspondence author:** Bensoussan, Yael Department of Otolaryngology-Head and Neck Surgery, University of South Florida, Tampa, Florida, USA.

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Document 74

## **Machine Learning Smart System for Parkinson Disease Classification Using the Voice as a Biomarker**

**Author:** Tougui, Ilias 1 ; Jilbab, Abdelilah 1 ; Mhamdi, Jamal El 1

1 E2SN, ENSIAS, Mohammed V University in Rabat, Rabat, Morocco, Morocco

**Publication info:** Healthcare informatics research 28.3: 210-221. (Jul 2022)

### **Abstract (summary): OBJECTIVES**

This study presents PD Predict, a machine learning system for Parkinson disease classification using voice as a biomarker.

## METHODS

We first created an original set of recordings from the mPower study, and then extracted several audio features, such as mel-frequency cepstral coefficient (MFCC) components and other classical **speech** features, using a windowing procedure. The generated dataset was then divided into training and holdout sets. The training set was used to train two **machine learning** pipelines, and their performance was estimated using a nested subject-wise cross-validation approach. The holdout set was used to assess the generalizability of the pipelines for unseen data. The final pipelines were implemented in PD Predict and accessed through a prediction endpoint developed using the Django REST Framework. PD Predict is a two-component system: a desktop application that records audio recordings, extracts audio features, and makes predictions; and a server-side web application that implements the **machine learning** pipelines and processes incoming requests with the extracted audio features to make predictions. Our system is deployed and accessible via the following link: <https://pdpredict.herokuapp.com/>.

## RESULTS

Both **machine learning** pipelines showed moderate performance, between 65% and 75% using the nested subject-wise cross-validation approach. Furthermore, they generalized well to unseen data and they did not overfit the training set.

## CONCLUSIONS

The architecture of PD Predict is clear, and the performance of the implemented **machine learning** pipelines is promising and confirms the usability of smartphone microphones for capturing digital **biomarkers** of disease.

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**Correspondence author:** Tougui, Ilias E2SN, ENSIAS, Mohammed V University in Rabat, Rabat, Morocco.

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Document 75

## **Unaligned Multimodal Sequences for Depression Assessment From **Speech****

**Author:** Zhao, Ziping; Wang, Keru

**Publication info:** Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference 2022 : 3409-3413. (Jul 2022)

**Abstract (summary):** A growing area of mental health research pertains to how an individual's degree of depression might be automatically assessed through analyzing multimodal-based objective **markers**. However, when combined with **machine learning**, this research can be challenging due to the existence of unaligned multimodal sequences and the limited amount of annotated training data. In this paper, a novel cross-modal framework for automatic depression severity assessment is proposed. The low-level descriptions (LLDs) from multiple clues (such as text, audio and video) are extracted, after which multimodal fusion via cross-modal attention mechanism is utilized to facilitate the learning of more accurate feature representations. For the features extracted from each modality, the cross-modal attention mechanism is utilized to continuously update the input sequence of the target mode, until the score of the patient's health questionnaire (PHQ-8) can finally be obtained. Moreover, Self-Attention Generative Adversarial Networks (SAGAN) is employed to increase the amount of training data available for depression severity analysis. Experimental results on the depression sub-challenge dataset of the Audio/Visual Emotion Challenge (AVEC 2017 and AVEC 2019) demonstrate the effectiveness of our proposed method.

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**First available:** 2022-09-10

**Language:** English

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**MeSH:** Algorithms (major); Depression -- diagnosis; Emotions; Humans; Machine Learning; Speech (major)

**Notes:** Indexing method: Automated;; Publication model: Print;; Cited medium: Internet

**Publication date:** Jul 2022

**Publication type:** Journal

**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

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Document 76

## **Structural Correlates of Overt Sentence Reading in Mild Cognitive Impairment and Mild-to-Moderate Alzheimer's Disease**

**Author:** De Looze, Céline 1 ; Dehsarvi, Amir 2 ; Suleyman, Narin 2 ; Crosby, Lisa 3 ; Hernández, Belinda 4 ; Coen, Robert F. 3 ; Lawlor, Brian A. 5 ; Reilly, Richard B. 6

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**Publication info:** Current Alzheimer Research 19.8: 606-617. Bentham Science Publishers. (Jul 2022)

**Abstract (summary):** Background: Overt sentence reading in mild cognitive impairment (MCI) and mild-to-moderate Alzheimer's disease (AD) has been associated with slowness of speech, characterized by a higher number of pauses, shorter speech units and slower speech rate and attributed to reduced working memory/ attention and language capacity. Objective: This preliminary case-control study investigates whether the temporal organization of speech is associated with the volume of brain regions involved in overt sentence reading and explores the discriminative ability of temporal speech parameters and standard volumetric MRI measures for the classification of MCI and AD. Methods: Individuals with MCI, mild-to-moderate AD, and healthy controls (HC) had a structural MRI scan and read aloud sentences varying in cognitive-linguistic demand (length). The association between speech features and regional brain volumes was examined by linear mixed-effect modeling. Genetic programming was used to explore the discriminative ability of temporal and MRI features. Results: Longer sentences, slower speech rate, and a higher number of pauses and shorter interpausal units were associated with reduced volumes of the reading network. Speech-based classifiers performed similarly to the MRI-based classifiers for MCI-HC (67% vs. 68%) and slightly better for AD-HC (80% vs. 64%) and AD-MCI (82% vs. 59%). Adding the speech features to the MRI features slightly improved the performance of MRI-based classification for AD-HC and MCI-HC but not HC-MCI. Conclusion: The temporal organization of speech in overt sentence reading reflects underlying volume reductions. It may represent a sensitive marker for early assessment of structural changes and cognitive-linguistic deficits associated with healthy aging, MCI, and AD.

**Accession number:** 2018662726

**Author e-mail address:** deloozec@tcd.ie

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**Correspondence author:** De Looze, Céline Trinity Centre for Biomedical Engineering, School of Engineering, Trinity College Dublin, Dublin, Ireland.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-11-30

**Device trade name:** Device trade name Name: Achieva; Manufacturer: Philips;

Name: FreeSurfer software version 6.0; Manufacturer: Undefined;

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.2174/1567205019666220805110248>

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**First available:** 2022-11-25

**Grant:** 13533. , CARDI. Centre for Ageing Research and Development in Ireland.

This study was supported by a Centre for Aging Research and Development in Ireland (CARDI) Leadership Fellowship. Award N: 13533.

**Identifier (keyword):** Alzheimer disease, cognitive aging, functional neuroimaging, genetic programming, machine learning, mild cognitive impairment, sentence reading, temporal speech features

**Language:** English

**Language of abstract:** English

**Number of references:** 96

**Publication date:** Jul 2022

**Publication type:** Journal

**Publisher:** Bentham Science Publishers

**Publisher location:** United Arab Emirates

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**Subject:** Embase;MEDLINE;FreeSurfer software version 6.0 +;imaging software;MRI scanner;aged;Alzheimer disease -- diagnosis (major);amygdala;angular gyrus;Article;attention;brain region;brain size;case control study;cephalometry;cerebellum;classifier;clinical article;cognition;cognitive aging;cognitive linguistic demand +;cohort analysis;controlled study;disease classification;disease severity;entorhinal cortex;feature extraction;female;functional neuroimaging;fusiform gyrus;Go No Go task;gray matter;hemisphere;hippocampus;human;inferior frontal gyrus;inferior parietal lobule;inferior temporal gyrus;insula;language;male;memory;middle temporal gyrus;mild cognitive impairment -- diagnosis (major);Mini Mental State Examination;Montreal cognitive assessment;neuroanatomy (major);neuroimaging;neuropsychological test;nuclear magnetic resonance imaging;overt sentence reading + (major);parietal gyrus;pars opercularis;pars orbitalis;pars triangularis;precuneus;reading (major);repeatable battery for the assessment of neuropsychological status +;slowness;speech disorder;speech rate;speech test;standard;superior frontal gyrus;superior temporal gyrus;supramarginal gyrus;sustained attention to response task +;temporal cortex;voice parameter;volumetry;working memory

**Updates:** 2022-11-252022-11-30

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Document 77

### **Multimodal phenotyping of psychiatric disorders from social interaction: Protocol of a clinical multicenter prospective study**

**Author:** König, Alexandra 1 ; Müller, Philipp 2 ; Tröger, Johannes 2 ; Lindsay, Hali 2 ; Alexandersson, Jan 2 ; Hinze, Jonas 3 ; Riemenschneider, Matthias 3 ; Postin, Danilo 4 ; Ettore, Eric 5 ; Lecomte, Amandine 6 ; Musiol, Michel 6 ; Amblard, Maxime 6 ; Bremond, François 1 ; Balazia, Michal 7 ; Hurlemann, Renee 4

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**Publication info:** Personalized Medicine in Psychiatry 33-34 Elsevier Inc. (Jul 1, 2022)

**Abstract (summary):** Identifying objective and reliable **markers** to tailor diagnosis and treatment of psychiatric patients remains a challenge, as conditions like major depression, bipolar disorder, or schizophrenia are qualified by complex behavior observations or subjective self-reports instead of easily measurable somatic features. Recent progress in computer vision, **speech** processing and **machine learning** has enabled detailed and objective characterization of human behavior in social interactions. However, the application of these technologies to personalized psychiatry is limited due to the lack of sufficiently large corpora that combine multi-modal measurements with longitudinal assessments of patients covering more than a single disorder. To close this gap, we introduce Mephesto, a multi-centre, multi-disorder longitudinal corpus creation effort designed to develop and validate novel multi-modal **markers** for psychiatric conditions. Mephesto will consist of multi-modal audio-, video-, and physiological recordings as well as clinical assessments of psychiatric patients covering a six-week main study period as well as several follow-up recordings spread across twelve months. We outline the rationale and study protocol and introduce four cardinal use cases that will build the foundation of a new state of the art in personalized treatment strategies for psychiatric disorders.

**Accession number:** 2018394453

**Author e-mail address:** alexandra.konig@inria.fr

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**Correspondence author:** König, Alexandra Institut national de recherche en informatique et en automatique (INRIA), Stars Team, 2004 Route des Lucioles, Valbonne, 06902, France.

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**Grant:** This research is funded by the MEPHESTO project (BMBF Grant Number 01IS20075; DRI-0120105/291).

**Identifier (keyword):** Digital phenotyping, Physiological sensors, Psychiatry, Social interaction, **Speech** analysis, Video analysis

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**Language of abstract:** English

**Number of references:** 95

**Publication date:** Jul 1, 2022

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**Subject:** Embase;accelerometer;wearable sensor;Article;artificial intelligence;audio recording;Beck Depression Inventory;behavior;bipolar disorder -- diagnosis;body temperature;Brief Negative Symptoms Scale +;Childhood Trauma Questionnaire;clinical assessment;clinical protocol;data analysis;differential diagnosis;digital phenotyping + (major);digital technology (major);ecological momentary assessment;electrodermal response;follow up;heart rate variability;human;information processing;longitudinal study;major depression -- diagnosis;mental disease -- disease management (major);mental patient;Montgomery Asberg Depression Rating Scale;negative syndrome;observational study;phenotype (major);Positive and Negative Syndrome Scale;prediction;prospective study;psychiatric diagnosis;psychotrauma -- diagnosis;quality of life;relapse;schizophrenia;schizophrenia assessment;self report;social interaction (major);social synchronization;speech analysis;therapeutic alliance;thought disorder;trail making test;treatment outcome;videoconferencing;videorecording;WHOQOL-100;Young Mania Rating Scale

**Updates:** 2022-06-032022-07-12

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Document 78

## **Exploring Longitudinal Cough, Breath, and Voice Data for COVID-19 Progression Prediction via Sequential Deep Learning: Model Development and Validation**

**Author:** Dang, Ting 1 ; Han, Jing 1 ; Xia, Tong 1 ; Spathis, Dimitris 1 ; Bondareva, Erika 1 ; Siegele-Brown, Chloë 1 ; Chauhan, Jagmohan 2 ; Grammenos, Andreas 1 ; Hasthanasombat, Apinan 1 ; Floto, R Andres 1 ; Cicuta, Pietro 1 ; Mascolo, Cecilia 1

1 Department of Computer Science and Technology, University of Cambridge, Cambridge, United Kingdom, United Kingdom 2 Department of Computer Science and Technology, University of Cambridge, Cambridge, United Kingdom, Electronics and Computer Science, University of Southampton, Southampton, United Kingdom, United Kingdom

**Publication info:** Journal of medical Internet research 24.6: e37004. (Jun 21, 2022)

## **Abstract (summary): BACKGROUND**

Recent work has shown the potential of using audio data (eg, cough, breathing, and **voice**) in the screening for COVID-19. However, these approaches only focus on one-off detection and detect the infection, given the current audio sample, but do not monitor disease progression in COVID-19. Limited exploration has been put forward to continuously monitor COVID-19 progression, especially recovery, through longitudinal audio data. Tracking disease progression characteristics and patterns of recovery could bring insights and lead to more timely treatment or treatment adjustment, as well as better resource management in health care systems.

## **OBJECTIVE**

The primary objective of this study is to explore the potential of longitudinal audio samples over time for COVID-19 progression prediction and, especially, recovery trend prediction using sequential **deep learning** techniques.

## **METHODS**

Crowdsourced respiratory audio data, including breathing, cough, and **voice** samples, from 212 individuals over 5-385 days were analyzed, alongside their self-reported COVID-19 test results. We developed and validated a **deep learning**-enabled tracking tool using gated recurrent units (GRUs) to detect COVID-19 progression by exploring the audio dynamics of the individuals' historical audio **biomarkers**. The investigation comprised 2 parts: (1) COVID-19 detection in terms of positive and negative (healthy) tests using sequential audio signals, which was primarily assessed in terms of the area under the receiver operating characteristic curve (AUROC), sensitivity, and specificity, with 95% CIs, and (2) longitudinal disease progression prediction over time in terms of probability of positive tests, which was evaluated using the correlation between the predicted probability trajectory and self-reported labels.

## **RESULTS**

We first explored the benefits of capturing longitudinal dynamics of audio **biomarkers** for COVID-19 detection. The strong performance, yielding an AUROC of 0.79, a sensitivity of 0.75, and a specificity of 0.71 supported the effectiveness of the approach compared to methods that do not leverage longitudinal dynamics. We further examined the predicted disease progression trajectory, which displayed high consistency with longitudinal test results with a correlation of 0.75 in the test cohort and 0.86 in a subset of the test cohort with 12 (57.1%) of 21 COVID-19-positive participants who

reported disease recovery. Our findings suggest that monitoring COVID-19 evolution via longitudinal audio data has potential in the tracking of individuals' disease progression and recovery.

## CONCLUSIONS

An audio-based COVID-19 progression monitoring system was developed using **deep learning** techniques, with strong performance showing high consistency between the predicted trajectory and the test results over time, especially for recovery trend predictions. This has good potential in the postpeak and postpandemic era that can help guide medical treatment and optimize hospital resource allocations. The changes in longitudinal audio samples, referred to as audio dynamics, are associated with COVID-19 progression; thus, modeling the audio dynamics can potentially capture the underlying disease progression process and further aid COVID-19 progression prediction. This framework provides a flexible, affordable, and timely tool for COVID-19 tracking, and more importantly, it also provides a proof of concept of how telemonitoring could be applicable to respiratory diseases monitoring, in general.

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**Copyright:** ©Ting Dang, Jing Han, Tong Xia, Dimitris Spathis, Erika Bondareva, Chloë Siegele-Brown, Jagmohan Chauhan, Andreas Grammenos, Apinan Hasthanasombat, R Andres Floto, Pietro Cicuta, Cecilia Mascolo. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 21.06.2022.

**Correspondence author:** Dang, Ting Department of Computer Science and Technology, University of Cambridge, Cambridge, United Kingdom.

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**Identifier (keyword):** COVID-19, COVID-19 progression, audio, **deep learning**, longitudinal study, mobile health

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** COVID-19 (major);Cough -- diagnosis;Deep Learning (major);Disease Progression;Humans;Voice (major)

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**Publisher location:** CANADA

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Document 79

## **Motor Signatures in Digitized Cognitive and Memory Tests Enhances Characterization of Parkinson's Disease**

**Author:** Ryu, Jihye 1 ; Torres, Elizabeth B. 2

1 Department of Psychology, Rutgers University, NB, NJ 08854, United States 2 Rutgers University Center for Cognitive Science, Computational Biomedicine Imaging and Modeling Center at Computer Science Department, Psychology Department, Rutgers University, Piscataway, NJ 08854, United States

**Publication info:** Sensors (Basel, Switzerland) 22.12 NLM (Medline). (Jun 11, 2022)

**Abstract (summary):** Although interest in using wearable sensors to characterize movement disorders is growing, there is a lack of methodology for developing clinically interpretable **biomarkers**. Such **digital biomarkers** would provide a more objective diagnosis, capturing finer degrees of motor deficits, while retaining the information of traditional clinical tests. We aim at digitizing traditional tests of cognitive and memory performance to derive motor biometrics of pen-strokes and **voice**, thereby complementing clinical tests with objective criteria, while enhancing the overall characterization of Parkinson's disease (PD). 35 participants including patients with PD, healthy young and age-matched controls performed a series of drawing and memory tasks, while their pen movement and **voice** were digitized. We examined the moment-to-moment variability of time series reflecting the pen speed and **voice** amplitude. The stochastic signatures of the fluctuations in pen drawing speed and **voice** amplitude of patients with PD show a higher signal-to-noise ratio compared to those of neurotypical controls. It appears that contact motions of the pen strokes on a tablet evoke sensory feedback for more immediate and predictable control in PD, while **voice** amplitude loses its neurotypical richness. We offer new standardized data types and analytics to discover the hidden motor aspects within the cognitive and memory clinical assays.



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**Identifier (keyword):** biometrics, digitalbiomarkers, micro-movement spikes, Parkinson's disease, stochastic analysis

**Language:** English

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**Publication date:** Jun 11, 2022

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**Publisher:** NLM (Medline)

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**Subject:** MEDLINE;biological marker;cerebrovascular accident (major);cognition;human;movement (physiology);Parkinson disease -- diagnosis (major)

**Updates:** 2022-06-302022-07-01

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Document 80

### **Subtle Sounds: Component Sound Capture, Extraction and Analysis from Patient Encounters for Enhanced Diagnostics**

**Author:** Elliott, Jordan M. 1 ; Landin, Jesus 2 ; Mohammed, Will 2 ; Thomas, Tamillia 3 ; Summerville, Jacob 3 ; Slepian, Marvin J. 1

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**Publication info:** ASAIO Journal, suppl. Supplement 2 68 : 140. Lippincott Williams and Wilkins. (Jun 2022)

**Abstract (summary):** Purpose: Patient examination during a healthcare encounter involves recognition and processing of multiple sensory inputs by the healthcare provider. Beyond symptom verbal description, stethoscope-based chest examination may reveal abnormal lung sounds, such as crackles and wheezes, or heart sounds, such as gallops or murmurs, adding diagnostic value. While these soundbased information elements aid in medical decision-making, they are often associated with a wide range of pathologies, requiring additional, expensive tests for further diagnosis definition. We developed an enhanced diagnostic system for sound-based capture and analysis to yield additional acoustic information and **biomarkers**, ultimately for improved patient care. Methods: A smart room system was developed to capture patientphysician interaction including handheld device to capture heart, lung and GI sounds for analysis. The system has an integrated analysis program allowing extraction of acoustic features including: spectral flatness, zero crossing rate and spectral centroid. Initial testing was conducted on sound capture, quality, and feature analysis. Results: A smart room configuration was successfully designed allowing sound capture. A prototype handheld device was fabricated, as well as development of a server for data collection and analysis. The system is currently able to record chest and lung sounds via the digital stethoscope, as well as patient **speech**. Work is ongoing on an acoustic feature extraction and **biomarker** generation analysis. Enhanced sound capture and analysis offers significant potential to elevate clinical diagnostics of complex diseases manifesting acoustic elements as components of their pathophysiology. (Figure Presented).

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**Conference country:** United States

**Conference end date:** 2022-06-11

**Conference location:** Chicago, IL

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**Conference title:** 67th Annual Conference of the American Society for Artificial Internal Organs, ASAIO 2022

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Elliott, Jordan M. Biomedical Engineering, University of Arizona, Tucson, AZ, United States.

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**Language of abstract:** English

**Publication date:** Jun 2022

**Publication type:** Journal

**Publisher:** Lippincott Williams and Wilkins

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**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;abnormal respiratory sound (major);adult;conference abstract;controlled study;diagnosis;diagnostic value;feature extraction (major);handheld device;heart;human;medical decision making;patient care;speech;stethoscope;thorax

**Updates:** 2022-09-14

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Document 81

### **Vocal markers of autism: Assessing the generalizability of machine learning models**

**Author:** Rybner, Astrid 1 ; Jessen, Emil Trenckner 1 ; Mortensen, Marie Damsgaard 1 ; Larsen, Stine Nyhus 1 ; Grossman, Ruth 2 ; Bilenberg, Niels 3 ; Cantio, Cathriona 4 ; Jepsen, Jens Richardt Møllegaard 5 ; Weed, Ethan 6 ; Simonsen, Arndis 7 ; Fusaroli, Riccardo 8

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Denmark, Linguistic Data Consortium, University of Pennsylvania, Philadelphia, Pennsylvania, USA, USA

**Publication info:** Autism research : official journal of the International Society for Autism Research 15.6: 1018-1030. (Jun 2022)

**Abstract (summary):** Machine learning (ML) approaches show increasing promise in their ability to identify vocal markers of autism. Nonetheless, it is unclear to what extent such markers generalize to new speech samples collected, for example, using a different speech task or in a different language. In this paper, we systematically assess the generalizability of ML findings across a variety of contexts. We train promising published ML models of vocal markers of autism on novel cross-linguistic datasets following a rigorous pipeline to minimize overfitting, including cross-validated training and ensemble models. We test the generalizability of the models by testing them on (i) different participants from the same study, performing the same task; (ii) the same participants, performing a different (but similar) task; (iii) a different study with participants speaking a different language, performing the same type of task. While model performance is similar to previously published findings when trained and tested on data from the same study (out-of-sample performance), there is considerable variance between studies. Crucially, the models do not generalize well to different, though similar, tasks and not at all to new languages. The ML pipeline is openly shared. Generalizability of ML models of vocal markers of autism is an issue. We outline three recommendations for strategies researchers could take to be more explicit about generalizability and improve it in future studies. LAY SUMMARY: Machine learning approaches promise to be able to identify autism from voice only. These models underestimate how diverse the contexts in which we speak are, how diverse the languages used are and how diverse autistic voices are. Machine learning approaches need to be more careful in defining their limits and generalizability.

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**Copyright:** © 2022 International Society for Autism Research and Wiley Periodicals LLC.

**Correspondence author:** Rybner, Astrid Linguistics, Cognitive Science and Semiotics, School of Communication and Culture, Aarhus University, Aarhus, Denmark.

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**Identifier (keyword):** autism spectrum disorder, biobehavioral markers, generalizability, machine learning, voice

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Autism Spectrum Disorder (major);Autistic Disorder (major) -- diagnosis;Biomarkers;Humans;Machine Learning;Speech;Voice (major)

**Notes:** Indexing method: Automated;; Publication model: Print-Electronic;; Cited medium:Internet

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**Publisher location:** UNITED STATES

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**Substance:** Substance Substance: Biomarkers; CAS: 0;

**Updates:** 2022-04-062022-06-022022-06-032022-07-11

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Document 82

### **Clinical Feasibility of Speech Phenotyping for Remote Assessment of Neurodegenerative and Psychiatric Disorders (RHAPSODY): a study protocol**

**Author:** Taylor, R. 1 ; Hampsey, E. 1 ; Mészáros, M. 2 ; Skirrow, C. 2 ; Strawbridge, R. 1 ; Chok, L. 2 ; Aarsland, D. 1 ; Al-Chalabi, A. 1 ; Chaudhuri, K.R. 3 ; Weston, J. 2 ; Fristed, E. 2 ; Young, A. 1 ; Awogbemila, O. 4

1 King's College London, Institute of Psychiatry, Psychology, and Neuroscience, London, United Kingdom 2 Novoic Limited, London, United Kingdom 3 King's College London, Institute of Psychiatry, Psychology, and Neuroscience, London, United Kingdom, Kings College Hospital and Kings College, Parkinson Foundation International Centre of Excellence, London, United Kingdom 4 Kings College Hospital and Kings College, Parkinson Foundation International Centre of Excellence, London, United Kingdom

**Publication info:** European Psychiatry, suppl. Supplement 1 65 : S163. Cambridge University Press. (Jun 2022)

**Abstract (summary):** Introduction: The diagnosis of neurodegenerative and psychiatric disorders (NPDs) in primary care can suffer from inefficiencies resulting in misdiagnoses and delayed diagnosis, limiting effective treatment options. The development of speech and language-based profiling biomarkers could aid in achieving earlier motor diagnosis for PD for instance, or more accurate diagnosis of clinically similar or late presenting NPDs. Objectives: RHAPSODY aims to

investigate the feasibility of the remote administration of a battery of **speech** tasks in eliciting continuous narrative **speech** across a range of NPDs. The project also aims to determine the feasibility of using acoustic and linguistic **biomarkers** from **speech** data to support the clinical assessment and disambiguation of common NPDs. Methods: All participants (n=250) will take part in a single virtual telemedicine video conference with a researcher in which they are screened and complete a battery of **speech** tasks, in addition to cohort-specific screening measures. Over the following month, participants will be asked to complete a series of short, self-administered **speech** assessments via a smartphone application. Results: The **speech** tasks will be audio-recorded and analysed on Novoic's technology platform. Objectives will be analysed using measures including average length of **speech** elicitation for **speech** tasks, intra- and inter-subject variance, differences in linguistic patterns, and response rates to **speech** assessments. Conclusions: The analyses could help to identify and validate **speech**-derived clinical **biomarkers** to support clinicians in detecting and disambiguating between NPDs with heterogeneous presentations. This should further support earlier intervention, improved treatment options and improved quality of life.

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**Conference end date:** 2022-06-07

**Conference location:** Virtual

**Conference start date:** 2022-06-04

**Conference title:** 30th th European Congress of Psychiatry, EPA 2022

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**Correspondence author:** Taylor, R. King's College London, Institute of Psychiatry, Psychology, and Neuroscience, London, United Kingdom.

**Database:** Embase®; 1947 to date (1947 - current)

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**DOI:** <http://dx.doi.org/10.1192/j.eurpsy.2022.435>

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**Identifier (keyword):** affective disorders, **Artificial intelligence**, Neurodegenerative Disorders, **Speech**

**Language:** English

**Language of abstract:** English

**Publication date:** Jun 2022

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**Subject:** Embase;biological marker;adult;artificial intelligence (major);clinical assessment;cohort analysis;conference abstract;controlled study;degenerative disease (major);diagnosis;feasibility study (major);female;human;major clinical study;male;mental disease (major);mood disorder (major);phenotype (major);quality of life;smartphone;speech (major);speech test;telemedicine;videoconferencing

**Updates:** 2022-12-08

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Document 83

## **Voice Biomarkers of Recovery From Acute Respiratory Illness**

**Author:** Tracey, Brian 1 ; Patel, Shyamal 2 ; Zhang, Yao 3 ; Chappie, Kara 3 ; Volfson, Dmitri 4 ; Parisi, Federico 5 ; Adans-Dester, Catherine 5 ; Bertacchi, Francesco 5 ; Bonato, Paolo 5 ; Wacnik, Paul 3

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**Publication info:** IEEE Journal of Biomedical and Health Informatics 26.6: 2787-2795. Institute of Electrical and Electronics Engineers Inc. (Jun 1, 2022)

**Abstract (summary):** Voice analysis is an emerging technology which has the potential to provide low-cost, at-home monitoring of symptoms associated with a variety of health conditions. While voice has received significant attention for monitoring neurological disease, few studies have focused on voice changes related to flu-like symptoms. Herein, we investigate the relationship between changes in acoustic features of voice and self-reported symptoms during recovery from a flu-like illness in a cohort of 29 subjects. Acoustic features were automatically extracted from 'sick' and 'well' visit data collected in the laboratory setting, and feature down-selection was used to identify those that change significantly between visits. The selected acoustic features were extracted from at-home data and used to construct a combined distance metric that correlated with self-reported symptoms (0.63 rank correlation). Changes in self-reported symptoms corresponding to 10% of the ordinal scale used in the study were detected with an area under the curve of 0.72. The results show that acoustic features

derived from **voice** recordings may provide an objective measure for diagnosing and monitoring symptoms of respiratory illnesses.

**Accession number:** 2016203782

**Author e-mail address:** brian.tracey@takeda.com, shyamal.patel@gmail.com, yao.zhang@pfizer.com, kara.chappie@pfizer.com, dmitri.volfson@takeda.com, fparisi@partners.org, cadans-destier@partners.org, fbertacchi@g.harvard.edu, pbonato@ieee.org, paul.wacnik@pfizer.com

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Tracey, Brian Signal Insights Llc, Arlington, MA, 02474, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1109/JBHI.2021.3137050>

**Embase document status:** Embase; MEDLINE

**First available:** 2022-01-06

**Identifier (keyword):** biomedical acoustics, Biomedical signal processing, **speech** analysis, wearable sensors

**Language:** English

**Language of abstract:** English

**Number of references:** 30

**Publication date:** Jun 1, 2022

**Publication type:** Journal

**Publisher:** Institute of Electrical and Electronics Engineers Inc.

**Publisher location:** United States

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**Subject:** Embase;MEDLINE;**biological marker** -- endogenous compound (major);motion analysis system;wearable sensor;acoustics (major);algorithm;area under the curve;Article;disease severity;dyspnea;entropy;**feature extraction** (major);flu like syndrome;heart rate variability;human;influenza;lung congestion;mathematical model;neurologic disease;nose obstruction;phenotype;psychometry;remission;respiratory tract disease (major);rhinorrhea;signal processing;sneezing;sore throat;spectroscopy;stimulus;time series analysis;**voice analysis** (major)

**Updates:** 2022-01-062022-01-202022-04-142022-06-142022-06-17



## **WATCH-PD: Detecting Early-Stage PD Status using Feature Engineering and Machine Learning in Remote Sensor-Based Assessments**

**Author:** Anderson, D. 1 ; Merickel, M. 1 ; Severson, B. 1 ; Amato, D. 1 ; Kangaroo, T. 2 ; Edgerton, J. 3 ; Dorsey, R. 4 ; Adams, J.L. 4 ; Jezewski, S. 1 ; Keil, A. 1 ; Johnson, S. 1 ; Kantartjis, M. 1 ; Polyak, S. 1 ; Severson, J. 1 ; Cosman, J. 5

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**Publication info:** Movement Disorders, suppl. Supplement 1 37 : S3. John Wiley and Sons Inc. (Jun 2022)

**Abstract (summary):** Objective: To use feature engineering and machine learning to evaluate digital biomarkers of early-stage Parkinson's disease (PD) in the WATCH-PD study. Background: WATCH-PD - a one-year longitudinal device study - aims to relate remotely monitored sensor-based assessments to clinician-rated earlystage PD. Here, we used a combination of feature engineering and machine learning to evaluate the sensitivity of these digital endpoints to detect earlystage PD status. Methods: 17 study sites enrolled PD (n=82) and healthy control (HC; n=50) participants in a one-year longitudinal study. Brain Baseline assessments of cognition, psychomotor performance, speech, and mobility were administered both on-site and at home throughout the study. Continuous data were collected actively and passively on study provisioned Apple iPhones and Watches. Feature engineering routines estimated distributional properties of time- and frequency-dependent features derived from signal processing routines performed on continuous voice and accelerometry data sources. Machine learning algorithms were performed iteratively using Monte Carlo simulation (n=100). Each iteration randomly sorted features into independent training (90% of participants) and test sets. Feature selection was performed using linear regression to identify the most group-selective features. Logistic regression models of PD status were trained on independent features. Accuracy, sensitivity, and specificity were calculated from model predictions in the test set. Results: At the time of analysis, participants completed 551 and 1,642 clinic and home sessions, respectively. Feature engineering yielded 3,622 features, 39.5% of which were selective for PD status. Features consistently selected across each Monte Carlo simulation (n=52) were associated with tremor-related activity during postural stability and at standing rest, wrist-to-trunk movement synchronization and tremor-related activity during active walking, and finger tapping efficiency. Model predictions yielded 85% accuracy, 83% sensitivity, and 86% specificity. Conclusions: Remotely monitored sensor-based WATCH-PD assessments produced digital endpoints that predicted early-stage PD status with good accuracy, sensitivity, and specificity. Digital endpoints of primary interest were associated with tremor-

and gait-related metrics. Further work is necessary to determine how well these digital endpoints track PD severity and progression.

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**Conference country:** United States

**Conference end date:** 2022-06-05

**Conference location:** Phoenix, AZ

**Conference start date:** 2022-06-02

**Conference title:** PSG 34th Annual Symposium on Etiology, Pathogenesis, and Treatment of Parkinson's Disease and Other Movement Disorders

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**Correspondence author:** Anderson, D. Clinical Ink, Horsham, PA, United States.

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**Date created:** 2022-07-16

**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1002/mds.29002>

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**First available:** 2022-07-19

**Language:** English

**Language of abstract:** English

**Publication date:** Jun 2022

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc.

**Publisher location:** Netherlands

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**Subject:** Embase;accelerometry;adult;algorithm (major);apple;brain;cognition assessment;conference abstract;controlled study;disease assessment;feature selection;female;finger;gait;human;linear regression analysis;longitudinal study;machine learning (major);major clinical study;male;Monte Carlo method;nonhuman;Parkinson disease;prediction;psychomotor performance;sensitivity and specificity;sensor (major);signal processing;speech;tremor;trunk;voice;walking;wrist

**Updates:** 2022-07-19

## **Vocal markers of autism: Assessing the generalizability of machine learning models**

**Author:** Rybner, Astrid 1 ; Jessen, Emil Trenckner 1 ; Mortensen, Marie Damsgaard 1 ; Larsen, Stine Nyhus 1 ; Grossman, Ruth 2 ; Bilenberg, Niels 3 ; Cantio, Cathriona 4 ; Jepsen, Jens Richardt Møllegaard 5 ; Weed, Ethan 6 ; Simonsen, Arndis 7 ; Fusaroli, Riccardo 8

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**Publication info:** Autism Research 15.6: 1018-1030. John Wiley and Sons Inc. (Jun 2022)

**Abstract (summary):** Machine learning (ML) approaches show increasing promise in their ability to identify vocal markers of autism. Nonetheless, it is unclear to what extent such markers generalize to new speech samples collected, for example, using a different speech task or in a different language. In this paper, we systematically assess the generalizability of ML findings across a variety of contexts. We train promising published ML models of vocal markers of autism on novel cross-linguistic datasets following a rigorous pipeline to minimize overfitting, including cross-validated training and ensemble models. We test the generalizability of the models by testing them on (i) different participants from the same study, performing the same task; (ii) the same participants, performing a different (but similar) task; (iii) a different study with participants speaking a different language, performing the same type of task. While model performance is similar to previously published findings when trained and tested on data from the same study (out-of-sample performance), there is considerable variance between studies. Crucially, the models do not generalize well to different, though similar, tasks and not at all to new languages. The ML pipeline is openly shared. Generalizability of ML models of vocal markers of autism is an issue. We outline three recommendations for strategies researchers could take to be more explicit about generalizability and improve it in future studies. Lay Summary: Machine learning approaches promise to be able to identify autism from voice only. These models underestimate how diverse the contexts in which we speak are, how diverse the languages used are and how diverse

autistic voices are. **Machine learning** approaches need to be more careful in defining their limits and generalizability.

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**Author e-mail address:** fusaroli@gmail.com

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**Correspondence author:** Fusaroli, Riccardo Linguistics, Cognitive Science and Semiotics, School of Communication and Culture, Aarhus University, Aarhus, Denmark.

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**Identifier (keyword):** autism spectrum disorder, biobehavioral **markers**, generalizability, **machine learning**, **voice**

**Language:** English

**Language of abstract:** English

**Number of references:** 63

**Publication date:** Jun 2022

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc

**Publisher location:** United States

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**Subject:** Embase;MEDLINE;adolescent;Article;autism (major);child;controlled study;cross validation;female;human;language ability;language processing;language test;machine learning;major clinical study;male;publication;school child;scientist;vocalization (major);voice analysis

**Updates:** 2022-04-112022-06-062022-06-13

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Document 86

## **Measuring neuropsychiatric symptoms in early dementia patients using speech analysis**

**Author:** König, A. 1 ; Mallick, E. 2 ; Linz, N. 2 ; Zegahri, R. 3 ; Manera, V. 3 ; Robert, P. 3

1 Institut National de Recherche En Informatique Et En Automatique (INRIA), Stars Team, Nice, France 2 KI:Elements, UG, Saarbrücken, Germany 3 FRIS-University Côte d'azur, Cobtek (Cognitionbehaviour-Technology) Lab, Nice, France

**Publication info:** European Psychiatry, suppl. Supplement 1 65 : S174. Cambridge University Press. (Jun 2022)

**Abstract (summary):** Introduction: Certain neuropsychiatric symptoms (NPS), namely apathy, depression and anxiety demonstrated great value in predicting dementia progression representing eventually an opportunity window for timely diagnosis and treatment. However, sensitive and objective markers of these symptoms are still missing. Objectives: To investigate the association between automatically extracted speech features and NPS in early-stage dementia patients. Methods: Speech of 141 patients aged 65 or older with neurocognitive disorder was recorded while performing two short narrative speech tasks. Presence of NPS was assessed by the Neuropsychiatric Inventory. Paralinguistic markers relating to prosodic, formant, source, and temporal qualities of speech were automatically extracted, correlated with NPS. Machine learning experiments were carried out to validate the diagnostic power of extracted markers. Results: Different speech variables seem to be associated with specific neuropsychiatric symptoms of dementia; apathy correlates with temporal aspects, anxiety with voice quality and this was mostly consistent between male and female after correction for cognitive impairment. Machine learning regressors are able to extract information from speech features and perform above baseline in predicting anxiety, apathy and depression scores. Conclusions: Different NPS seem to be characterized by distinct speech features which in turn were easily extractable automatically from short vocal tasks. These findings support the use of speech analysis for detecting subtypes of NPS. This could have great implications for future clinical trials.

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**Conference end date:** 2022-06-07

**Conference location:** Virtual

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**Conference title:** 30th th European Congress of Psychiatry, EPA 2022

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**Correspondence author:** König, A. Institut National de Recherche En Informatique Et En Automatique (INRIA), Stars Team, Nice, France.

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**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1192/j.eurpsy.2022.461>

**Embase document status:** Embase

**First available:** 2022-12-08

**Identifier (keyword):** apathy, Depression, Neuropsychiatric symptoms, **speech** analysis

**Language:** English

**Language of abstract:** English

**Publication date:** Jun 2022

**Publication type:** Journal

**Publisher:** Cambridge University Press

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;adult;anxiety;apathy (major);cognitive defect;conference abstract;controlled study;dementia (major);depression (major);disorders of higher cerebral function;female;human;**machine learning** (major);major clinical study;male;mental disease (major);narrative;neuropsychiatric inventory;paralanguage;**speech**;**speech analysis** (major);speech test;**voice**

**Updates:** 2022-12-08

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Document 87

## **DIGITAL BIOMARKERS FOR PREDICTING PTSD, DEPRESSION, AND BURNOUT IN EMERGENCY DEPARTMENT CLINICIANS**

**Author:** Schultebrucks, Katharina 1 ; Chang, Bernard 1

1 Department of Emergency Medicine, Columbia University, New York, NY, United States

**Publication info:** Psychosomatic Medicine 84.5: A84. Lippincott Williams and Wilkins. (Jun 2022)

**Abstract (summary):** Background: The importance to protect emergency department (ED) clinicians' mental health has been dramatically reinforced in the COVID-19 pandemic leading to a high prevalence of Posttraumatic Stress Disorder (PTSD) and other stress-associated adverse mental health effects in ED clinicians. This study proposes an innovative approach using digital phenotyping to develop Digital Biomarkers as predictors of stress pathologies. Furthermore, we determine how candidate digital biomarkers relate to physiological markers of chronic stress. Methods: We used computer vision and voice analysis to extract facial, voice, speech, and movement characteristics from an unstructured clinical interview. Previously, we tested the approach to identify digital biomarkers in a cohort of trauma survivors to discriminate PTSD. Here, we adapted the approach to test its potential to develop digital biomarkers as predictors of stress pathologies in ED clinicians. Results: Video- and audio-based markers were able to accurately discriminate PTSD (AUC=0.90) and depression status (AUC=0.86) in trauma survivors. Building on these results, we will present pilot findings from an ongoing longitudinal study of COVID-19 frontline workers. Conclusion: Digital biomarkers identified in direct clinical observation during free speech may be used to classify stress pathologies in ED clinicians. Digital biomarkers could improve the scalability and sensitivity of clinical assessments using low burden, passive evaluations of well-being, which is critical among this high-risk population.

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**Conference country:** United States

**Conference end date:** 2022-03-26

**Conference location:** Long Beach, CA

**Conference start date:** 2022-03-23

**Conference title:** 79th Annual Scientific Meeting Achieving Health Equity: Opportunities for Psychosomatic Science

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**Correspondence author:** Schultebrucks, Katharina Department of Emergency Medicine, Columbia University, New York, NY, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-08-25

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**Document type:** Conference Abstract

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**First available:** 2022-08-25

**Language:** English

**Language of abstract:** English

**Publication date:** Jun 2022

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**Publisher:** Lippincott Williams and Wilkins

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker (major);adult;burnout (major);chronic stress;clinical assessment;clinical observation;computer vision;conference abstract;controlled study;coronavirus disease 2019;depression (major);emergency ward (major);face;female;frontline staff;high risk population;human;interview;longitudinal study;male;phenotype;posttraumatic stress disorder (major);risk assessment;speech;survivor;videorecording;vision;voice;voice analysis;wellbeing

**Updates:** 2022-08-25

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Document 88

## **Using digital health tools for the Remote Assessment of Treatment Prognosis in Depression (RAPID): A study protocol for a feasibility study**

**Author:** De Angel, Valeria 1 ; Lewis, Serena 2 ; Munir, Sara 3 ; Matcham, Faith 4 ; Dobson, Richard 5 ; Hotopf, Matthew 1

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**Publication info:** BMJ Open 12.5 BMJ Publishing Group. (May 6, 2022)

**Abstract (summary):** Introduction Digital health tools such as smartphones and wearable devices could improve psychological treatment outcomes in depression through more accurate and comprehensive measures of patient behaviour. However, in this emerging field, most studies are



small and based on student populations outside of a clinical setting. The current study aims to determine the feasibility and acceptability of using smartphones and wearable devices to collect behavioural and clinical data in people undergoing therapy for depressive disorders and establish the extent to which they can be potentially useful **biomarkers** of depression and recovery after treatment. **Methods and analysis** This is an observational, prospective cohort study of 65 people attending psychological therapy for depression in multiple London-based sites. It will collect continuous passive data from smartphone sensors and a Fitbit fitness tracker, and deliver questionnaires, **speech** tasks and cognitive assessments through smartphone-based apps. Objective data on sleep, physical activity, location, Bluetooth contact, smartphone use and heart rate will be gathered for 7 months, and compared with clinical and contextual data. A mixed methods design, including a qualitative interview of patient experiences, will be used to evaluate key feasibility indicators, **digital** phenotypes of depression and therapy prognosis. Patient and public involvement was sought for participant-facing documents and the study design of the current research proposal. **Ethics and dissemination** Ethical approval has been obtained from the London Westminster Research Ethics Committee, and the Health Research Authority, Integrated Research Application System (project ID: 270918). Privacy and confidentiality will be guaranteed and the procedures for handling, processing, storage and destruction of the data will comply with the General Data Protection Regulation. Findings from this study will form part of a doctoral thesis, will be presented at national and international meetings or academic conferences and will generate manuscripts to be submitted to peer-reviewed journals.

**Accession number:** 638076974

**Author e-mail address:** valeria.de\_angel@kcl.ac.uk

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**Correspondence author:** De Angel, Valeria Department Of Psychological Medicine, Institute Of Psychiatry, Psychology And Neuroscience, King's College London, London, United Kingdom.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-06-12

**Device company:** Device company Device trade name: Undefined; Manufacturer: Fitbit;

**Device trade name:** Device trade name Name: Android; Manufacturer: Undefined;

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**Document type:** Article

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Centre at South London and Maudsley NHS Foundation Trust and King's College London, UK; (2) Health Data Research UK, which is funded by the UK Medical Research Council, Engineering and Physical Sciences Research Council, Economic and Social Research Council, Department of Health and Social Care (England), Chief Scientist Office of the Scottish Government Health and Social Care Directorates, Health and Social Care Research and Development Division (Welsh Government), Public Health Agency (Northern Ireland), British Heart Foundation and Wellcome Trust; (3) The BigData@Heart consortium, funded by the Innovative Medicines Initiative-2 Joint Undertaking under grant agreement number 116074. This joint undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA; it is chaired by DE Grobbee and SD Anker, partnering with 20 academic and industry partners and ESC; (4) the National Institute for Health Research (NIHR) University College London Hospitals Biomedical Research Centre; (5) the NIHR Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London; (6) the UK Research and Innovation London Medical Imaging and Artificial Intelligence Centre for Value Based Healthcare; (7) the NIHR Applied Research Collaboration South London (NIHR ARC South London) at King's College Hospital NHS Foundation Trust.

**Identifier (keyword):** Anxiety disorders, Depression, Health informatics, Mental health, Mood disorders

**Language:** English

**Language of abstract:** English

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**Publication date:** May 6, 2022

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**Publisher:** BMJ Publishing Group

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**Subject:** Embase;MEDLINE;biological marker;activity tracker;Android +;computer;mobile health application;smartphone (major);wearable sensor (major);adult;Article;clinical study;clinical trial;clinical trial protocol;cognition assessment;cohort analysis;depression -- therapy (major);digital technology (major);experience;feasibility study;heart rate;human;interview;major clinical study;observational study;patient participation;physical activity;prognosis;prospective study;psychotherapy (major);qualitative research;sleep;speech test;study design

**Updates:** 2022-06-072022-06-13

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Document 89

## **Towards sound based testing of COVID-19-Summary of the first Diagnostics of COVID-19 using Acoustics (DiCOVA) Challenge**

**Author:** Sharma, Neeraj Kumar 1 ; Muguli, Ananya 1 ; Krishnan, Prashant 1 ; Kumar, Rohit 1 ; Chetupalli, Srikanth Raj 1 ; Ganapathy, Sriram 1

1 Learning and Extraction of Acoustic Patterns (LEAP) Lab, Electrical Engineering, Indian Institute of Science, Bangalore, India, India

**Publication info:** Computer speech & language 73 : 101320. (May 2022)

**Abstract (summary):** The technology development for point-of-care tests (POCTs) targeting respiratory diseases has witnessed a growing demand in the recent past. Investigating the presence of acoustic **biomarkers** in modalities such as cough, breathing and **speech** sounds, and using them for building POCTs can offer fast, contactless and inexpensive testing. In view of this, over the past year, we launched the "Coswara" project to collect cough, breathing and **speech** sound recordings via worldwide crowdsourcing. With this data, a call for development of diagnostic tools was announced in the Interspeech 2021 as a special session titled "Diagnostics of COVID-19 using Acoustics (DiCOVA) Challenge". The goal was to bring together researchers and practitioners interested in developing acoustics-based COVID-19 POCTs by enabling them to work on the same set of development and test datasets. As part of the challenge, datasets with breathing, cough, and **speech** sound samples from COVID-19 and non-COVID-19 individuals were released to the participants. The challenge consisted of two tracks. The Track-1 focused only on cough sounds, and participants competed in a leaderboard setting. In Track-2, breathing and **speech** samples were provided for the participants, without a competitive leaderboard. The challenge attracted 85 plus registrations with 29 final submissions for Track-1. This paper describes the challenge (datasets, tasks, baseline system), and presents a focused summary of the various systems submitted by the participating teams. An analysis of the results from the top four teams showed that a fusion of the scores from these teams yields an area-under-the-receiver operating curve (AUC-ROC) of 95.1% on the blind test data. By summarizing the lessons learned, we foresee the challenge overview in this paper to help accelerate technological development of acoustic-based POCTs.

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**Correspondence author:** Sharma, Neeraj Kumar Learning and Extraction of Acoustic Patterns (LEAP) Lab, Electrical Engineering, Indian Institute of Science, Bangalore, India.

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**Date created:** 2021-11-29

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**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1016/j.csl.2021.101320>

**First available:** 2021-11-29

**Identifier (keyword):** Acoustics, COVID-19, Healthcare, Machine learning, Respiratory diagnosis

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Document 90

## **Parkinson's Disease Detection Based on Running Speech Data from Phone Calls**

**Author:** Laganas, Christos 1 ; Iakovakis, Dimitrios 1 ; Hadjidimitriou, Stelios 1 ; Charisis, Vasileios 1 ; Dias, Sofia B. 2 ; Bostantzopoulou, Sevasti 3 ; Katsarou, Zoe 4 ; Klingelhofer, Lisa 5 ; Reichmann, Heinz 5 ; Trivedi, Dhaval 6 ; Chaudhuri, K. Ray 6 ; Hadjileontiadis, Leontios J. 7

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**Publication info:** IEEE Transactions on Biomedical Engineering 69.5: 1573-1584. IEEE Computer Society. (May 1, 2022)

**Abstract (summary):** Objective: Parkinson's Disease (PD) is a progressive neurodegenerative disorder, manifesting with subtle early signs, which, often hinder timely and early diagnosis and treatment. The development of accessible, technology-based methods for longitudinal PD symptoms tracking in daily living, offers the potential for transforming disease assessment and accelerating diagnosis. Methods: A privacy-aware method for classifying patients and healthy controls (HC), on the grounds of speech impairment present in PD, is proposed. Voice features from running speech signals were extracted from passively-captured recordings over voice calls. Language-aware training of multiple- and single-instance learning classifiers was employed to fuse and predict on voice features and demographic data from a multilingual cohort of 498 subjects (392/106 self-reported HC/PD patients). Results: By means of leave-one-subject-out cross-validation, the bestperforming models yielded 0.69/0.68/0.63/0.83 area under the Receiver Operating Characteristic curve (AUC) for the binary classification of PD patient vs. HC in sub-cohorts of English/Greek/German/Portuguese-speaking subjects, respectively. Out-of sample testing of the best performing models was conducted in an additional dataset, generated by 63 clinically-assessed subjects (24/39 HC/early PD patients). Testing has resulted in 0.84/0.93/0.83 AUC for the English/Greek/German-speaking sub-cohorts, respectively. Conclusions: The proposed approach outperforms other methods proposed for language-aware PD detection considering the ecological validity of the voice data. Significance: This paper introduces for the first time a highfrequency, privacy-aware and unobtrusive PD screening tool based on analysis of voice samples captured during routine phone calls.

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**Identifier (keyword):** digital **biomarkers**, **machine learning**, Parkinson's disease, **speech** processing, **voice** impairment

**Language:** English

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**Number of references:** 59

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**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;**biological marker** (major);microphone;mobile application;smartphone;adult;Article;**binary classification**;clinical article;cohort analysis;controlled study;**cross validation**;English (language);**feature extraction**;German (language);Greek (language);human;**machine learning** (major);multilingualism;Parkinson disease -- diagnosis (major);Portuguese (language);self report;signal processing (major);**speech** (major);**speech analysis** (major);**speech disorder**;voice analysis

**Updates:** 2021-10-142021-10-252022-05-052023-01-27

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Document 91

## **Noninvasive **Voice Biomarker** Is Associated With Incident Coronary Artery Disease Events at Follow-up**

**Author:** Sara, Jaskanwal Deep Singh 1 ; Maor, Elad 2 ; Orbelo, Diana 3 ; Gulati, Rajiv 1 ; Lerman, Lliach O. 4 ; Lerman, Amir 1

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**Publication info:** Mayo Clinic Proceedings 97.5: 835-846. Elsevier Ltd. (May 2022)

**Abstract (summary):** Objective: To evaluate the association between a preidentified **voice biomarker** and incident coronary artery disease (CAD) events. Methods: Patients referred for clinically indicated coronary angiography underwent a total of three 30-second **voice** recordings using the **Vocalis** Health smartphone application between January 1, 2015, and February 28, 2017. A pre-established **voice biomarker** was derived from each individual recording, and the mean **biomarker** value was calculated for each patient. Individuals were clinically observed through December 31,

2019. The prespecified primary outcome was a composite of presenting to the emergency department with chest pain, being admitted to the hospital with chest pain, or having an acute coronary syndrome; the prespecified secondary outcome was a composite of a positive stress test result at follow-up or the presence of CAD at follow-up coronary angiography. Results: In the final analysis, 108 patients were included (mean age, 59.47±11.44 years; male, 59 [54.6%]). The median follow-up time was 24 months (range, 1 to 60 months). In multivariable Cox proportional hazards models adjusting for CAD grade on baseline angiography, a high baseline mean **voice biomarker** was significantly associated with both the primary (hazard ratio, 2.61; 95% CI, 1.42 to 4.80; P=.002) and secondary (hazard ratio, 3.13; 95% CI, 1.13 to 8.68; P=.03) composite outcomes. Conclusion: This study found a significant association between a noninvasive **voice biomarker** and incident CAD events at follow-up. These results may have important clinical implications for the remote and noninvasive screening of patients to identify those at risk of coronary disease and its complications.

**Accession number:** 2017891188

**Author e-mail address:** lerman.amir@mayo.edu

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Lerman, Amir Department of Cardiovascular Medicine, Mayo Clinic College of Medicine, 200 First St SW, MN, Rochester, 55905.

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**Number of references:** 25

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**Subject:** Embase;MEDLINE;biological marker -- endogenous compound (major);creatinine -- endogenous compound;high density lipoprotein cholesterol -- endogenous compound;low density lipoprotein cholesterol -- endogenous compound;triacylglycerol -- endogenous compound;mobile application;smartphone;acute coronary syndrome;adult;Article;audio recording;cholesterol blood level;cohort analysis;coronary angiography;coronary artery disease (major);diabetes mellitus;electrocardiography;emergency ward;event free survival;exercise test;feature extraction;female;follow up;human;hyperlipidemia;hypertension;ischemic heart disease;major clinical study;male;middle aged;non invasive procedure (major);non ST segment elevation myocardial infarction;nuclear stress test;ST segment elevation myocardial infarction;stable angina pectoris;stress echocardiography;thorax pain;unstable angina pectoris;voice

**Substance:** Substance Substance: creatinine; CAS: 19230-81-060-27-5;

**Updates:** 2022-05-102022-10-192022-10-24

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Document 92

## Deep Phenotyping in Difficult to Diagnosis Cases - A Novel Methodology

**Author:** Butala, A. 1 ; Motley, S. 1 ; Paul, A. 1 ; Moro-Velazquez, L. 1 ; Dehak, N. 1

1 , Baltimore, MD, United States

**Publication info:** Movement Disorders Clinical Practice 9.SUPPL 1: S63-S64. Wiley-Blackwell. (May 2022)

**Abstract (summary):** Objective: We present a novel, developing methodology that uses the simultaneous collection and post-processing of different biosignals to precisely characterize motor and non-motor findings in subjects with difficult to diagnose movement disorders. Background: Diagnosis requires detailed, but subjective, clinical observation. Current biomarkers fail to reliably distinguish iPD from associated conditions.1 Late diagnoses negatively impact quality of life and confer higher costs on the healthcare system.2 Methods: We hypothesize that our approach of physiological recording, signal processing and machine-learning will permit more precise and objective characterization of subdued biosignals. We capture the biosignals from participants using an eye-tracker, microphone, and digital tablet simultaneously. The bio-signals are then processed to obtain interpretable features such as reaction time after stimulus, number of saccades per task, saccade precision, speech articulatory and phonatory features, and writing vs in-air time, among others. Results: Here we analyze the results of four subjects:S-1: 59 yoW with Parkinsonism, rapidly progressive complex ataxia & dysautonomia. Biosignal recordings revealed subtle square wave jerks, vertical gaze restriction, increased saccade latency, and right-beating-nystagmus not evident on clinical exam. S-2: 34 yoM with early-onset asymmetric hemibody dystonia-parkinsonism was



recorded. While EOM signals did not reveal decrementing amplitude with saccades, **speech** recordings showed relatively subtle **dysphonia** and disarticulation. S-3: 63 yo man with Probable iPD, previously denying symptoms suggestive of atypical parkinsonism, was found to have occult square wave jerks, overshoot and impaired performance on antisaccades. Conclusion: In this report, we showed how multimodal, synchronized biosignals and **machine learning** analytic methods can elicit subtle clinical signs. S-1's biosignals lead to a diagnosis of Gerstmann-Sträussler- Scheinker syndrome (PRNP) after WES. S-2 was later diagnosed with Rapid-Onset Dystonia Parkinsonism (ATP1A3). S-3 maintains a working diagnosis of Probable iPD, though has recognized some cognitive impairment in follow-up. This is a small sample of a larger, ongoing corpus to train **AI** in distinguishing iPD and related diseases. This approach could be a portable, scalable, cost-effective, and non-invasive clinical adjunct with subspecialist level expertise.

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**Conference country:** United States

**Conference end date:** 2022-05-28

**Conference location:** Miami, FL

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**Conference title:** Pan American Parkinson's Disease and Movement Disorders Congress, PAS 2022

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**Correspondence author:** Butala, A. , Baltimore, MD, United States.

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**Subject:** Embase;biological marker;endogenous compound;prion protein;adult;analytic method;ataxia;autonomic dysfunction;clinical observation;cognitive defect;conference abstract;controlled study;diagnosis;disarticulation;dysphonia;dystonia;eye movement monitor;follow up;gaze;health care cost;health care system;human;machine learning (major);major clinical study;male;microphone;motor dysfunction;optokinetic nystagmus;parkinsonism;phenotype (major);quality of life;reaction time;saccadic eye movement;signal processing;speech;writing

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Document 93

## **Neural correlates of individual differences in predicting ambiguous sounds comprehension level**

**Author:** Lin, Yi 1 ; Tsao, Yu 2 ; Hsieh, Po-Jang 3

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**Publication info:** NeuroImage 251 Academic Press Inc. (May 1, 2022)

**Abstract (summary):** This study investigated brain activation during auditory processing as a biomarker for the prediction of future perceptual learning performance. Cochlear implant simulated sounds (vocoded sounds) are degraded signals. Participants with normal hearing who were trained with these ambiguous sounds showed varied speech comprehension levels. We discovered that the neuronal signatures from untrained participants forecasted their future ambiguous speech comprehension levels. Participants' brain activations for auditory information processing were measured before (t1) they underwent a five-day vocoded sounds training session. We showed that the pre-training (t1) activities in the inferior frontal gyrus (IFG) correlate with the fifth-day (t2) vocoded sound comprehension performance. To further predict participants' future (t2) performances, we split the participants into two groups (i.e., good and bad learners) based on their fifth-day performance; a linear support vector machine (SVM) was trained to classify (predict) the remaining participants' groups. We found that pre-training (t1) fMRI activities in the bilateral IFG, angular gyrus (AG), and supramarginal gyrus (SMG) showed discriminability between future (t2) good and bad learners. These findings suggest that neural correlates of individual differences in auditory processing can potentially be used to predict participants' future cognition and behaviors.

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**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Hsieh, Po-Jang National Taiwan University, Taiwan.

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**Identifier (keyword):** Behavioral **biomarker**, Individual differences, Vocoded **speech**

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**Subject:** Embase;MEDLINE;**biological marker** (major);nuclear magnetic resonance scanner;SIEMENS MAGNETOM Prisma +;acoustic nerve fiber;adult;angular gyrus;Article;auditory evoked potential (major);auditory nervous system;auditory perception test (major);behavior assessment;brain function (major);cognition;controlled study;correlation analysis;female;functional magnetic resonance imaging;human;human experiment;individuality (major);inferior frontal gyrus;information processing;male;normal human;**phonetics**;prediction;signal detection;**speech discrimination** (major);speech perception;**support vector machine**;supramarginal gyrus;verbal memory;working memory;young adult

**Updates:** 2022-03-012022-03-08

## Development of a novel digital speech composite measure for Frontotemporal Dementia

**Author:** Robin, Jessica; Xu, Mengdan; Kaufman, Liam; Simpson, William; McCaughey, Stella; Wolfus, Charles; Jackson, Sam; Ward, Michael

**Publication info:** Neurology 98.18 SUPPL Lippincott Williams and Wilkins. (May 2022)

**Abstract (summary):** Objective: The objective for this study was to examine longitudinal change in speech patterns in Frontotemporal Dementia (FTD) and to develop a novel composite measure for assessing speech and language abilities. Background: Current tools to assess speech and language abilities in FTD often involve specialized neuropsychological testing, which can be lengthy, costly and burdensome to patients and their caregivers. Digital tools can be used to objectively measure speech abilities remotely with lower patient burden and higher functional relevance to everyday life. Design/Methods: 36 participants with subtypes of FTD were enrolled in a remote, longitudinal study collecting digital speech assessments over 12 months. Speech samples were analyzed using Winterlight's speech analysis platform, generating >500 variables describing the acoustic and linguistic features of the speech sample. Using linear mixed models, we determined which speech variables demonstrated significant change over time and developed a novel composite score based on these variables. Results: Nine speech variables demonstrated significant change over time, controlling for effects of age, sex and stimulus. These nine selected variables were combined to create a novel speech composite score, reflecting different aspects of speech and language including the ratio of words to pauses, the types of words used, the information content and the complexity of sentences. When compared to healthy control participants, the FTD group had lower scores at baseline on the novel composite score. The composite score showed significant decline over time ( $\beta = -0.055$ ,  $p < 0.001$ ) and high test-retest reliability ( $ICC = 0.76$ ,  $p < 0.001$ ). Conclusions: This study demonstrated that digital speech assessments can be used to characterize speech and language abilities in FTD. We developed a novel composite measure sensitive to disease-related differences and progression. Future work will further validate this score using clinical standards and biomarkers, and integrate these measures into clinical trials.

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**Conference location:** Virtual

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**Conference title:** 74th Annual Meeting of the American Academy of Neurology, AAN 2022

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**Correspondence author:** Robin, Jessica

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**Publication date:** May 2022

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**Publisher:** Lippincott Williams and Wilkins

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**Subject:** Embase;biological marker;adult;caregiver;clinical article;conference abstract;controlled study;female;frontotemporal dementia (major);human;language ability;longitudinal study;male;neuropsychological test;speech (major);speech analysis;test retest reliability

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## **Speech as a Biomarker for COVID-19 Detection Using Machine Learning**

**Author:** Usman, Mohammed 1 ; Gunjan, Vinit Kumar 2 ; Wajid, Mohd 3 ; Zubair, Mohammed 1 ; Siddiquee, Kazy Noor-E-Alam 4

1 Department of Electrical Engineering, King Khalid University, Abha 61411, Saudi Arabia, Saudi Arabia 2 Department of Computer Science and Engineering, CMR Institute of Technology, Hyderabad, India, India 3 Department of Electronics Engineering, ZHCET, Aligarh Muslim University, Aligarh 202002, India, India 4 Department of Computer Science and Engineering, University of Science and Technology, Chittagong, Bangladesh, Bangladesh

**Publication info:** Computational intelligence and neuroscience 2022 : 6093613. (Apr 18, 2022)

**Abstract (summary):** The use of speech as a biomedical signal for diagnosing COVID-19 is investigated using statistical analysis of speech spectral features and classification algorithms based on machine learning. It is established that spectral features of speech, obtained by computing the

short-time Fourier Transform (STFT), get altered in a statistical sense as a result of physiological changes. These spectral features are then used as input features to machine learning-based classification algorithms to classify them as coming from a COVID-19 positive individual or not. Speech samples from healthy as well as "asymptomatic" COVID-19 positive individuals have been used in this study. It is shown that the RMS error of statistical distribution fitting is higher in the case of speech samples of COVID-19 positive speech samples as compared to the speech samples of healthy individuals. Five state-of-the-art machine learning classification algorithms have also been analyzed, and the performance evaluation metrics of these algorithms are also presented. The tuning of machine learning model parameters is done so as to minimize the misclassification of COVID-19 positive individuals as being COVID-19 negative since the cost associated with this misclassification is higher than the opposite misclassification. The best performance in terms of the "recall" metric is observed for the Decision Forest algorithm which gives a recall value of 0.7892.

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**Copyright:** Copyright © 2022 Mohammed Usman et al.

**Correspondence author:** Usman, Mohammed Department of Electrical Engineering, King Khalid University, Abha 61411, Saudi Arabia.

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Document 96

## Feasibility of a **Machine Learning**-Based Smartphone Application in Detecting Depression and Anxiety in a Generally Senior Population

**Author:** Lin, David 1 ; Nazreen, Tahmida 1 ; Rutowski, Tomasz 1 ; Lu, Yang 1 ; Harati, Amir 1 ; Shriberg, Elizabeth 1 ; Chlebek, Piotr 1 ; Aratow, Michael 1

1 Ellipsis Health, San Francisco, CA, United States, United States

**Publication info:** Frontiers in psychology 13 : 811517. (Apr 8, 2022)

### **Abstract (summary):** Background

Depression and anxiety create a large health burden and increase the risk of premature mortality. Mental health screening is vital, but more sophisticated screening and monitoring methods are needed. The Ellipsis Health App addresses this need by using semantic information from recorded **speech** to screen for depression and anxiety.

### Objectives

The primary aim of this study is to determine the feasibility of collecting weekly **voice** samples for mental health screening. Additionally, we aim to demonstrate portability and improved performance of Ellipsis' **machine learning** models for patients of various ages.

### Methods

Study participants were current patients at Desert Oasis Healthcare, mean age 63 years (SD = 10.3). Two non-randomized cohorts participated: one with a documented history of depression within 24 months prior to the study (Group Positive), and the other without depression (Group Negative). Participants recorded 5-min **voice** samples weekly for 6 weeks via the Ellipsis Health App. They also completed PHQ-8 and GAD-7 questionnaires to assess for depression and anxiety, respectively.

### Results

Protocol completion rate was 61% for both groups. Use beyond protocol was 27% for Group Positive and 9% for Group Negative. The Ellipsis Health App showed an AUC of 0.82 for the combined groups when compared to the PHQ-8 and GAD-7 with a threshold score of 10. Performance was high for

senior participants as well as younger age ranges. Additionally, many participants spoke longer than the required 5 min.

## Conclusion

The Ellipsis Health App demonstrated feasibility in using **voice** recordings to screen for depression and anxiety among various age groups and the **machine learning** models using Transformer methodology maintain performance and improve over LSTM methodology when applied to the study population.

**Accession number:** 35478769

**Copyright:** Copyright © 2022 Lin, Nazreen, Rutowski, Lu, Harati, Shriberg, Chlebek and Aratow.

**Correspondence author:** Lin, David Ellipsis Health, San Francisco, CA, United States.

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**Identifier (keyword):** NLP, **artificial intelligence**, behavioral health monitoring, **biomarkers**, **machine learning**, mental health screening, smartphone, **speech**

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

**Notes:** All authors were employed by the company Ellipsis Health Inc. The authors declare that this study received funding from Ellipsis Health Inc. Ellipsis Health Inc. had the following involvement in the study: study design, collection, analysis, interpretation of data, the writing of this article and the decision to submit it for publication.;; Publication model: Electronic-eCollection;; Cited medium:Print

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## Toward Automated Articulation Rate Analysis via Connected Speech in Dysarthrias

**Author:** Illner, Vojtěch 1 ; Tykalová, Tereza 1 ; Novotný, Michal 1 ; Klempíř, Jiří 2 ; Dušek, Petr 2 ; Ruzs, Jan 3

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**Publication info:** Journal of speech, language, and hearing research : JSLHR 65.4: 1386-1401. (Apr 4, 2022)

### Abstract (summary): PURPOSE

This study aimed to evaluate the reliability of different approaches for estimating the articulation rates in connected speech of Parkinsonian patients with different stages of neurodegeneration compared to healthy controls.

### METHOD

Monologues and reading passages were obtained from 25 patients with idiopathic rapid eye movement sleep behavior disorder (iRBD), 25 de novo patients with Parkinson's disease (PD), 20 patients with multiple system atrophy (MSA), and 20 healthy controls. The recordings were subsequently evaluated using eight syllable localization algorithms, and their performances were compared to a manual transcript used as a reference.

### RESULTS

The Google & Pyphen method, based on automatic speech recognition followed by hyphenation, outperformed the other approaches (automated vs. hand transcription:  $r > .87$  for monologues and  $r > .91$  for reading passages,  $p < .001$ ) in precise feature estimates and resilience to dysarthric speech. The Praat script algorithm achieved sufficient robustness (automated vs. hand transcription:  $r > .65$  for monologues and  $r > .78$  for reading passages,  $p < .001$ ). Compared to the control group, we detected a slow rate in patients with MSA and a tendency toward a slower rate in patients with iRBD, whereas the articulation rate was unchanged in patients with early untreated PD.

## CONCLUSIONS

The state-of-the-art **speech** recognition tool provided the most precise articulation rate estimates. If **speech** recognizer is not accessible, the freely available Praat script based on simple intensity thresholding might still provide robust properties even in severe **dysarthria**. Automated articulation rate assessment may serve as a natural, inexpensive **biomarker** for monitoring disease severity and a differential diagnosis of Parkinsonism.

**Accession number:** 35302874

**Correspondence author:** Illner, Vojtěch Department of Circuit Theory, Faculty of Electrical Engineering, Czech Technical University in Prague, Czech Republic.

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**MeSH:** Dysarthria -- diagnosis;Dysarthria -- etiology;Humans;Multiple System Atrophy (major);Parkinson Disease (major) -- complications;Parkinson Disease (major) -- diagnosis;Reproducibility of Results;**Speech**

**Notes:** Indexing method: Automated;; Publication model: Print-Electronic;; Cited medium:Internet

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Document 98

## Neurogenerative Disease Diagnosis in Cepstral Domain Using MFCC with Deep Learning

**Author:** Alghamdi, Norah Saleh 1 ; Zakariah, Mohammed 2 ; Hoang, Vinh Truong 3 ; Elahi, Mohammad Mamun 4

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**Publication info:** Computational and mathematical methods in medicine 2022 : 4364186. (Apr 4, 2022)

**Abstract (summary):** Because underlying cognitive and neuromuscular activities regulate speech signals, biomarkers in the human voice can provide insight into neurological illnesses. Multiple motor and nonmotor aspects of neurologic voice disorders arise from an underlying neurologic condition such as Parkinson's disease, multiple sclerosis, myasthenia gravis, or ALS. Voice problems can be caused by disorders that affect the corticospinal system, cerebellum, basal ganglia, and upper or lower motoneurons. According to a new study, voice pathology detection technologies can successfully aid in the assessment of voice irregularities and enable the early diagnosis of voice pathology. In this paper, we offer two deep-learning-based computational models, 1-dimensional convolutional neural network (1D CNN) and 2-dimensional convolutional neural network (2D CNN), that simultaneously detect voice pathologies caused by neurological illnesses or other causes. From the German corpus Saarbruecken Voice Database (SVD), we used voice recordings of sustained vowel /a/ generated at normal pitch. The collected voice signals are padded and segmented to maintain homogeneity and increase the number of samples. Convolutional layers are applied to raw data, and MFCC features are extracted in this project. Although the 1D CNN had the maximum accuracy of 93.11% on test data, model training produced overfitting and 2D CNN, which generalized the data better and had lower train and validation loss despite having an accuracy of 84.17% on test data. Also, 2D CNN outperforms state-of-the-art studies in the field, implying that a model trained on handcrafted features is better for speech processing than a model that extracts features directly.

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**MeSH:** Deep Learning (major);Humans;Neural Networks, Computer;Speech;Voice (major);Voice Disorders (major) -- diagnosis

**Notes:** The authors declare that there is no conflict of interest regarding the publication of this paper.;; Indexing method: Automated;; Publication model: Electronic-eCollection;; Cited medium:Internet

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**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

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Document 99

## IDENTIFICATION OF VOCAL BIOMARKERS FOR SCREENING DIABETES AND MONITORING HEALTH OF PEOPLE WITH DIABETES: PRELIMINARY RESULTS FROM THE COLIVE VOICE STUDY

**Author:** Elbeji, A. 1 ; Aguayo, G. 2 ; Fischer, A. 2 ; Fagherazzi, G. 2

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**Publication info:** Diabetes Technology and Therapeutics 24.SUPPL 1: A224. Mary Ann Liebert Inc. (Apr 2022)

**Abstract (summary):** Background and Aims: People with diabetes have distinct vocal signatures than the general population, however, few studies investigated how to use this specificity for

screening purposes. **Voice** is a rich source of information that may be used to develop digital **biomarkers** for diagnosing diseases or tracking symptoms thanks to advances in **artificial intelligence** and signal processing. Our aim is to compare audio features of people with type 1 diabetes (T1D), type 2 diabetes (T2D), and people without diabetes. Methods: Colive **Voice** (<https://www.colivevoice.org/>) is an international platform for the identification of **vocal biomarkers** for chronic diseases. Classification of the diabetes status and type was performed using linear discriminant analysis (LDA) based on audio features extracted from standardized recordings (here, three consecutive forced coughs) with the OpenSMILE library. A one-way ANOVA was used to analyze the distribution of the components obtained in the three groups. Results: We included 31 participants (5 with T1D, 6 with T2D, and 20 without diabetes). The average age of the participants was 49 years old, and 70% were female. The LDA explained 100% of the variance and identified audio features that accurately distinguished the three categories ( $p < 0.001$ ). Conclusions: These findings suggest the feasibility of screening for T1D and T2D based solely on **voice** characteristics. More volunteers are needed in Colive **Voice** to confirm these findings, but also to develop **vocal biomarkers** for monitoring symptoms including diabetes distress, hypoglycemia, and fatigue, which might be integrated into medical devices such as closed-loop insulin systems.

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**Conference end date:** 2022-04-30

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**Conference title:** 15th International Conference on Advanced Technologies and Treatments for Diabetes, ATTD 2022

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**Correspondence author:** Elbeji, A. Luxembourg Institute of Health, Department of Population Health, Luxembourg, Luxembourg.

**Database:** Embase®; 1947 to date (1947 - current)

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**Language:** English

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**Publication date:** Apr 2022

**Publication type:** Journal

**Publisher:** Mary Ann Liebert Inc.

**Publisher location:** Netherlands

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**Subject:** Embase;biological marker;insulin;adult;analysis of variance;chronic disease;clinical article;conference abstract;controlled study;coughing;diabetes mellitus;discriminant analysis;distress syndrome;fatigue;feasibility study;female;human;hypoglycemia;insulin dependent diabetes mellitus;male;medical device;middle aged;non insulin dependent diabetes mellitus;preliminary data (major);voice (major)

**Substance:** Substance Substance: insulin; CAS: 9004-10-8;

**Updates:** 2022-06-20

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Document 100

## **Utilizing Conversational Artificial Intelligence, Voice, and Phonocardiography Analytics in Heart Failure Care**

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2 Department of Cardiovascular Medicine, Mayo Clinic, Mayo Medical School, 200 Second Street, Southwest, Rochester, MN, 55901, United States

**Publication info:** Heart Failure Clinics 18.2: 311-323. Elsevier Inc. (Apr 2022)

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**First available:** 2022-03-11

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**Identifier (keyword):** Artificial intelligence, Conversational AI, Heart failure, Machine learning, Phonocardiography, Voicebiomarker, Voice technology

**Language:** English

**Number of references:** 31

**Publication date:** Apr 2022

**Publication type:** Journal

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**Subject:** Embase;MEDLINE;biological marker (major);chatbot (major);virtual assistant;artificial intelligence (major);diagnostic accuracy;electronic health record;health care delivery;heart failure (major);heart left ventricle function;home;hospital;human;human computer interaction;left ventricular systolic dysfunction;machine learning;natural language processing;phonocardiography (major);prognosis;Review;voice analysis (major)

**Updates:** 2022-03-112022-03-302022-04-012022-05-26

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Document 101

## **Deep learning-based classification of posttraumatic stress disorder and depression following trauma utilizing visual and auditory markers of arousal and mood**

**Author:** Schultebrasucks, Katharina 1 ; Yadav, Vijay 2 ; Shalev, Arie Y. 3 ; Bonanno, George A. 4 ; Galatzer-Levy, Isaac R. 5

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**Publication info:** Psychological medicine 52.5: 957-967. NLM (Medline). (Apr 1, 2022)

**Abstract (summary):** BACKGROUND: Visual and auditory signs of patient functioning have long been used for clinical diagnosis, treatment selection, and prognosis. Direct measurement and quantification of these signals can aim to improve the consistency, sensitivity, and scalability of clinical assessment. Currently, we investigate if machine learning-based computer vision (CV), semantic, and acoustic analysis can capture clinical features from free speech responses to a brief interview 1 month post-trauma that accurately classify major depressive disorder (MDD) and posttraumatic stress disorder (PTSD). METHODS: N = 81 patients admitted to an emergency department (ED) of a Level-1 Trauma Unit following a life-threatening traumatic event participated in an open-ended qualitative interview with a para-professional about their experience 1 month following admission. A deep neural network was utilized to extract facial features of emotion and their intensity, movement parameters, speech prosody, and natural language content. These features were utilized as inputs to classify PTSD and MDD cross-sectionally. RESULTS: Both video- and audio-based markers contributed to good discriminatory classification accuracy. The algorithm discriminates PTSD status at 1 month after ED admission with an AUC of 0.90 (weighted average precision = 0.83, recall = 0.84, and f1-score = 0.83) as well as depression status at 1 month after ED admission with an AUC of 0.86 (weighted average precision = 0.83, recall = 0.82, and f1-score = 0.82). CONCLUSIONS: Direct clinical observation during post-trauma free speech using deep learning identifies digital markers that can be utilized to classify MDD and PTSD status.

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**Identifier (keyword):** Computer vision, deep learning, depression, digital biomarker, emergency department, landmark feature, posttraumatic stress, resilience, voice analysis

**Language:** English

**Language of abstract:** English

**Publication date:** Apr 1, 2022

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**Subject:** MEDLINE;biological marker (major);arousal;depression;human;major depression -- diagnosis (major);posttraumatic stress disorder -- diagnosis (major);psychology

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Document 102

**Remote data collection speech analysis and prediction of the identification of Alzheimer's disease biomarkers in people at risk for Alzheimer's disease dementia: The Speech on the Phone Assessment (SPeAk) prospective observational study protocol**

**Author:** Gregory, Sarah 1 ; Linz, Nicklas 2 ; König, Alexandra 3 ; Langel, Kai 4 ; Pullen, Hannah 1 ; Luz, Saturnino 5 ; Harrison, John 6 ; Ritchie, Craig W 1

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**Publication info:** BMJ Open 12.3 BMJ Publishing Group. (Mar 15, 2022)

**Abstract (summary):** Introduction Identifying cost-effective, non-invasive biomarkers of Alzheimer's disease (AD) is a clinical and research priority. Speech data are easy to collect, and studies suggest it can identify those with AD. We do not know if speech features can predict AD biomarkers in a preclinical population. Methods and analysis The Speech on the Phone Assessment (SPeAk) study is a prospective observational study. SPeAk recruits participants aged 50 years and over who have previously completed studies with AD biomarker collection. Participants complete a baseline telephone assessment, including spontaneous speech and cognitive tests. A 3-month visit will repeat the cognitive tests with a conversational artificial intelligence bot. Participants complete acceptability questionnaires after each visit. Participants are randomised to receive their cognitive test results either after each visit or only after they have completed the study. We will combine SPeAk data with AD biomarker data collected in a previous study and analyse for correlations between extracted speech features and AD biomarkers. The outcome of this analysis will inform the development of an algorithm for prediction of AD risk based on speech features. Ethics and dissemination This study has been approved by the Edinburgh Medical School Research Ethics Committee (REC reference 20-EMREC-007). All participants will provide informed consent before completing any study-related

procedures, participants must have capacity to consent to participate in this study. Participants may find the tests, or receiving their scores, causes anxiety or stress. Previous exposure to similar tests may make this more familiar and reduce this anxiety. The study information will include signposting in case of distress. Study results will be disseminated to study participants, presented at conferences and published in a peer reviewed journal. No study participants will be identifiable in the study results.

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**Author e-mail address:** Sarah.Gregory@ed.ac.uk

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**Correspondence author:** Gregory, Sarah Edinburgh Dementia Prevention, Centre for Clinical Brain Sciences, The University of Edinburgh Centre for Clinical Brain Sciences, Edinburgh, United Kingdom.

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**Identifier (keyword):** delirium &cognitive disorders, dementia, old age psychiatry

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**Publication date:** Mar 15, 2022

**Publication type:** Journal

**Publisher:** BMJ Publishing Group

**Publisher location:** United Kingdom

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**Subject:** Embase;MEDLINE;biological marker (major);adult;Alzheimer disease (major);Article;artificial intelligence (major);cognition assessment;data analysis;data correlation;dementia (major);disease marker;disease risk assessment (major);follow up;human;information processing;informed

consent;observational study;program acceptability;prospective study;questionnaire;rescreening;Rey auditory verbal learning test;sample size;sociodemographics;sound analysis;speech analysis (major);task performance;telemedicine (major);test retest reliability;verbal communication;Wechsler adult intelligence scale

**Updates:** 2022-03-292022-04-05

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Document 103

## **Cascaded Deep Learning Frameworks in Contribution to the Detection of Parkinson's Disease**

**Author:** Chintalapudi, Nalini 1 ; Battineni, Gopi 1 ; Hossain, Mohmmad Amran 1 ; Amenta, Francesco 1

1 Centre of Clinical Research, School of Medicinal and Health Products Sciences, University of Camerino, 62032 Camerino, Italy, Italy

**Publication info:** Bioengineering (Basel, Switzerland) 9.3 (Mar 12, 2022)

**Abstract (summary):** Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor impairment, as well as tremors, stiffness, and rigidity. Besides the typical motor symptomatology, some Parkinsonians experience non-motor symptoms such as hyposmia, constipation, urinary dysfunction, orthostatic hypotension, memory loss, depression, pain, and sleep disturbances. The correct diagnosis of PD cannot be easy since there is no standard objective approach to it. After the incorporation of machine learning (ML) algorithms in medical diagnoses, the accuracy of disease predictions has improved. In this work, we have used three deep-learning-type cascaded neural network models based on the audial voice features of PD patients, called Recurrent Neural Networks (RNN), Multilayer Perception (MLP), and Long Short-Term Memory (LSTM), to estimate the accuracy of PD diagnosis. A performance comparison between the three models was performed on a sample of the subjects' voice biomarkers. Experimental outcomes suggested that the LSTM model outperforms others with 99% accuracy. This study has also presented loss function curves on the relevance of good-fitting models to the detection of neurodegenerative diseases such as PD.

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**Correspondence author:** Chintalapudi, Nalini Centre of Clinical Research, School of Medicinal and Health Products Sciences, University of Camerino, 62032 Camerino, Italy.

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**Document type:** Journal Article

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**Identifier (keyword):** Parkinson's disease, deep learning, early detection, model fitting, neural networks

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Document 104

## **NON-INVASIVE VOICE BIOMARKER IS ASSOCIATED WITH INCIDENT CORONARY ARTERY DISEASE EVENTS AT FOLLOW-UP**

**Author:** Sara, Jaskanwal Deep Singh 1 ; Maor, Elad 1 ; Gulati, Rajiv 1 ; Lerman, Lilach O. 1 ; Lerman, Amir 1

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**Publication info:** Journal of the American College of Cardiology, suppl. Supplement 79.9: 2023. Elsevier Inc. (Mar 8, 2022)

**Abstract (summary):** Background: We evaluate the association between a voice biomarker and coronary artery disease (CAD) events at follow-up. Methods: Patients referred for coronary angiography underwent 3 voice recordings using Vocalis Health's smartphone application between January 1 2015 and February 28 2017. A prespecified voice biomarker was derived using Artificial Intelligence from each recording, and the mean biomarker value was calculated for each patient. The prespecified primary outcome was a composite of presenting with or being hospitalized for chest pain or having an acute coronary syndrome, and the prespecified secondary outcome was a composite of a positive stress test and/or the presence of CAD at follow-up angiography. Results:

One hundred and eight patients were included (mean age: 59.47 ± 11.44 years, males: 54.6%, median follow-up: 24 months). Patients were divided into those with a high (T3) versus low (T1-T2) mean **voice biomarker** value. Patients with a high **voice biomarker** had a higher frequency of the primary composite end-point (21 (58.3%) vs. 22 (30.6%), p=0.0056; Figure). In multivariable Cox proportional hazards models a high mean **voice biomarker** was associated with the primary and secondary outcomes (HR 2.611, 95% CI 1.421 - 4.798, p=0.002; and HR 3.132, 95% CI 1.130 - 8.679, p=0.028). Conclusion: We demonstrate an association between a **voice biomarker** and CAD events at follow-up, suggesting a potential role for **voice** analysis in the remote screening of patients at risk of CAD and its complications. [Formula presented]

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**Subject:** Embase;**biological marker** (major);acute coronary syndrome;adult;**artificial intelligence**;complication;conference abstract;controlled study;coronary angiography;coronary artery disease (major);follow up (major);human;major clinical study;male;middle aged;outcome assessment;physiological stress;smartphone;thorax pain;**voice** (major);**voice analysis**

**Updates:** 2022-03-26

## Applications of artificial intelligence to aid early detection of dementia: A scoping review on current capabilities and future directions

**Author:** Li, Renjie 1 ; Wang, Xinyi 2 ; Lawler, Katherine 3 ; Garg, Saurabh 1 ; Bai, Quan 1 ; Alty, Jane 3

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**Publication info:** Journal of Biomedical Informatics 127 Academic Press Inc. (Mar 2022)

**Abstract (summary):** Background & Objective: With populations aging, the number of people with dementia worldwide is expected to triple to 152 million by 2050. Seventy percent of cases are due to Alzheimer's disease (AD) pathology and there is a 10–20 year 'pre-clinical' period before significant cognitive decline occurs. We urgently need, cost effective, objective biomarkers to detect AD, and other dementias, at an early stage. Risk factor modification could prevent 40% of cases and drug trials would have greater chances of success if participants are recruited at an earlier stage. Currently, detection of dementia is largely by pen and paper cognitive tests but these are time consuming and insensitive to the pre-clinical phase. Specialist brain scans and body fluid biomarkers can detect the earliest stages of dementia but are too invasive or expensive for widespread use. With the advancement of technology, Artificial Intelligence (AI) shows promising results in assisting with detection of early-stage dementia. This scoping review aims to summarise the current capabilities of AI-aided digital biomarkers to aid in early detection of dementia, and also discusses potential future research directions. Methods & Materials: In this scoping review, we used PubMed and IEEE Xplore to identify relevant papers. The resulting records were further filtered to retrieve articles published within five years and written in English. Duplicates were removed, titles and abstracts were screened and full texts were reviewed. Results: After an initial yield of 1,463 records, 1,444 records were screened after removal of duplication. A further 771 records were excluded after screening titles and abstracts, and 496 were excluded after full text review. The final yield was 177 studies. Records were grouped into different artificial intelligence based tests: (a) computerized cognitive tests (b) movement tests (c) speech, conversion, and language tests and (d) computer-assisted interpretation of brain scans. Conclusions: In general, AI techniques enhance the performance of dementia screening tests because more features can be retrieved from a single test, there are less errors due to subjective judgements and AI shifts the automation of dementia screening to a higher level. Compared with traditional cognitive tests, AI-based computerized cognitive tests improve the discrimination sensitivity

by around 4% and specificity by around 3%. In terms of **speech**, conversation and language tests, combining both acoustic features and linguistic features achieve the best result with accuracy around 94%. **Deep learning** techniques applied in brain scan analysis achieves around 92% accuracy. Movement tests and setting smart environments to capture daily life behaviours are two potential future directions that may help discriminate dementia from normal aging. **AI**-based smart environments and multi-modal tests are promising future directions to improve detection of dementia in the earliest stages.

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**Correspondence author:** Li, Renjie School of Information and Communication Technology, University of Tasmania, TAS, 7005, Australia.

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**Grant:** This work was supported by the J.O. and J.R. Wicking Trust (Equity Trustees), the University of Tasmania and the National Health and Medical Research Council (grant 2004051).

**Identifier (keyword):** Alzheimer's, **Artificial Intelligence**, Dementia, Digital **biomarkers**, Pre-clinical, Screening tests

**Language:** English

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**Number of references:** 254

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**Subject:** Embase;MEDLINE;biological marker (major);Addenbrooke cognitive examination revised;Alzheimer disease -- diagnosis;artificial intelligence (major);behavior assessment;brain scintiscanning;clock drawing test;cognition assessment;computer analysis;computerized cognitive test +;conversation;daily life activity;data analysis;dementia -- diagnosis (major);diagnostic accuracy;early diagnosis (major);human;Mini Mental State Examination;Montreal cognitive assessment;movement test +;psychoacoustics;psycholinguistics;Review;screening test;sensitivity and specificity;speech and language assessment

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Document 106

## **VoiceLens: A multi-view multi-class disease classification model through daily-life speech data**

**Author:** Bhattacharjee, Soumyadeep 1 ; Xu, Wenyao 2

1 Gifted Math Program, State University of New York at Buffalo, United States, Williamsville East High School, East Amherst, NY, United States sbhattac@buffalo.edu 2 The State University of New York at Buffalo, NY, United States wenyaoxu@buffalo.edu

**Publication info:** Smart Health 23 Elsevier B.V. (Mar 2022)

**Abstract (summary):** Biomarkers in the human voice can offer insight into neurological disorders because voice signals are influenced by the underlying cognitive and neuromuscular functions. In the past decade, there is an increasing research attention on voice-based neural disorder detection using machine learning techniques. However, existing works only attempt to detect a single neurological disorder (e.g., Parkinson's or Huntington's). In this work, we present the first computational model, namely VoiceLens, that detects multiple neurological disorders at the same time. The proposed VoiceLens framework combines the effectiveness of the powerful Mel-Frequency-Cepstral-Coefficients (MFCC) within a two-phase multi-class classification module to build an accurate voice-based disease prediction model. The first phase captures the fine-grained details of these disorders and their sequential variation patterns within a stacked Long-Short-Term-Memory (LSTM) network to make the baseline disease detection, i.e., healthy v.s. pathology. In the second phase, the detected pathology samples are further analyzed by a deep multi-layer learned descriptor to identify the disease types. The VoiceLens method is developed and evaluated using a large-scale Saarbruecken-Voice-Database comprising of samples from 2000 individuals with multiple disease patterns, including Laryngeal Cancers, Dish-Syndrome, and Parkinson's disease. Experimental results show the remarkable performance of VoiceLens by reporting Accuracy up to 97.5% in the disease detection, where the model also obtains 98.00% and 97.13% for F1-Score and Recall. Also, compared with existing machine learning models, the proposed VoiceLens system demonstrates around 15% (and 12%) average gain in the Accuracy (and F1-score) in a multi-disease identification test including six (6) different pathology classes and one (1) healthy class.



**Accession number:** 2015914102

**Author e-mail address:** sbhattac@buffalo.edu, wenyaoxu@buffalo.edu

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**Correspondence author:** Bhattacharjee, Soumyadeep Gifted Math Program, State University of New York at Buffalo, United States.

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**Device trade name:** Device trade name Name: Python 3.7; Manufacturer: Undefined;

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**Identifier (keyword):** Audio analysis, Disease prediction, Health care analytics, Multi-class classification, **Speech** processing

**Language:** English

**Language of abstract:** English

**Number of references:** 58

**Publication date:** Mar 2022

**Publication type:** Journal

**Publisher:** Elsevier B.V.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;chatbot;information processing device;personal computer;Python 3.7 +;voice amplification device;adult;Article;**Bayesian learning**;computer model (major);computer prediction;controlled study;decision tree;**deep learning**;**deep neural network**;disease classification (major);female;human;larynx cancer;**long short term memory network**;**machine learning** (major);major clinical study;male;**multiclass classification**;Parkinson disease;**random forest**;software;sound analysis;**speech**;**support vector machine**;voice disorder

Document 107

## Voice in Parkinson's Disease: A Machine Learning Study

**Author:** Suppa, Antonio 1 ; Costantini, Giovanni 2 ; Asci, Francesco 3 ; Di Leo, Pietro 2 ; Al-Wardat, Mohammad Sami 4 ; Di Lazzaro, Giulia 5 ; Scalise, Simona 6 ; Pisani, Antonio 7 ; Saggio, Giovanni 2

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**Publication info:** Frontiers in Neurology 13 Frontiers Media S.A. (Feb 15, 2022)

**Abstract (summary):** Introduction: Parkinson's disease (PD) is characterized by specific voice disorders collectively termed hypokinetic dysarthria. We here investigated voice changes by using machine learning algorithms, in a large cohort of patients with PD in different stages of the disease, OFF and ON therapy. Methods: We investigated 115 patients affected by PD (mean age:  $68.2 \pm 9.2$  years) and 108 age-matched healthy subjects (mean age:  $60.2 \pm 11.0$  years). The PD cohort included 57 early-stage patients (Hoehn & Yahr  $\leq 2$ ) who never took L-Dopa for their disease at the time of the study, and 58 mid-advanced-stage patients (Hoehn & Yahr  $>2$ ) who were chronically-treated with L-Dopa. We clinically evaluated voices using specific subitems of the Unified Parkinson's Disease Rating Scale and the Voice Handicap Index. Voice samples recorded through a high-definition audio recorder underwent machine learning analysis based on the support vector machine classifier. We also calculated the receiver operating characteristic curves to examine the diagnostic accuracy of the analysis and assessed possible clinical-instrumental correlations. Results: Voice is abnormal in early-stage PD and as the disease progresses, voice increasingly degrades as demonstrated by high accuracy in the discrimination between healthy subjects and PD patients in the early-stage and mid-advanced-stage. Also, L-dopa therapy improves but not restore voice in PD as shown by high accuracy in the comparison between patients OFF and ON therapy. Finally, for the first time we achieved significant clinical-instrumental correlations by using a new score (LR value) calculated by machine learning. Conclusion: Voice is abnormal in early-stage PD, progressively degrades in mid-advanced-stage and can be improved but not restored by L-Dopa. Lastly, machine learning allows tracking disease severity and quantifying the symptomatic effect of L-Dopa on voice parameters with previously unreported high accuracy, thus representing a potential new biomarker of PD.

**Accession number:** 637377789

**Author e-mail address:** saggio@uniroma2.it

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Saggio, Giovanni Department of Electronic Engineering, University of Rome Tor Vergata, Rome, Italy.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-03-21

**Device trade name:** Device trade name Name: H4n Zoom; Manufacturer: Undefined;

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.3389/fneur.2022.831428>

**Embase document status:** Embase

**First available:** 2022-03-09

**Identifier (keyword):** hypokinetic **dysarthria**, L-Dopa, **machine learning**, Parkinson's disease, **voice analysis**

**Language:** English

**Language of abstract:** English

**Number of references:** 45

**Publication date:** Feb 15, 2022

**Publication type:** Journal

**Publisher:** Frontiers Media S.A.

**Publisher location:** Switzerland

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;levodopa -- drug therapy -- Parkinson disease;levodopa -- drug therapy -- **voice disorder**;levodopa -- special situation for pharmacovigilance -- aged;H4n Zoom +;tape recorder;adult;aged;Article;chronic drug administration;**classifier**;clinical assessment tool;cohort analysis;controlled study;correlation analysis;diagnostic accuracy;diagnostic test accuracy study;disease course;disease severity;**dysarthria**;Hoehn and Yahr scale;human;**machine learning**;major clinical study;middle aged;Parkinson disease -- diagnosis (major);Parkinson disease -- drug therapy -- levodopa (major);receiver operating characteristic;scoring system;**support vector machine**;Unified Parkinson Disease Rating Scale;very elderly;**voice analysis**;**voice disorder** -- diagnosis (major);**voice disorder** -- drug therapy -- levodopa (major);Voice Handicap Index +

**Substance:** Substance Substance: levodopa; CAS: 59-92-7;

**Updates:** 2022-03-092022-03-25

## **Evaluating the Feasibility and Acceptability of an Artificial-Intelligence-Enabled and Speech-Based Distress Screening Mobile App for Adolescents and Young Adults Diagnosed with Cancer: A Study Protocol**

**Author:** Zhang, Anao 1 ; Kamat, Aarti 2 ; Acquati, Chiara 3 ; Aratow, Michael 4 ; Kim, Johnny S 5 ; DuVall, Adam S 6 ; Walling, Emily 2

1 School of Social Work, University of Michigan, Ann Arbor, MI 48109, USA, Adolescent and Young Adult Oncology Program, University of Michigan Health, Ann Arbor, MI 48109, USA, USA 2 Adolescent and Young Adult Oncology Program, University of Michigan Health, Ann Arbor, MI 48109, USA, Department of Pediatrics, University of Michigan Health, Ann Arbor, MI 48109, USA, USA 3 Graduate College of Social Work, University of Houston, Houston, TX 77204, USA, Department of Health Disparities Research, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA, USA 4 Ellipsis Health, San Francisco, CA 94102, USA, USA 5 Graduate School of Social Work, University of Denver, Denver, CO 80208, USA, USA 6 Department of Medicine, University of Chicago, Chicago, IL 60637, USA, USA

**Publication info:** Cancers 14.4 (Feb 12, 2022)

**Abstract (summary):** Adolescents and young adults (AYAs) diagnosed with cancer are an age-defined population, with studies reporting up to 45% of the population experiencing psychological distress. Although it is essential to screen and monitor for psychological distress throughout AYAs' cancer journeys, many cancer centers fail to effectively implement distress screening protocols largely due to busy clinical workflow and survey fatigue. Recent advances in mobile technology and speech science have enabled flexible and engaging methods to monitor psychological distress. However, patient-centered research focusing on these methods' feasibility and acceptability remains lacking. Therefore, in this project, we aim to evaluate the feasibility and acceptability of an artificial intelligence (AI)-enabled and speech-based mobile application to monitor psychological distress among AYAs diagnosed with cancer. We use a single-arm prospective cohort design with a stratified sampling strategy. We aim to recruit 60 AYAs diagnosed with cancer and to monitor their psychological distress using an AI-enabled speech-based distress monitoring tool over a 6 month period. The primary feasibility endpoint of this study is defined by the number of participants completing four out of six monthly distress assessments, and the acceptability endpoint is defined both quantitatively using the acceptability of intervention measure and qualitatively using semi-structured interviews.

**Accession number:** 35205663

**Correspondence author:** Zhang, Anao School of Social Work, University of Michigan, Ann Arbor, MI 48109, USA. , Adolescent and Young Adult Oncology Program, University of Michigan Health, Ann Arbor, MI 48109, USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2022-02-25

**Date revised:** 2022-03-01

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.3390/cancers14040914>

**First available:** 2022-02-25

**Identifier (keyword):** acceptability, adolescent and young adult cancer, artificial intelligence, distress, feasibility, vocalbiomarkers, voice analysis

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Electronic;; Cited medium:Print

**Publication date:** Feb 12, 2022

**Publication type:** Journal

**Publisher location:** SWITZERLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2022-02-252022-02-282022-03-01

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Document 109

## **Digital Phenotyping in Clinical Neurology**

**Author:** Gupta, Anoopum S. 1

1 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States agupta@mgh.harvard.edu

**Publication info:** Seminars in Neurology 42.1: 48-59. Thieme Medical Publishers, Inc. (Feb 1, 2022)

**Abstract (summary):** Internet-connected devices, including personal computers, smartphones, smartwatches, and voice assistants, have evolved into powerful multisensor technologies that billions

of people interact with daily to connect with friends and colleagues, access and share information, purchase goods, play games, and navigate their environment. **Digital** phenotyping taps into the data streams captured by these devices to characterize and understand health and disease. The purpose of this article is to summarize opportunities for **digital** phenotyping in neurology, review studies using everyday technologies to obtain motor and cognitive information, and provide a perspective on how neurologists can embrace and accelerate progress in this emerging field.

**Accession number:** 636994001

**Author e-mail address:** agupta@mgh.harvard.edu

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Gupta, Anoopum S. , 100 Cambridge Street, Boston, MA, 02114, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-11-16

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1055/s-0041-1741495>

**Embase document status:** Embase; MEDLINE

**First available:** 2022-01-26

**Identifier (keyword):** **biomarkers**, **digital** phenotyping, outcome measures, quantitative phenotyping

**Language:** English

**Language of abstract:** English

**Number of references:** 168

**Publication date:** Feb 1, 2022

**Publication type:** Journal

**Publisher:** Thieme Medical Publishers, Inc.

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;**biological marker** (major);personal computer;smart watch;smartphone;arm movement;Article;behavior;body equilibrium;clinical research;cognition;**digital technology** (major);eye movement;gait;gaze;human;Internet;motor performance;neurologist;neurology (major);nonhuman;phenotype (major);speech and language

**Updates:** 2022-01-262022-01-312022-05-272022-11-16

## **COVID-19 detection in cough, breath and speech using deep transfer learning and bottleneck features**

**Author:** Pahar, Madhurananda 1 ; Klopper, Marisa 2 ; Warren, Robin 2 ; Niesler, Thomas 1

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**Publication info:** Computers in Biology and Medicine 141 Elsevier Ltd. (Feb 2022)

**Abstract (summary):** We present an experimental investigation into the effectiveness of transfer learning and bottleneck feature extraction in detecting COVID-19 from audio recordings of cough, breath and speech. This type of screening is non-contact, does not require specialist medical expertise or laboratory facilities and can be deployed on inexpensive consumer hardware such as a smartphone. We use datasets that contain cough, sneeze, speech and other noises, but do not contain COVID-19 labels, to pre-train three deep neural networks: a CNN, an LSTM and a Resnet50. These pre-trained networks are subsequently either fine-tuned using smaller datasets of coughing with COVID-19 labels in the process of transfer learning, or are used as bottleneck feature extractors. Results show that a Resnet50 classifier trained by this transfer learning process delivers optimal or near-optimal performance across all datasets achieving areas under the receiver operating characteristic (ROC AUC) of 0.98, 0.94 and 0.92 respectively for all three sound classes: coughs, breaths and speech. This indicates that coughs carry the strongest COVID-19 signature, followed by breath and speech. Our results also show that applying transfer learning and extracting bottleneck features using the larger datasets without COVID-19 labels led not only to improved performance, but also to a marked reduction in the standard deviation of the classifier AUCs measured over the outer folds during nested cross-validation, indicating better generalisation. We conclude that deep transfer learning and bottleneck feature extraction can improve COVID-19 cough, breath and speech audio classification, yielding automatic COVID-19 detection with a better and more consistent overall performance.

**Accession number:** 2016043546

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**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

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**Document status:** Revised

**Document type:** Article

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RCD. Division of Research Capacity Development.

SAMRC. South African Medical Research Council.

SAMRC. South African Medical Research Council.

EMC.

National Treasury.

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**Identifier (keyword):** Bottleneck features, Breath, Cough, COVID-19, Speech, Transfer learning

**Language:** English

**Language of abstract:** English

**Number of references:** 47

**Publication date:** Feb 2022

**Publication type:** Journal

**Publisher:** Elsevier Ltd

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**Subject:** Embase;MEDLINE;Article;audio recording (major);breathing (major);classifier;controlled study;coronavirus disease 2019 -- diagnosis (major);coughing (major);cross validation;deep neural network;detection algorithm;diagnostic test accuracy study;feature extraction;feature selection;human;k fold cross validation;nested cross validation;pandemic;sneezing;speech (major);support vector machine;transfer of learning (major);tuberculosis

**Updates:** 2022-01-132022-01-212022-04-06

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Document 111

## **Voice characteristics from isolated rapid eye movement sleep behavior disorder to early Parkinson's disease**

**Author:** Jeancolas, Laetitia 1 ; Mangone, Graziella 2 ; Petrovska-Delacrétaz, Dijana 3 ; Benali, Habib 4 ; Benkelfat, Badr-Eddine 3 ; Arnulf, Isabelle 5 ; Corvol, Jean-Christophe 2 ; Vidailhet, Marie 2 ; Lehéricy, Stéphane 6

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**Publication info:** Parkinsonism & related disorders 95 : 86-91. (Feb 2022)

### **Abstract (summary): BACKGROUND**

Speech disorders are amongst the first symptoms to appear in Parkinson's disease (PD).

## **OBJECTIVES**

We aimed to characterize PD voice signature from the prodromal stage (isolated rapid eye movement sleep behavior disorder, iRBD) to early PD using an automated acoustic analysis and compare male and female patients. We carried out supervised learning classifications to automatically detect patients using voice only.

## METHODS

**Speech** samples were acquired in 256 French speakers (117 participants with early PD, 41 with iRBD, and 98 healthy controls), with a professional quality microphone, a computer microphone and their own telephone. High-level features related to prosody, **phonation**, **speech** fluency and rhythm abilities were extracted. Group analyses were performed to determine the most discriminant features, as well as the impact of sex, **vocal** tasks, and microphone type. These **speech** features were used as inputs of a **support vector machine** and were combined with classifiers using low-level features.

## RESULTS

PD related impairments were found in prosody, pause durations and rhythmic abilities, from the prodromal stage. These alterations were more pronounced in men than in women. Early PD detection was achieved with a balanced accuracy of 89% in males and 70% in females. Participants with iRBD were detected with a balanced accuracy of 63% (reaching 70% in the subgroup with mild motor symptoms).

## CONCLUSION

This study provides new insight in the characterization of sex-dependent early PD **speech** impairments, and demonstrates the valuable benefit of including automated **voice** analysis in future diagnostic procedures of prodromal PD.

**Accession number:** 35063866

**Author e-mail address:** laetitia.jeancolas@icm-institute.org

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**Correspondence author:** Jeancolas, Laetitia Paris Brain Institute - ICM, Centre de NeuroImagerie de Recherche - CENIR, Paris, France; Laboratoire SAMOVAR, Télécom SudParis, Institut Polytechnique de Paris, France.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2022-04-29

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**Document type:** Journal Article, Research Support, Non-U.S. Gov't

**DOI:** <http://dx.doi.org/10.1016/j.parkreldis.2022.01.003>

**First available:** 2022-01-22

**Identifier (keyword):** Acoustic analysis, Parkinson's disease, REM sleep behavior disorder, **Speech disorders**, Supervised classification

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Female;Humans;Male;Parkinson Disease (major) -- complications;Parkinson Disease (major) -- diagnosis;Prodromal Symptoms;REM Sleep Behavior Disorder (major) -- diagnosis;REM Sleep Behavior Disorder (major) -- etiology;**Speech Disorders**;Voice (major)

**Notes:** Indexing method: Automated;; Publication model: Print-Electronic;; Cited medium:Internet

**Publication date:** Feb 2022

**Publication type:** Journal

**Publisher location:** ENGLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2022-01-222022-01-242022-01-252022-01-312022-02-012022-03-222022-04-282022-04-29

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Document 112

## **AI-Based human audio processing for COVID-19: A comprehensive overview**

**Author:** Deshpande, Gauri 1 ; Batliner, Anton 2 ; Schuller, Björn W 3

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**Publication info:** Pattern recognition 122 : 108289. (Feb 2022)

**Abstract (summary):** The Coronavirus (COVID-19) pandemic impelled several research efforts, from collecting COVID-19 patients' data to screening them for virus detection. Some COVID-19 symptoms are related to the functioning of the respiratory system that influences **speech** production; this suggests research on identifying **markers** of COVID-19 in **speech** and other human generated audio signals. In this article, we give an overview of research on human audio signals using '**Artificial Intelligence**' techniques to screen, diagnose, monitor, and spread the awareness about COVID-19. This overview will be useful for developing automated systems that can help in the context of COVID-19, using non-obtrusive and easy to use bio-signals conveyed in human non-**speech** and **speech** audio productions.

**Accession number:** 34483372

**Copyright:** © 2021 Elsevier Ltd. All rights reserved.

**Correspondence author:** Deshpande, Gauri Chair of Embedded Intelligence for Health Care and Wellbeing, University of Augsburg, Germany. , TCS Research Pune, India.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2021-09-06

**Date revised:** 2022-12-15

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1016/j.patcog.2021.108289>

**First available:** 2021-09-06

**Identifier (keyword):** Audio processing, COVID-19, Computational paralinguistics, Digital health

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.;; Publication model: Print-Electronic;; Cited medium:Print

**Publication date:** Feb 2022

**Publication type:** Journal

**Publisher location:** ENGLAND

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Document 113

## **Facial and **Vocal** Markers of Schizophrenia Measured Using Remote Smartphone Assessments: Observational Study**

**Author:** Abbas, Anzar 1 ; Hansen, Bryan J 2 ; Koesmahargyo, Vidya 1 ; Yadav, Vijay 1 ; Rosenfield, Paul J 3 ; Patil, Omkar 2 ; Dockendorf, Marissa F 2 ; Moyer, Matthew 2 ; Shipley, Lisa A 2 ; Perez-Rodriguez, M Mercedes 3 ; Galatzer-Levy, Isaac R 4

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**Publication info:** JMIR formative research 6.1: e26276. (Jan 21, 2022)

## **Abstract (summary): BACKGROUND**

**Machine learning**-based facial and **vocal** measurements have demonstrated relationships with schizophrenia diagnosis and severity. Demonstrating utility and validity of remote and automated assessments conducted outside of controlled experimental or clinical settings can facilitate scaling such measurement tools to aid in risk assessment and tracking of treatment response in populations that are difficult to engage.

## **OBJECTIVE**

This study aimed to determine the accuracy of **machine learning**-based facial and **vocal** measurements acquired through automated assessments conducted remotely through smartphones.

## **METHODS**

Measurements of facial and **vocal** characteristics including facial expressivity, **vocal** acoustics, and **speech** prevalence were assessed in 20 patients with schizophrenia over the course of 2 weeks in response to two classes of prompts previously utilized in experimental laboratory assessments: evoked prompts, where subjects are guided to produce specific facial expressions and **speech**; and spontaneous prompts, where subjects are presented stimuli in the form of emotionally evocative imagery and asked to freely respond. Facial and **vocal** measurements were assessed in relation to schizophrenia symptom severity using the Positive and Negative Syndrome Scale.

## **RESULTS**

**Vocal** markers including **speech** prevalence, **vocal** jitter, fundamental frequency, and **vocal** intensity demonstrated specificity as markers of negative symptom severity, while measurement of facial expressivity demonstrated itself as a robust marker of overall schizophrenia symptom severity.

## **CONCLUSIONS**

Established facial and **vocal** measurements, collected remotely in schizophrenia patients via smartphones in response to automated task prompts, demonstrated accuracy as markers of schizophrenia symptom severity. Clinical implications are discussed.

**Accession number:** 35060906

**Copyright:** ©Anzar Abbas, Bryan J Hansen, Vidya Koesmahargyo, Vijay Yadav, Paul J Rosenfield, Omkar Patil, Marissa F Dockendorf, Matthew Moyer, Lisa A Shipley, M Mercedes Perez-Rodriguez, Isaac R Galatzer-Levy. Originally published in JMIR Formative Research (<https://formative.jmir.org>), 21.01.2022.

**Correspondence author:** Abbas, Anzar AiCure, New York, NY, United States.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2022-01-21

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**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.2196/26276>

**First available:** 2022-01-21

**Identifier (keyword):** computer vision, digital biomarkers, facial expressivity, negative symptoms, phenotyping, vocal acoustics

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Electronic;; Cited medium:Internet

**Publication date:** Jan 21, 2022

**Publication type:** Journal

**Publisher location:** CANADA

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**Updates:** 2022-01-212022-01-242022-02-092022-02-162022-03-202022-03-22

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Document 114

## **Heterogeneous digital biomarker integration out-performs patient self-reports in predicting Parkinson's disease**

**Author:** Deng, Kaiwen 1 ; Li, Yueming 1 ; Zhang, Hanrui 1 ; Wang, Jian 2 ; Albin, Roger L 3 ; Guan, Yuanfang 4

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**Publication info:** Communications biology 5.1: 58. (Jan 17, 2022)

**Abstract (summary):** Parkinson's disease (PD) is one of the first diseases where digital **biomarkers** demonstrated excellent performance in differentiating disease from healthy individuals. However, no study has systematically compared and leveraged multiple types of digital **biomarkers** to predict PD. Particularly, **machine learning** works on the fine-motor skills of PD are limited. Here, we developed **deep learning** methods that achieved an AUC (Area Under the receiver operator characteristic Curve) of 0.933 in identifying PD patients on 6418 individuals using 75048 tapping accelerometer and position records. Performance of tapping is superior to gait/rest and **voice**-based models obtained from the same benchmark population. Assembling the three models achieved a higher AUC of 0.944. Notably, the models not only correlated strongly to, but also performed better than patient self-reported symptom scores in diagnosing PD. This study demonstrates the complementary predictive power of tapping, gait/rest and **voice** data and establishes integrative **deep learning**-based models for identifying PD.

**Accession number:** 35039601

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**Copyright:** © 2022. The Author(s).

**Correspondence author:** Deng, Kaiwen Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2022-03-03

**Date created:** 2022-01-18

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**Document status:** Revised

**Document type:** Comparative Study, Journal Article, Research Support, N.I.H., Extramural, Research Support, Non-U.S. Gov't

**DOI:** <http://dx.doi.org/10.1038/s42003-022-03002-x>

**First available:** 2022-01-18

**Grant:** P50 NS123067. NINDS NIH HHS. United States.

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**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Adult;Aged;Aged, 80 and over;Area Under Curve;Biomarkers -- analysis (major);Female;Humans;Male;Middle Aged;Parkinson Disease -- diagnosis (major);Self Report (major);Wearable Electronic Devices -- statistics & numerical data (major);Young Adult

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Document 115

## **Automated text-level semantic markers of Alzheimer's disease**

**Author:** Sanz, Camila 1 ; Carrillo, Facundo 2 ; Slachevsky, Andrea 3 ; Forno, Gonzalo 4 ; Gorno Tempini, Maria Luisa 5 ; Villagra, Roque 6 ; Ibáñez, Agustín 7 ; Tagliazucchi, Enzo 8 ; García, Adolfo M 9

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**Publication info:** Alzheimer's & dementia (Amsterdam, Netherlands) 14.1: e12276. (Jan 14, 2022)

## **Abstract (summary): INTRODUCTION**

Automated **speech** analysis has emerged as a scalable, cost-effective tool to identify persons with Alzheimer's disease dementia (ADD). Yet, most research is undermined by low interpretability and specificity.

## **METHODS**

Combining statistical and **machine learning** analyses of natural **speech** data, we aimed to discriminate ADD patients from healthy controls (HCs) based on automated measures of domains typically affected in ADD: semantic granularity (coarseness of concepts) and ongoing semantic variability (conceptual closeness of successive words). To test for specificity, we replicated the analyses on Parkinson's disease (PD) patients.

## **RESULTS**

Relative to controls, ADD (but not PD) patients exhibited significant differences in both measures. Also, these features robustly discriminated between ADD patients and HC, while yielding near-chance classification between PD patients and HCs.

## **DISCUSSION**

Automated discourse-level semantic analyses can reveal objective, interpretable, and specific **markers** of ADD, bridging well-established neuropsychological targets with digital assessment tools.

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**Correspondence author:** Sanz, Camila Departamento de Física Universidad de Buenos Aires and Instituto de Física de Buenos Aires (IFIBA-CONICET) Pabellón I Ciudad Universitaria (1428) CABA Buenos Aires Argentina.

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**Grant:** R01 AG057234. NIA NIH HHS. United States.

**Identifier (keyword):** Alzheimer's disease dementia, Parkinson's disease, automated speech analysis, semantic granularity, semantic variability

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

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**Source attribution:** Medline, © Publisher specific

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Document 116

## **Detecting Heart Failure With Self-Supervised Mode-Based Memory Fusion Voice Analysis**

**Author:** Kaye, D. 1 ; Partovi, A. 1 ; Tang, J. 1 ; Barker, S. 1

1 Alfred Hospital, Melbourne, Australia

**Publication info:** Heart Lung and Circulation, suppl. Supplement 3 31 : S78-S79. Elsevier Ltd. (Jan 2022)

**Abstract (summary):** Congestive heart failure (CHF) is a chronic and progressive disease that affects millions of people worldwide, severely impacting their quality of life. The risk of missed cases affects life expectancy; thus it is critical to develop applications to continuously monitor CHF symptoms and disease progression in a patient-centric and cost-effective way. Breathlessness is the most common symptom of heart failure and one of the major contributors to hospitalisation. In this research, we seek to monitor breathlessness as a proxy for monitoring CHF at early stage of disease and have proposed a non-invasive method to monitor it through **voice** recordings. We introduced a new dataset, containing **voice** recordings from both healthy subjects (n=40), of which 20 are selected from pre-existed database, and heart failure participants (n=40). The severity of CHF is assessed based on composite clinical details including NYHA classification, quality of life questionnaire, CHF **biomarkers**, echocardiogram, and electrocardiogram and haemodynamic evaluation. We have proposed a novel **machine learning** model (mode-based memory fusion neural network) to improve the overall performance of CHF recognition, and achieved 90% accuracy under a subject-independent evaluation setting, highlighting the applicability of such methods for tele-health and home monitoring applications. We use two approaches to validate our paradigm: (1) Leave One Subject Out (LOSO) and (2) Leave One Subject Group Out (LOSGO). As seen in Table 1, our Memory Fusion model outperforms the average accuracy compared to other **machine learning** models. Figure 1 displays the high-level architecture of the memory fusion model. [Formula presented] [Formula presented]

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**Conference title:** 70th Annual Scientific Meeting of the Cardiac Society of Australia and New Zealand

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**Publication date:** Jan 2022

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**Subject:** Embase;biological marker;adult;artificial neural network;clinical article;conference abstract;congestive heart failure;controlled study;dyspnea;echocardiography;electrocardiogram;electrocardiography (major);heart failure (major);hemodynamics;home monitoring;human;machine learning (major);memory (major);New York Heart Association class;non invasive procedure;quality of life;questionnaire;telehealth;voice;voice analysis (major)

**Updates:** 2022-08-08

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Document 117

## Extracting **Vocal Biomarkers** for Pulmonary Congestion With a Smartphone App

**Author:** Ravindra, Neal G. 1 ; Kao, David P. 2

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2 Divisions of Cardiology and Bioinformatics and Personalized Medicine, University of Colorado School of Medicine, Aurora, CO, United States David.Kao@cuanschutz.edu

**Publication info:** JACC: Heart Failure 10.1: 50-51. Elsevier Inc. (Jan 2022)

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**Device trade name:** Device trade name Name: iPhone; Manufacturer: Undefined;

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**Identifier (keyword):** heart failure, machine learning, remote monitoring, speech analysis

**Language:** English

**Number of references:** 6

**Publication date:** Jan 2022

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**Subject:** Embase;MEDLINE;biological marker -- endogenous compound (major);iPhone +;smartphone (major);acute heart failure;Editorial;functional assessment;health care quality;health status;hospital admission;human;lung congestion -- diagnosis (major);machine learning;mobile application (major);patient care;patient monitoring

**Updates:** 2021-12-202022-01-24

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Document 118

## **Affective Computing for Late-Life Mood and Cognitive Disorders**

**Author:** Smith, Erin 1 ; Storch, Eric A. 2 ; Vahia, Ipsit 3 ; Wong, Stephen T. C. 4 ; Lavretsky, Helen 5 ; Cummings, Jeffrey L. 6 ; Eyre, Harris A. 7

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CA, United States, Organisation for Economic Co-operation and Development (OECD), Paris, France, Global Brain Health Institute, University of California, San Francisco, San Francisco, CA, United States, Global Brain Health Institute, Trinity College Dublin, Dublin, Ireland, Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, United States, IMPACT, The Institute for Mental and Physical Health and Clinical Translation, Deakin University, Geelong, VIC, Australia

**Publication info:** Frontiers in Psychiatry 12 Frontiers Media S.A. (Dec 23, 2021)

**Abstract (summary):** Affective computing (also referred to as artificial emotion intelligence or emotion AI) is the study and development of systems and devices that can recognize, interpret, process, and simulate emotion or other affective phenomena. With the rapid growth in the aging population around the world, affective computing has immense potential to benefit the treatment and care of late-life mood and cognitive disorders. For late-life depression, affective computing ranging from vocal biomarkers to facial expressions to social media behavioral analysis can be used to address inadequacies of current screening and diagnostic approaches, mitigate loneliness and isolation, provide more personalized treatment approaches, and detect risk of suicide. Similarly, for Alzheimer's disease, eye movement analysis, vocal biomarkers, and driving and behavior can provide objective biomarkers for early identification and monitoring, allow more comprehensive understanding of daily life and disease fluctuations, and facilitate an understanding of behavioral and psychological symptoms such as agitation. To optimize the utility of affective computing while mitigating potential risks and ensure responsible development, ethical development of affective computing applications for late-life mood and cognitive disorders is needed.

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**Correspondence author:** Smith, Erin The PRODEO Institute, San Francisco, CA, United States.

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**Language:** English

**Language of abstract:** English

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**Subject:** Embase;biological marker;aging;agitation;Alzheimer disease;artificial intelligence (major);cognition assessment;cognitive defect (major);diagnostic test;disease association;emotion assessment;ethical theory;eye movement;facial expression;human;isolation;late life depression (major);loneliness;mood disorder assessment;patient care;personalized medicine;process development;Review;risk assessment;screening;social media;suicide

**Updates:** 2022-01-112022-01-18

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Document 119

## **Combining Polygenic Risk Score and Voice Features to Detect Major Depressive Disorders**

**Author:** Di, Yazheng 1 ; Wang, Jingying 2 ; Liu, Xiaoqian 1 ; Zhu, Tingshao 1

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**Publication info:** Frontiers in Genetics 12 Frontiers Media S.A. (Dec 20, 2021)

**Abstract (summary):** Background: The application of polygenic risk scores (PRSs) in major depressive disorder (MDD) detection is constrained by its simplicity and uncertainty. One promising way to further extend its usability is fusion with other biomarkers. This study constructed an MDD biomarker by combining the PRS and voice features and evaluated their ability based on large clinical samples. Methods: We collected genome-wide sequences and utterances edited from clinical interview speech records from 3,580 women with recurrent MDD and 4,016 healthy people. Then, we constructed PRS as a gene biomarker by p value-based clumping and thresholding and extracted voice features using the i-vector method. Using logistic regression, we compared the ability of gene or voice biomarkers with the ability of both in combination for MDD detection. We also tested more machine learning models to further improve the detection capability. Results: With a p-value threshold of 0.005, the combined biomarker improved the area under the receiver operating characteristic curve

(AUC) by 9.09% compared to that of genes only and 6.73% compared to that of **voice** only. Multilayer **perceptron** can further heighten the AUC by 3.6% compared to logistic regression, while **support vector machine** and random forests showed no better performance. Conclusion: The addition of **voice biomarkers** to genes can effectively improve the ability to detect MDD. The combination of PRS and **voice biomarkers** in MDD detection is feasible. This study provides a foundation for exploring the clinical application of genetic and **voice biomarkers** in the diagnosis of MDD.

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**Author e-mail address:** tszhu@psych.ac.cn

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**Correspondence author:** Zhu, Tingshao Key Laboratory of Behavioral Science, Institute of Psychology, Chinese Academy of Sciences, Beijing, China.

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**Grant:** This research is funded by the Key Research Program of the Chinese Academy of Sciences (ZDRW-XH-2019-4).

**Identifier (keyword):** **biomarkers**, computer technology, depression, major depressive disorder (MDD), polygenic risk score (PRS), **voicebiomarkers**

**Language:** English

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**Subject:** Embase;**biological marker**;adult;area under the curve;Article;**artificial neural network**;DNA sequencing;female;gene frequency;genetic analysis;genetic marker;genetic risk;genetic risk score



(major);genetic susceptibility;human;interview;learning algorithm;machine learning;major clinical study;major depression (major);male;multilayer perceptron;nerve cell network;perceptron;phonetics;receiver operating characteristic;semi structured interview;single nucleotide polymorphism;social psychology;support vector machine;voice (major);whole genome sequencing

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Document 120

## **Natural Language Processing markers in first episode psychosis and people at clinical high-risk**

**Author:** Morgan, Sarah E 1 ; Diederens, Kelly 2 ; Vértés, Petra E 3 ; Ip, Samantha H Y 4 ; Wang, Bo 5 ; Thompson, Bethany 2 ; Demjaha, Arsime 2 ; De Micheli, Andrea 6 ; Oliver, Dominic 7 ; Liakata, Maria 8 ; Fusar-Poli, Paolo 9 ; Spencer, Tom J 10 ; McGuire, Philip 2

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**Publication info:** Translational psychiatry 11.1: 630. (Dec 13, 2021)

**Abstract (summary):** Recent work has suggested that disorganised speech might be a powerful predictor of later psychotic illness in clinical high risk subjects. To that end, several automated

measures to quantify disorganisation of transcribed **speech** have been proposed. However, it remains unclear which measures are most strongly associated with psychosis, how different measures are related to each other and what the best strategies are to collect **speech** data from participants. Here, we assessed whether twelve automated Natural Language Processing markers could differentiate transcribed **speech** excerpts from subjects at clinical high risk for psychosis, first episode psychosis patients and healthy control subjects (total N = 54). In-line with previous work, several measures showed significant differences between groups, including semantic coherence, **speech** graph connectivity and a measure of whether **speech** was on-topic, the latter of which outperformed the related measure of tangentiality. Most NLP measures examined were only weakly related to each other, suggesting they provide complementary information. Finally, we compared the ability of transcribed **speech** generated using different tasks to differentiate the groups. **Speech** generated from picture descriptions of the Thematic Apperception Test and a story re-telling task outperformed free **speech**, suggesting that choice of **speech** generation method may be an important consideration. Overall, quantitative **speech** markers represent a promising direction for future clinical applications.

**Accession number:** 34903724

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**Correspondence author:** Morgan, Sarah E Department of Computer Science and Technology, University of Cambridge, Cambridge, CB3 0FD, UK. , Department of Psychiatry, University of Cambridge, Cambridge, CB2 0SZ, UK. , The Alan Turing Institute, London, NW1 2DB, UK.

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Document 121

### **Early detection of frontotemporal dementia (EDoF): A digital biomarker study**

**Author:** Convery, Rhian S. 1 ; Russell, Lucy L. 2 ; Bocchetta, Martina 1 ; Rohrer, Jonathan D. 1

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**Publication info:** Alzheimer's & dementia : the journal of the Alzheimer's Association, suppl. Supplement 11 17 : e053568. NLM (Medline). (Dec 1, 2021)

**Abstract (summary):** BACKGROUND: With the commencement of clinical trials in frontotemporal dementia (FTD), robust biomarkers that can detect the earliest signs of the disease and also measure treatment effect, are essential. Pen and paper assessments are laborious, administered infrequently, and can rely on subjective reporting. Using digital devices allows for more frequent, often continuous, assessment from home, whilst producing a wealth of objective data. The Early Detection of Frontotemporal dementia (EDoF) study aims to develop a series of digital measures that may be useful for the diagnosis of FTD and for outcome measures in trials. METHOD: The EDoF study includes: a computerised cognitive battery, a mobile eye tracking device, a novel app that passively measures cognitive function by monitoring smartphone metadata, speech and language analysis using machine learning algorithms, actigraphy, and gait analysis. These measures are being validated in a large control population before being tested in symptomatic and presymptomatic genetic FTD within the Genetic FTD Initiative (GENFI) study. RESULT: We are currently recruiting participants to the initial arms of the study, with over 1,300 healthy controls having already completed the computerized cognitive battery. The mobile eye tracking device measures eye movement abnormalities but also uses instructionless eye movement tasks to measure executive function and social cognition. Pilot eye tracking data shows abnormalities of these tasks in symptomatic FTD, and also for antisaccadic eye movements in presymptomatic FTD. Normative data for all of the measures will be generated helping to assess construct validity and retest reliability. CONCLUSION: EDoF is the first study aiming to use a comprehensive set of digital measures to detect early FTD. It may also prove useful for home monitoring within future therapeutic trials of FTD.

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**Language:** English

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**Subject:** MEDLINE; **biological marker** (major); actimetry; adult; algorithm; article; construct validity; controlled study; diagnosis; executive function; eye movement monitor; frontotemporal dementia (major); gait; home monitoring; human; language; **machine learning**; metadata; outcome assessment; reliability; saccadic eye movement; smartphone; social cognition; **speech analysis**

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Document 122

### **Connected **speech** markers of amyloid burden in primary progressive aphasia**

**Author:** Slegers, Antoine 1 ; Chafouleas, Geneviève 2 ; Montembeault, Maxime 3 ; Bedetti, Christophe 1 ; Welch, Ariane E. 3 ; Rabinovici, Gil D. 3 ; Langlais, Philippe 2 ; Gorno-Tempini, Maria L. 3 ; Brambati, Simona M. 4

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Psychology, Université de Montréal, Canada, Centre de Recherche de L'Institut Universitaire de Gériatrie de Montréal (CRIUGM), Montréal, Canada, Centre de recherche du Centre intégré universitaire de santé et de services sociaux du Nord-de-l'Île-de-Montréal, Montréal, Québec, Canada  
simona.maria.brambati@umontreal.ca

**Publication info:** Cortex 145 : 160-168. Masson SpA. (Dec 2021)

**Abstract (summary):** Introduction: Positron emission tomography (PET) amyloid imaging has become an important part of the diagnostic workup for patients with primary progressive aphasia (PPA) and uncertain underlying pathology. Here, we employ a semi-automated analysis of connected **speech** (CS) with a twofold objective. First, to determine if quantitative CS features can help select primary progressive aphasia (PPA) patients with a higher probability of a positive PET amyloid imaging result. Second, to examine the relevant group differences from a clinical perspective. Methods: 117 CS samples from a well-characterised cohort of PPA patients who underwent PET amyloid imaging were collected. Expert consensus established PET amyloid status for each patient, and 40% of the sample was amyloid positive. Results: Leave-one-out cross-validation yields 77% classification accuracy (sensitivity: 74%, specificity: 79%). Discussion: Our results confirm the potential of CS analysis as a screening tool. Discriminant CS features from lexical, syntactic, pragmatic, and semantic domains are discussed.

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R01 AG027859. , NIA. National Institute on Aging.

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**Identifier (keyword):** Alzheimer's disease, Biomarkers, Connected speech, Differential diagnosis, Natural language processing, Primary progressive aphasia, Telemedicine

**Language:** English

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**Subject:** Embase;MEDLINE;amyloid -- special situation for pharmacovigilance -- aged (major);Pittsburgh compound B -- special situation for pharmacovigilance -- aged (major);aged;Alzheimer disease;Article;automation;clinical feature;cohort analysis;connected speech + (major);controlled study;diagnostic accuracy;differential diagnosis;feature extraction;feature selection;female;gray matter;human;image analysis;leave one out cross validation;major clinical

study;male;meta analysis (topic);positron emission tomography (major);primary progressive aphasia -- diagnosis (major);quantitative analysis;retrospective study;semantics;sensitivity and specificity;speech analysis (major);telemedicine

**Substance:** Substance Substance: amyloid; CAS: 11061-24-8;

**Updates:** 2021-11-022021-12-242022-02-02

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Document 123

### **Vocal features obtained through automated methods in verbal fluency tasks can aid the identification of mixed episodes in bipolar disorder**

**Author:** Weiner, Luisa 1 ; Guidi, Andrea 2 ; Doignon-Camus, Nadège 3 ; Giersch, Anne 3 ; Bertschy, Gilles 4 ; Vanello, Nicola 2

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**Publication info:** Translational Psychiatry 11.1 Springer Nature. (Dec 2021)

**Abstract (summary):** There is a lack of consensus on the diagnostic thresholds that could improve the detection accuracy of bipolar mixed episodes in clinical settings. Some studies have shown that **voice** features could be reliable **biomarkers** of manic and depressive episodes compared to euthymic states, but none thus far have investigated whether they could aid the distinction between mixed and non-mixed acute bipolar episodes. Here we investigated whether **vocal** features acquired via verbal fluency tasks could accurately classify mixed states in bipolar disorder using **machine learning** methods. Fifty-six patients with bipolar disorder were recruited during an acute episode (19 hypomanic, 8 mixed hypomanic, 17 with mixed depression, 12 with depression). Nine different trials belonging to four conditions of verbal fluency tasks—letter, semantic, free word generation, and associational fluency—were administered. Spectral and prosodic features in three conditions were selected for the classification algorithm. Using the leave-one-subject-out (LOSO) strategy to train the classifier, we calculated the accuracy rate, the F1 score, and the Matthews correlation coefficient (MCC). For depression versus mixed depression, the accuracy and F1 scores were high, i.e., respectively 0.83 and 0.86, and the MCC was of 0.64. For hypomania versus mixed hypomania, accuracy and F1 scores were also high, i.e., 0.86 and 0.75, respectively, and the MCC was of 0.57. Given the high rates of correctly classified subjects, **vocal** features quickly acquired via verbal fluency

tasks seem to be reliable **biomarkers** that could be easily implemented in clinical settings to improve diagnostic accuracy.

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**Subject:** Embase;MEDLINE;**biological marker**;adult;article;**classification algorithm** (major);**classifier**;controlled study;correlation coefficient;diagnostic accuracy;diagnostic test accuracy study;female;human;hypomania;major clinical study;male;mixed mania and depression (major)

**Updates:** 2021-08-132021-08-25

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Document 124

**Correlating natural language processing and automated **speech** analysis with clinician assessment to quantify **speech**-language changes in mild cognitive impairment and Alzheimer's dementia**



**Author:** Yeung, Anthony 1 ; Iaboni, Andrea 2 ; Rochon, Elizabeth 3 ; Lavoie, Monica 4 ; Santiago, Calvin 5 ; Yancheva, Maria 6 ; Novikova, Jekaterina 6 ; Xu, Mengdan 6 ; Robin, Jessica 6 ; Kaufman, Liam D. 6 ; Mostafa, Fariya 6

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**Publication info:** Alzheimer's Research and Therapy 13.1 BioMed Central Ltd. (Dec 2021)

**Abstract (summary):** Background: Language impairment is an important marker of neurodegenerative disorders. Despite this, there is no universal system of terminology used to describe these impairments and large inter-rater variability can exist between clinicians assessing language. The use of natural language processing (NLP) and automated speech analysis (ASA) is emerging as a novel and potentially more objective method to assess language in individuals with mild cognitive impairment (MCI) and Alzheimer's dementia (AD). No studies have analyzed how variables extracted through NLP and ASA might also be correlated to language impairments identified by a clinician. Methods: Audio recordings (n=30) from participants with AD, MCI, and controls were rated by clinicians for word-finding difficulty, incoherence, perseveration, and errors in speech. Speech recordings were also transcribed, and linguistic and acoustic variables were extracted through NLP and ASA. Correlations between clinician-rated speech characteristics and the variables were compared using Spearman's correlation. Exploratory factor analysis was applied to find common factors between variables for each speech characteristic. Results: Clinician agreement was high in three of the four speech characteristics: word-finding difficulty (ICC = 0.92, p<0.001), incoherence (ICC = 0.91, p<0.001), and perseveration (ICC = 0.88, p<0.001). Word-finding difficulty and incoherence were useful constructs at distinguishing MCI and AD from controls, while perseveration and speech errors were less relevant. Word-finding difficulty as a construct was explained by three factors, including number and duration of pauses, word duration, and syntactic complexity. Incoherence was explained by two factors, including increased average word duration, use of past tense, and changes in age of acquisition, and more negative valence. Conclusions: Variables extracted through automated acoustic and linguistic analysis of MCI and AD speech were significantly correlated with clinician ratings of speech and language characteristics. Our results suggest that correlating NLP and ASA with clinician observations is an objective and novel approach to measuring speech and language changes in neurodegenerative disorders.

**Accession number:** 2012314662

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**Correspondence author:** Yeung, Anthony Department of Psychiatry, University of Toronto, 250 College Street, Toronto, ON, M5T 1R8, Canada.

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**Identifier (keyword):** Alzheimer's, Automated **speech** analysis, Dementia, **Machine learning**, **Markers**, Mild cognitive impairment, Natural language processing

**Language:** English

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**Subject:** Embase;MEDLINE;aged;Alzheimer disease (major);Article;audio recording;**automatic speech recognition** (major);clinical article;clinical assessment;controlled study;demography;exploratory factor analysis;female;human;language disability;linguistics;male;mild cognitive impairment (major);natural language processing (major);perseveration;quantitative analysis;sex ratio;**speech analysis** (major)

Document 125

## Acoustic and language analysis of **speech** for suicidal ideation among US veterans

**Author:** Belouali, Anas 1 ; Gupta, Samir 1 ; Sourirajan, Vaibhav 1 ; Yu, Jiawei 1 ; Allen, Nathaniel 2 ; Alaoui, Adil 1 ; Dutton, Mary Ann 3 ; Reinhard, Matthew J. 4

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**Publication info:** BioData Mining 14.1 BioMed Central Ltd. (Dec 2021)

**Abstract (summary):** Background: Screening for suicidal ideation in high-risk groups such as U.S. veterans is crucial for early detection and suicide prevention. Currently, screening is based on clinical interviews or self-report measures. Both approaches rely on subjects to disclose their suicidal thoughts. Innovative approaches are necessary to develop objective and clinically applicable assessments. **Speech** has been investigated as an objective **marker** to understand various mental states including suicidal ideation. In this work, we developed a **machine learning** and natural language processing classifier based on **speech markers** to screen for suicidal ideation in US veterans. Methodology: Veterans submitted 588 narrative audio recordings via a mobile app in a real-life setting. In addition, participants completed self-report psychiatric scales and questionnaires. Recordings were analyzed to extract **voice** characteristics including prosodic, **phonation**, and **glottal**. The audios were also transcribed to extract textual features for linguistic analysis. We evaluated the acoustic and linguistic features using both statistical significance and ensemble feature selection. We also examined the performance of different **machine learning** algorithms on multiple combinations of features to classify suicidal and non-suicidal audios. Results: A combined set of 15 acoustic and linguistic features of **speech** were identified by the ensemble feature selection. Random Forest classifier, using the selected set of features, correctly identified suicidal ideation in veterans with 86% sensitivity, 70% specificity, and an area under the receiver operating characteristic curve (AUC) of 80%. Conclusions: **Speech** analysis of audios collected from veterans in everyday life settings using smartphones offers a promising approach for suicidal ideation detection. A **machine learning** classifier may eventually help clinicians identify and monitor high-risk veterans.

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**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Belouali, Anas Innovation Center for Biomedical Informatics, Georgetown University Medical Center, Washington, DC, United States.

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UL1-TR001409. , GHUCCTS. Georgetown-Howard Universities Center for Clinical and Translational Science.

**Language:** English

**Language of abstract:** English

**Number of references:** 74

**Publication date:** Dec 2021

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**Publisher location:** United Kingdom

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;acoustics (major);adult;area under the curve;Article;audio recording;classifier;controlled study;demography;ensemble feature selection +;feature selection;follow up;human;language (major);learning algorithm;linguistics;machine learning;male;mobile application;Patient Health Questionnaire 9;random forest;receiver operating characteristic;self report;sensitivity and specificity;speech analysis (major);speech discrimination;suicidal ideation (major);task performance;United States;veteran

**Updates:** 2021-02-122021-07-02

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Document 126

## **Voice analyses using smartphone-based data in patients with bipolar disorder, unaffected relatives and healthy control individuals, and during different affective states**

**Author:** Faurholt-Jepsen, Maria 1 ; Rohani, Darius Adam 2 ; Busk, Jonas 3 ; Vinberg, Maj 4 ; Bardram, Jakob Eyvind 2 ; Kessing, Lars Vedel 1

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**Publication info:** International Journal of Bipolar Disorders 9.1 Springer Science and Business Media Deutschland GmbH. (Dec 2021)

**Abstract (summary):** Background: **Voice** features have been suggested as objective **markers** of bipolar disorder (BD). Aims: To investigate whether **voice** features from naturalistic phone calls could discriminate between (1) BD, unaffected first-degree relatives (UR) and healthy control individuals (HC); (2) affective states within BD. Methods: **Voice** features were collected daily during naturalistic phone calls for up to 972 days. A total of 121 patients with BD, 21 UR and 38 HC were included. A total of 107.033 **voice** data entries were collected [BD (n = 78.733), UR (n = 8004), and HC (n = 20.296)]. Daily, patients evaluated symptoms using a smartphone-based system. Affective states were defined according to these evaluations. Data were analyzed using random forest **machine learning** algorithms. Results: Compared to HC, BD was classified with a sensitivity of 0.79 (SD 0.11)/AUC = 0.76 (SD 0.11) and UR with a sensitivity of 0.53 (SD 0.21)/AUC of 0.72 (SD 0.12). Within BD, compared to euthymia, mania was classified with a specificity of 0.75 (SD 0.16)/AUC = 0.66 (SD 0.11). Compared to euthymia, depression was classified with a specificity of 0.70 (SD 0.16)/AUC = 0.66 (SD 0.12). In all models the user dependent models outperformed the user independent models. Models combining increased mood, increased activity and insomnia compared to periods without performed best with a specificity of 0.78 (SD 0.16)/AUC = 0.67 (SD 0.11). Conclusions: **Voice** features from naturalistic phone calls may represent a supplementary objective **marker** discriminating BD from HC and a state **marker** within BD.

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**Correspondence author:** Faurholt-Jepsen, Maria Copenhagen Affective Disorder Research Center (CADIC), Psychiatric Center Copenhagen, Rigshospitalet, Blegdamsvej 9, Copenhagen, 2100, Denmark.

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5164-00001B9. , IFD. Innovationsfonden.

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The authors would like to thank the patients for participating in the studies, the nurses and PhD students involved in the studies.

**Identifier (keyword):** Bipolar disorder, Classification, openSMILE, Random Forest, Voice analysis

**Language:** English

**Language of abstract:** English

**Number of references:** 47

**Publication date:** Dec 2021

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**Publisher:** Springer Science and Business Media Deutschland GmbH

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**Subject:** Embase;neuroleptic agent;smartphone (major);algorithm;anxiety disorder;Article;bipolar disorder (major);clinical assessment;controlled study;depression;disease severity;electroencephalography;female;Hamilton Depression Rating Scale;heart rate variability;human;ICD-10;learning algorithm;machine learning;major clinical study;male;mania;neuropsychiatry;polysomnography;psychosis;sleep time;support vector machine;voice analysis (major);Young Mania Rating Scale

**Updates:** 2021-12-062021-12-13

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Document 127

## Digital biomarkers in multiple sclerosis

**Author:** Dillenseger, Anja 1 ; Weidemann, Marie Luise 1 ; Trentzsch, Katrin 1 ; Inojosa, Hernan 1 ; Haase, Rocco 1 ; Schriefer, Dirk 1 ; Voigt, Isabel 1 ; Scholz, Maria 1 ; Akgün, Katja 1 ; Ziemssen, Tjalf 1

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**Publication info:** Brain Sciences 11.11 MDPI. (Nov 2021)

**Abstract (summary):** For incurable diseases, such as multiple sclerosis (MS), the prevention of progression and the preservation of quality of life play a crucial role over the entire therapy period. In MS, patients tend to become ill at a younger age and are so variable in terms of their disease course that there is no standard therapy. Therefore, it is necessary to enable a therapy that is as personalized as possible and to respond promptly to any changes, whether with noticeable symptoms or symptomless. Here, measurable parameters of biological processes can be used, which provide good information with regard to prognostic and diagnostic aspects, disease activity and response to therapy, so-called **biomarkers**. Increasing digitalization and the availability of easy-to-use devices and technology also enable healthcare professionals to use a new class of digital **biomarkers**—digital health technologies—to explain, influence and/or predict health-related outcomes. The technology and devices from which these digital **biomarkers** stem are quite broad, and range from wearables that collect patients' activity during digitalized functional tests (e.g., the Multiple Sclerosis Performance Test, dual-tasking performance and **speech**) to digitalized diagnostic procedures (e.g., optical coherence tomography) and software-supported magnetic resonance imaging evaluation. These technologies offer a time-saving way to collect valuable data on a regular basis over a long period of time, not only once or twice a year during patients' routine visit at the clinic. Therefore, they lead to real-life data acquisition, closer patient monitoring and thus a patient dataset useful for precision medicine. Despite the great benefit of such increasing digitalization, for now, the path to implementing digital **biomarkers** is widely unknown or inconsistent. Challenges around validation, infrastructure, evidence generation, consistent data collection and analysis still persist. In this narrative review, we explore existing and future opportunities to capture clinical digital **biomarkers** in the care of people with MS, which may lead to a digital twin of the patient. To do this, we searched published papers for existing opportunities to capture clinical digital **biomarkers** for different functional systems in the context of MS, and also gathered perspectives on digital **biomarkers** under development or already existing as a research approach.

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**Identifier (keyword):** Big data, Digital **biomarkers**, Digital health technology, Digital twin, EHealth, Multiple sclerosis, Personalized therapy, Precision medicine

**Language:** English

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**Number of references:** 172

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**Subject:** Embase;**biological marker** (major);dialysis fluid;smartphone;brain stem;cancer prognosis;cognitive function test;coordination;data analysis;disease severity;exercise;gait;gait disorder;health care;immunomodulation;lower limb;**machine learning**;mobile application;multiple sclerosis (major);nonhuman;nuclear magnetic resonance imaging;optical coherence tomography;performance;physical activity;prevalence;questionnaire;Review;risk assessment;sensory dysfunction;signal processing;**speech analysis**;treatment response;vision

**Updates:** 2021-11-292021-11-30



## Detection of COVID-19 from voice, cough and breathing patterns: Dataset and preliminary results

**Author:** Despotovic, Vladimir 1 ; Ismael, Muhannad 2 ; Cornil, Maël 2 ; Call, Roderick Mc 2 ; Fagherazzi, Guy 3

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**Publication info:** Computers in Biology and Medicine 138 Elsevier Ltd. (Nov 2021)

**Abstract (summary):** COVID-19 heavily affects breathing and voice and causes symptoms that make patients' voices distinctive, creating recognizable audio signatures. Initial studies have already suggested the potential of using voice as a screening solution. In this article we present a dataset of voice, cough and breathing audio recordings collected from individuals infected by SARS-CoV-2 virus, as well as non-infected subjects via large scale crowdsourced campaign. We describe preliminary results for detection of COVID-19 from cough patterns using standard acoustic features sets, wavelet scattering features and deep audio embeddings extracted from low-level feature representations (VGGish and OpenL3). Our models achieve accuracy of 88.52%, sensitivity of 88.75% and specificity of 90.87%, confirming the applicability of audio signatures to identify COVID-19 symptoms. We furthermore provide an in-depth analysis of the most informative acoustic features and try to elucidate the mechanisms that alter the acoustic characteristics of coughs of people with COVID-19.

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**Identifier (keyword):** Artificial intelligence, Cough, COVID-19, Digital biomarker, Voice

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**Subject:** Embase;MEDLINE;biological marker (major);acoustic analysis (major);acoustics;adult;aged;ageusia;anosmia;Article;artificial intelligence (major);audio recording;breathing pattern (major);classification;classifier;comorbidity;controlled study;convolutional neural network;coronavirus disease 2019 -- diagnosis (major);coughing (major);diagnostic accuracy;diagnostic test accuracy study;dry cough;English (language);feature extraction;feature selection;female;France;French (language);German (language);Germany;Gini coefficient;human;Luxembourg;machine learning;major clinical study;male;multicenter study;multilayer perceptron;noise reduction;non-smoker;phonation;random forest;sensitivity and specificity;Serbia;short time Fourier transform;smoking;voice (major)

**Updates:** 2021-10-192021-11-182022-02-02

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Document 129

## Using Digital Speech Assessments to Detect Early Signs of Cognitive Impairment

**Author:** Robin, Jessica 1 ; Xu, Mengdan 1 ; Kaufman, Liam D 1 ; Simpson, William 2

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**Publication info:** Frontiers in digital health 3 : 749758. (Oct 27, 2021)

**Abstract (summary):** Detecting early signs of cognitive decline is crucial for early detection and treatment of Alzheimer's Disease. Most of the current screening tools for Alzheimer's Disease represent a significant burden, requiring invasive procedures, or intensive and costly clinical testing. Recent findings have highlighted changes to **speech** and language patterns that occur in Alzheimer's Disease, and may be detectable prior to diagnosis. Automated tools to assess **speech** have been developed that can be used on a smartphone or tablet, from one's home, in under 10 min. In this study, we present the results of a study of older adults who completed a **digital speech** assessment task over a 6-month period. Participants were grouped according to those who scored above (N = 18) or below (N = 18) the recommended threshold for detecting cognitive impairment on the Montreal Cognitive Assessment (MoCA) and those with diagnoses of mild cognitive impairment (MCI) or early Alzheimer's Disease (AD) (N = 14). Older adults who scored above the MoCA threshold had better performance on **speech** composites reflecting language coherence, information richness, syntactic complexity, and word finding abilities. Those with MCI and AD showed more rapid decline in the coherence of language from baseline to 6-month follow-up, suggesting that this score may be useful both for detecting cognitive decline and monitoring change over time. This study demonstrates that automated **speech** assessments have potential as sensitive tools to detect early signs of cognitive impairment and monitor progression over time.

**Accession number:** 34778869

**Copyright:** Copyright © 2021 Robin, Xu, Kaufman and Simpson.

**Correspondence author:** Robin, Jessica Winterlight Labs, Toronto, ON, Canada.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2021-11-15

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**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.3389/fgth.2021.749758>

**First available:** 2021-11-15

**Identifier (keyword):** Alzheimer's disease, **digitalbiomarker**, language, mild cognitive impairment, **speech**

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** The authors of this article are employees of Winterlight Labs.;; Publication model: Electronic-Collection;; Cited medium:Internet

**Publication date:** Oct 27, 2021

**Publication type:** Journal

**Publisher location:** SWITZERLAND

**Source attribution:** Medline, © Publisher specific

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Document 130

## **Measuring neuropsychiatric symptoms in patients with early cognitive decline using speech analysis**

**Author:** König, Alexandra 1 ; Mallick, Elisa 1 ; Tröger, Johannes 1 ; Linz, Nicklas 1 ; Zeghari, Radia 1 ; Manera, Valeria 1 ; Robert, Philippe 1

1 Stars Team, Sophia Antipolis, Institut National de Recherche en Informatique et en Automatique (INRIA), Valbonne, France, Clinical Research, Ki:elements, Saarbrücken, Germany, CoBTek (Cognition-Behaviour-Technology) Lab, FRIS-University Côte d'Azur, Nice, France  
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**Publication info:** European Psychiatry 64.1 Cambridge University Press. (Oct 13, 2021)

**Abstract (summary):** Background Certain neuropsychiatric symptoms (NPS), namely apathy, depression, and anxiety demonstrated great value in predicting dementia progression, representing eventually an opportunity window for timely diagnosis and treatment. However, sensitive and objective markers of these symptoms are still missing. Therefore, the present study aims to investigate the association between automatically extracted speech features and NPS in patients with mild neurocognitive disorders. Methods Speech of 141 patients aged 65 or older with neurocognitive disorder was recorded while performing two short narrative speech tasks. NPS were assessed by the neuropsychiatric inventory. Paralinguistic markers relating to prosodic, formant, source, and temporal qualities of speech were automatically extracted, correlated with NPS. Machine learning experiments were carried out to validate the diagnostic power of extracted markers. Results Different speech variables are associated with specific NPS; apathy correlates with temporal aspects, and anxiety with voice quality - and this was mostly consistent between male and female after correction for cognitive impairment. Machine learning regressors are able to extract information from speech features and perform above baseline in predicting anxiety, apathy, and depression scores. Conclusions Different NPS seem to be characterized by distinct speech features, which are easily extractable automatically

from short **vocal** tasks. These findings support the use of **speech** analysis for detecting subtypes of NPS in patients with cognitive impairment. This could have great implications for the design of future clinical trials as this cost-effective method could allow more continuous and even remote monitoring of symptoms.

**Accession number:** 2015262461

**Author e-mail address:** alexandra.konig@inria.fr

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**Correspondence author:** König, Alexandra Stars Team, Sophia Antipolis, Institut National de Recherche en Informatique et en Automatique (INRIA), Valbonne, France.

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**Date created:** 2022-02-14

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**Document type:** Article

**DOI:** <http://dx.doi.org/10.1192/j.eurpsy.2021.2236>

**Embase document status:** Embase; MEDLINE

**First available:** 2021-11-02

**Grant:** It was partially funded by the MEPHESTO project (Grant DRI-0120105/291), the EIT Digital Well-being Activity (Grant 17074), ELEMENT, the University Côte d'Azur, and the IA Association, and supported by the Edmond & Lily Safra Foundation and Institute Claude Pompidou.

**Identifier (keyword):** Apathy, Depression, Mild neurocognitive disorders, Neuropsychiatric symptoms, **Speech** analysis, **Vocal** parameters

**Language:** English

**Language of abstract:** English

**Number of references:** 54

**Publication date:** Oct 13, 2021

**Publication type:** Journal

**Publisher:** Cambridge University Press

**Publisher location:** France

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;microphone;tablet computer;adult;aged;anxiety (major);apathy (major);Article;automation;controlled study;depression (major);disorders of higher cerebral function (major);**feature extraction** (major);female;human;**machine learning**;major clinical study;male;Mini

Mental State Examination;neuropsychiatric inventory;paralanguage;speech analysis (major);speech test;voice

**Updates:** 2021-11-022021-11-082022-02-15

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Document 131

## **Assessing Parkinson's Disease at Scale Using Telephone-Recorded Speech: Insights from the Parkinson's Voice Initiative**

**Author:** Arora, Siddharth 1 ; Tsanas, Athanasios 2

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**Publication info:** Diagnostics (Basel, Switzerland) 11.10 (Oct 14, 2021)

**Abstract (summary):** Numerous studies have reported on the high accuracy of using voice tasks for the remote detection and monitoring of Parkinson's Disease (PD). Most of these studies, however, report findings on a small number of voice recordings, often collected under acoustically controlled conditions, and therefore cannot scale at large without specialized equipment. In this study, we aimed to evaluate the potential of using voice as a population-based PD screening tool in resource-constrained settings. Using the standard telephone network, we processed 11,942 sustained vowel /a/ phonations from a US-English cohort comprising 1078 PD and 5453 control participants. We characterized each phonation using 304 dysphonia measures to quantify a range of vocal impairments. Given that this is a highly unbalanced problem, we used the following strategy: we selected a balanced subset (n = 3000 samples) for training and testing using 10-fold cross-validation (CV), and the remaining (unbalanced held-out dataset, n = 8942) samples for further model validation. Using robust feature selection methods we selected 27 dysphonia measures to present into a radial-basis-function support vector machine and demonstrated differentiation of PD participants from controls with 67.43% sensitivity and 67.25% specificity. These findings could help pave the way forward toward the development of an inexpensive, remote, and reliable diagnostic support tool for PD using voice as a digital biomarker.

**Accession number:** 34679590

**Correspondence author:** Arora, Siddharth Somerville College, University of Oxford, Oxford OX2 6HD, UK.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2021-10-23

**Date revised:** 2021-10-26

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.3390/diagnostics11101892>

**First available:** 2021-10-23

**Identifier (keyword):** Parkinson's disease, acoustic measures, **biomarker**, clinical decision support tool, **dysphonia** measures, sustained vowel **phonations**, telemonitoring

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Electronic;; Cited medium:Print

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**Publisher location:** SWITZERLAND

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**Updates:** 2021-10-232021-10-252021-10-26

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Document 132

## **Detecting Subclinical Social Anxiety Using Physiological Data From a Wrist-Worn Wearable: Small-Scale Feasibility Study**

**Author:** Shaukat-Jali, Ruksana 1 ; van Zalk, Nejra 1 ; Boyle, David Edward 1

1 Dyson School of Design Engineering, Imperial College London, London, United Kingdom, United Kingdom

**Publication info:** JMIR formative research 5.10: e32656. (Oct 7, 2021)

### **Abstract (summary): BACKGROUND**

Subclinical (ie, threshold) social anxiety can greatly affect young people's lives, but existing solutions appear inadequate considering its rising prevalence. Wearable sensors may provide a novel way to detect social anxiety and result in new opportunities for monitoring and treatment, which would be greatly beneficial for persons with social anxiety, society, and health care services. Nevertheless, indicators such as skin temperature measured by wrist-worn sensors have not been used in prior work on physiological social anxiety detection.

## OBJECTIVE

This study aimed to investigate whether subclinical social anxiety in young adults can be detected using physiological data obtained from wearable sensors, including heart rate, skin temperature, and electrodermal activity (EDA).

## METHODS

Young adults (N=12) with self-reported subclinical social anxiety (measured using the widely used self-reported version of the Liebowitz Social Anxiety Scale) participated in an impromptu **speech** task. Physiological data were collected using an E4 Empatica wearable device. Using the preprocessed data and following a supervised **machine learning** approach, various classification algorithms such as **Support Vector Machine**, Decision Tree, Random Forest, and K-Nearest Neighbours (KNN) were used to develop models for 3 different contexts. Models were trained to differentiate (1) between baseline and socially anxious states, (2) among baseline, anticipation anxiety, and reactive anxiety states, and (3) social anxiety among individuals with social anxiety of differing severity. The predictive capability of the singular modalities was also explored in each of the 3 supervised learning experiments. The generalizability of the developed models was evaluated using 10-fold cross-validation as a performance index.

## RESULTS

With modalities combined, the developed models yielded accuracies between 97.54% and 99.48% when differentiating between baseline and socially anxious states. Models trained to differentiate among baseline, anticipation anxiety, and reactive anxiety states yielded accuracies between 95.18% and 98.10%. Furthermore, the models developed to differentiate between social anxiety experienced by individuals with anxiety of differing severity scores successfully classified with accuracies between 98.86% and 99.52%. Surprisingly, EDA was identified as the most effective singular modality when differentiating between baseline and social anxiety states, whereas ST was the most effective modality when differentiating anxiety among individuals with social anxiety of differing severity.

## CONCLUSIONS

The results indicate that it is possible to accurately detect social anxiety as well as distinguish between levels of severity in young adults by leveraging physiological data collected from wearable sensors.

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**Copyright:** ©Ruksana Shaukat-Jali, Nejra van Zalk, David Edward Boyle. Originally published in JMIR Formative Research (<https://formative.jmir.org>), 07.10.2021.

**Correspondence author:** Shaukat-Jali, Ruksana Dyson School of Design Engineering, Imperial College London, London, United Kingdom.



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**Date created:** 2021-10-07

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**Document type:** Journal Article

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**Identifier (keyword):** anxiety, digital **biomarkers**, digital phenotyping, mHealth, **machine learning**, mental health, new methods, physiological measurement, sensor, social anxiety, wearable, wearable sensors, young adults

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Electronic;; Cited medium:Internet

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Document 133

## **Symposium Title: Computational Psychophysiology**

**Author:** Hu, Bin 1

1 Lanzhou University

**Publication info:** International Journal of Psychophysiology, suppl. Supplement 168 : S57. Elsevier B.V. (Oct 2021)

**Abstract (summary):** Emotion, mind and behavior are fundamental to human life, influencing everyday tasks such as learning, social communication, and even rational decision-making. To study human brain, mind, emotion and behavior need to be analyzed in combination, a feat that requires advanced computational approaches. The **affective computing** is proposed to develop new technologies and theories that advance basic understanding of affect, cognition, behavior, and their

roles in human experience. As a novel multidisciplinary science, research of affective requires integration of multiple areas such as computer science, cognitive neuroscience, neuropsychology, physiology, psychiatry, and biomedical engineering. The goal of this session is to gather the state-of-the-art achievements in this field and discuss the technological and scientific development in order to promote its further development. The research interests include but are not limited to: • Quantification of human emotion, cognition, and affective process • Methods for multi-modal (e.g., ERPs, MEG, MRI, **speech**) recognition emotional/mental states • Algorithms and features for the recognition of emotion, mental state and body gestures • Computational **biomarkers** of mental emotional disorders • Emotion/cognition-based applications in HCI/HRI • Computational methods for influencing the emotional/ mental state of people • Biomedical sensor technology &wearable computing

**Accession number:** 2014456642

**Conference country:** China

**Conference end date:** 2021-09-11

**Conference location:** Chengdu

**Conference start date:** 2021-09-07

**Conference title:** Proceedings of the 20th World Congress of Psychophysiology (IOP 2021) of the International Organization of Psychophysiology (IOP)

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**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1016/j.ijpsycho.2021.07.172>

**Embase document status:** Embase

**First available:** 2021-09-09

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**Language of abstract:** English

**Publication date:** Oct 2021

**Publication type:** Journal

**Publisher:** Elsevier B.V.

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**Subject:** Embase;**biological marker**;achievement;algorithm (major);biomedical engineering;brain;cognitive neuroscience;computer;conference abstract;controlled study;decision

making;emotional disorder;gesture;human;learning;mental health;neuropsychology;nuclear magnetic resonance imaging;psychiatry;psychophysiology (major);sensor;speech

**Updates:** 2021-09-09

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Document 134

## VOICE-BASED MONITORING OF COPD

**Author:** Mohammed Daanish Ali Khan, Mir; Pradeep Naval, Prakhar; Kulshreshtha, Rajat; Venneti, Satya; Singh, Anil

**Publication info:** Chest, suppl. Supplement 160.4: A2173-A2174. Elsevier Inc. (Oct 2021)

**Abstract (summary):** TOPIC: Pulmonary Rehabilitation TYPE: Original Investigations PURPOSE: COPD is a common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation with a projected increase in prevalence over the coming decades. Periodic assessment of COPD is needed to determine the level of airflow limitation and assess impact on a patient's health status, risk of future exacerbations, hospital admissions, mortality and to help guide therapy. Previously, COPD was viewed as a disease mostly characterized by dyspnea, now it is recognized that COPD impacts patients beyond this. As a result, a comprehensive assessment of symptoms is recommended. The COPD assessment test (CAT) is an 8 item measure of health status impairment and is commonly used to assess symptoms. Voice is an important biomarker of many medical conditions including diseases of the respiratory system which leave signatures in breath and speech. We build on our previous work of voice-based prediction of FEV1 and FVC (Ashraf, Obaid, et al. Chest 158.4 (2020): A1687, Walter, Kristin. JAMA 325.12 (2021): 1130-1131) to create a voice based early warning system for COPD exacerbation utilizing the CAT score. METHODS: We present the results of a prospective cohort study correlating voice and breath samples to CAT scores. We collected a total of 418 sessions from 9 participants aged 42 to 75 at a large suburban general hospital in Western Pennsylvania over the course of a year. Each participant provided biweekly voice and breath samples, along with self-reported CAT scores. We recorded audio samples on a commodity smart tablet using a proprietary software and analyzed recorded data off-line on the secure Telling.ai cloud. Based on input from health care providers, we weighted CAT questions pertaining to cough, sputum, wheezing and tightness of the chest more heavily than other questions. We extracted audio features from the recordings and developed a regression algorithm using k fold cross validation to predict deviation in the weighted CAT score from a baseline, and a binary classification retrospective prediction algorithm to predict a clinically important weighted CAT score increase (2 point or more) upto 7 days in advance. RESULTS: Our weighted CAT deviation from baseline regressor and retrospective exacerbation classification models had the following results, averaged across all folds, for all participants:(R squared = 0.972, Mean absolute error =0.449, Mean squared error = 0.572, Pearson Coefficient Correlation r = 0.998, two-tailed p-value <0.0000001)and(Accuracy = 94.086%, Sensitivity = 94.229%, Specificity = 94.414%)respectively. CONCLUSIONS: We demonstrate that changes in voice and breath correlate strongly with changes in

symptoms scores 0.97 R<sup>2</sup> and MAE = 0.45 and furthermore, that signatures in **voice** can be detected even before the symptoms present themselves (2 point or more weighted CAT score increase upto 7 days in advance) with 94.23% sensitivity and 94.41% specificity. This technology requires no additional custom-built hardware, is cost effective, non-invasive and practical for ubiquitous and frequent use on mobile phones. **CLINICAL IMPLICATIONS:** The solution is ideally suited for personalized, predictive and frequent monitoring to enable the development of clinical decision support systems. This technique offers the promise of early interventions to reduce exacerbation frequency and severity, advancing personalized medicine for chronic and acute respiratory care. **DISCLOSURES:** Employee relationship with Telling.ai Please note: \$20001 - \$100000 by Mir Mohammed Daanish Ali Khan, source=Web Response, value=Salary Employee relationship with Telling.ai Please note: \$20001 - \$100000 by Rajat Kulshreshtha, source=Web Response, value=Salary Employee relationship with Telling.ai Please note: >\$100000 by Prakhar Pradeep Naval, source=Web Response, value=Salary Speaker/Speaker's Bureau relationship with boeringer Ingleheim Please note: 2019-2020 Added 04/29/2021 by Anil Singh, source=Web Response, value=Honoraria Speaker/Speaker's Bureau relationship with astra zeneca Please note: 2019-2020 Added 04/29/2021 by Anil Singh, source=Web Response, value=Honoraria Chief Technical Officer relationship with Telling.ai Please note: >\$100000 by Satya Venneti, source=Web Response, value=Salary

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**Subject:** Embase;biological marker;adult;aged;binary classification (major);breathing disorder;chest tightness;chronic obstructive lung disease (major);clinical assessment;clinical decision support system;cohort analysis;computer;conference abstract;controlled study;coughing;disease exacerbation;dyspnea;early intervention;employee;female;forced expiratory volume;forced vital capacity;general hospital;health care personnel;health status;hospital admission;human;human tissue;k fold cross validation;major clinical study;male;mobile phone;mortality;Pennsylvania;personalized medicine;prediction;prevalence;proprietary software;prospective study;pulmonary rehabilitation;respiratory care;risk assessment;salary;sensitivity and specificity;speech;sputum;tablet computer (major);validation process;voice (major);wheezing

**Updates:** 2021-10-11

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Document 135

## **A deep learning algorithm for objective assessment of hypernasality in children with cleft palate**

**Author:** Mathad, Vikram C. 1 ; Scherer, Nancy 1 ; Chapman, Kathy 2 ; Liss, Julie M. 1 ; Berisha, Visar 3

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**Publication info:** IEEE Transactions on Biomedical Engineering 68.10: 2986-2996. IEEE Computer Society. (Oct 2021)

**Abstract (summary):** Objectives: Evaluation of hypernasality requires extensive perceptual training by clinicians and extending this training on a large scale internationally is untenable; this compounds the health disparities that already exist among children with cleft. In this work, we present the objective hypernasality measure (OHM), a speech-based algorithm that automatically measures hypernasality in speech, and validate it relative to a group of trained clinicians. Methods: We trained a deep neural network (DNN) on approximately 100 hours of a publicly-available healthy speech corpus to detect the presence of nasal acoustic cues generated through the production of nasal consonants and nasalized phonemes in speech. Importantly, this model does not require any clinical data for training. The posterior probabilities of the deep learning model were aggregated at the sentence and speaker-levels to compute the OHM. Results: The results showed that the OHM was significantly correlated with perceptual hypernasality ratings from the Americleft database ( $r = 0.797$ ,  $p < 0.001$ ) and the New Mexico Cleft Palate Center (NMPC) database ( $r = 0.713$ ,  $p < 0.001$ ). In addition, we

evaluated the relationship between the OHM and articulation errors; the sensitivity of the OHM in detecting the presence of very mild hypernasality; and established the internal reliability of the metric. Further, the performance of the OHM was compared with a DNN regression algorithm directly trained on the hypernasal speech samples. Significance: The results indicate that the OHM is able to measure the severity of hypernasality on par with American-trained clinicians on this dataset.

**Accession number:** 634216402

**Author e-mail address:** vchikkaw@asu.edu

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Mathad, Vikram C. Department of Speech and Hearing Sciences, Arizona State University, Tempe, AZ, 85281, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document type:** Article

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**First available:** 2021-02-26

**Grant:** The work was supported by NIH under Grant NIDCR DE026252.

**Identifier (keyword):** Cleft palate, Clinical speech analysis, Deepneural networks, Hypernasality, Speech assessment, Vocalbiomarkers

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**Number of references:** 38

**Publication date:** Oct 2021

**Publication type:** Journal

**Publisher:** IEEE Computer Society

**Publisher location:** United States

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**Subject:** Embase;MEDLINE;biological marker (major);Article;child;cleft palate (major);comparative study;consonant;cross validation;data base;deep learning (major);deep neural network;external validity;feed forward neural network;human;hypernasality (major);internal validity;learning algorithm (major);nasality;phoneme;reliability;signal noise ratio;speech analysis;speech rate

Document 136

## **Feasibility of using an automated analysis of formulation effort in patients' spoken seizure descriptions in the differential diagnosis of epileptic and nonepileptic seizures**

**Author:** Pevy, Nathan 1 ; Christensen, Heidi 2 ; Walker, Traci 3 ; Reuber, Markus 4

1 Sheffield Institute for Translational Neuroscience (SiTraN), University of Sheffield, Sheffield, United Kingdom ndpevy1@sheffield.ac.uk 2 Department of Computer Science, University of Sheffield, Sheffield, United Kingdom 3 Division of Human Communication Sciences, University of Sheffield, Sheffield, United Kingdom 4 Academic Neurology Unit, University of Sheffield, Royal Hallamshire Hospital, Sheffield, United Kingdom

**Publication info:** Seizure 91 : 141-145. W.B. Saunders Ltd. (Oct 2021)

**Abstract (summary):** Objective: There are three common causes of Transient Loss of Consciousness (TLOC), syncope, epileptic and psychogenic nonepileptic seizures (PNES). Many individuals who have experienced TLOC initially receive an incorrect diagnosis and inappropriate treatment. Whereas syncope can be distinguished relatively easily with a small number of "yes"/"no" questions, the differentiation of the other two causes of TLOC is more challenging. Previous qualitative research based on the methodology of Conversation Analysis has demonstrated that the descriptions of epileptic seizures contain more formulation effort than accounts of PNES. This research investigates whether features likely to reflect the level of formulation effort can be automatically elicited from audio recordings and transcripts of **speech** and used to differentiate between epileptic and nonepileptic seizures. Method: Verbatim transcripts of conversations between patients and neurologists were manually produced from video and audio recordings of 45 interactions (21 epilepsy and 24 PNES). The subsection of each transcript containing the person's account of their first seizure was manually extracted for the analysis. Seven automatically detectable features were designed as **markers** of formulation effort. These features were used to train a Random Forest **machine learning** classifier. Result: There were significantly more hesitations and repetitions in descriptions of epileptic than nonepileptic seizures. Using a nested leave-one-out cross validation approach, 71% of seizures were correctly classified by the Random Forest classifier. Discussion: This pilot study provides proof of principle that linguistic features that have been automatically extracted from audio recordings and transcripts could be used to distinguish between epileptic seizures and PNES and thereby contribute to the differential diagnosis of TLOC. Future research should explore whether additional observations can be incorporated into a diagnostic stratification tool and compare the performance of these features when they are combined with additional information provided by patients and witnesses about seizure manifestations and medical history.

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**Author e-mail address:** ndpevy1@sheffield.ac.uk

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Pevy, Nathan Sheffield Institute of Translational Neuroscience (SiTraN), University of Sheffield, Sheffield, United Kingdom.

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**Embase document status:** Embase; MEDLINE

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**Grant:** We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. This research project was funded by Epilepsy Research UK.

**Identifier (keyword):** Classification, Diagnosis, Epilepsy, Natural language processing, Nonepileptic seizures, **Speech analysis**

**Language:** English

**Language of abstract:** English

**Number of references:** 32

**Publication date:** Oct 2021

**Publication type:** Journal

**Publisher:** W.B. Saunders Ltd

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**Subject:** Embase;MEDLINE;electroencephalograph;Article;audio recording;**classifier**;clinical article;decision tree;differential diagnosis;electroencephalography;epilepsy -- diagnosis (major);feasibility study;female;human;**machine learning**;male;medical history;natural language processing;pilot study;psychogenic nonepileptic seizure -- diagnosis (major);qualitative research;**random forest**;**speech analysis**;**speech discrimination**;transcription initiation;unconsciousness;validation process;videorecording

**Updates:** 2021-07-132021-12-23



## Quantified language connectedness in schizophrenia-spectrum disorders

**Author:** Voppel, A E 1 ; de Boer, J N 2 ; Brederoo, S G 1 ; Schnack, H G 3 ; Sommer, Iec 1

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Department of Biomedical Sciences of Cells and Systems, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; Department of Psychiatry, UMCU Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands, the Netherlands 3 Department of Psychiatry, UMCU Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands; Utrecht University, Utrecht Institute of Linguistics OTS, Utrecht, the Netherlands, the Netherlands

**Publication info:** Psychiatry research 304 : 114130. (Oct 2021)

**Abstract (summary):** Language abnormalities are a core symptom of schizophrenia-spectrum disorders and could serve as a potential diagnostic marker. Natural language processing enables quantification of language connectedness, which may be lower in schizophrenia-spectrum disorders. Here, we investigated connectedness of spontaneous **speech** in schizophrenia-spectrum patients and controls and determine its accuracy in classification. Using a semi-structured interview, **speech** of 50 patients with a schizophrenia-spectrum disorder and 50 controls was recorded. Language connectedness in a semantic word2vec model was calculated using consecutive word similarity in moving windows of increasing sizes (2-20 words). Mean, minimal and variance of similarity were calculated per window size and used in a random forest classifier to distinguish patients and healthy controls. Classification based on connectedness reached 85% cross-validated accuracy, with 84% specificity and 86% sensitivity. Features that best discriminated patients from controls were variance of similarity at window sizes between 5 and 10. We show impaired connectedness in spontaneous **speech** of patients with schizophrenia-spectrum disorders even in patients with low ratings of positive symptoms. Effects were most prominent at the level of sentence connectedness. The high sensitivity, specificity and tolerability of this method show that language analysis is an accurate and feasible **digital** assistant in diagnosing schizophrenia-spectrum disorders.

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**Correspondence author:** Voppel, A E Department of Biomedical Sciences of Cells and Systems, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands.

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**DOI:** <http://dx.doi.org/10.1016/j.psychres.2021.114130>

**First available:** 2021-08-02

**Identifier (keyword):** Biomarker, Natural language processing, Psychosis, Semantic model, Speech, Word similarity

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Humans;Language;Language Disorders (major);Schizophrenia (major) -- complications;Semantics;Speech

**Notes:** Indexing method: Automated;; Publication model: Print-Electronic;; Cited medium:Internet

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**Publisher location:** IRELAND

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**Updates:** 2021-08-022021-08-032021-08-042021-08-052021-08-062021-08-092021-08-102021-08-122021-08-162021-08-172021-08-182021-08-192021-08-202021-08-232021-08-242021-08-262021-09-112021-09-132021-10-262021-10-28

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Document 138

## **Editorial: Digital Linguistic Biomarkers: Beyond Paper and Pencil Tests**

**Author:** Gagliardi, Gloria 1 ; Kokkinakis, Dimitrios 2 ; Duñabeitia, Jon Andoni 3

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Nebrija en Cognición, Nebrija University, Madrid, Spain, UiT The Arctic University of Norway, Tromsø, Norway, Norway

**Publication info:** Frontiers in psychology 12 : 752238. (Sep 16, 2021)

**Accession number:** 34603170

**Correspondence author:** Gagliardi, Gloria Department of Classical Philology and Italian Studies, University of Bologna, Bologna, Italy.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Document type:** Editorial

**DOI:** <http://dx.doi.org/10.3389/fpsyg.2021.752238>

**First available:** 2021-10-04

**Identifier (keyword):** clinical linguistics, computational linguistics, computer-aided diagnosis, linguistic **biomarkers**, linguistic-based diagnosis, **machine learning**, natural language processing, **speech** processing and recognition

**Language:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.;; Publication model: Electronic-eCollection;; Cited medium:Print

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**Publication type:** Journal

**Publisher location:** SWITZERLAND

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Document 139

## **Exploring Test-Retest Reliability and Longitudinal Stability of **Digital Biomarkers** for Parkinson Disease in the m-Power Data Set: Cohort Study**

**Author:** Sahandi Far, Mehran 1 ; Eickhoff, Simon B 1 ; Goni, Maria 1 ; Dukart, Juergen 1

1 Institute of Neuroscience and Medicine, Brain & Behaviour (INM-7), Research Centre Jülich, Jülich, Germany, Institute of Systems Neuroscience, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany, Germany

**Publication info:** Journal of medical Internet research 23.9: e26608. (Sep 13, 2021)

## **Abstract (summary): BACKGROUND**

**Digital biomarkers** (DB), as captured using sensors embedded in modern smart devices, are a promising technology for home-based sign and symptom monitoring in Parkinson disease (PD).

## **OBJECTIVE**

Despite extensive application in recent studies, test-retest reliability and longitudinal stability of DB have not been well addressed in this context. We utilized the large-scale m-Power data set to establish the test-retest reliability and longitudinal stability of gait, balance, **voice**, and tapping tasks in an unsupervised and self-administered daily life setting in patients with PD and healthy controls (HC).

## **METHODS**

Intraclass correlation coefficients were computed to estimate the test-retest reliability of features that also differentiate between patients with PD and healthy volunteers. In addition, we tested for longitudinal stability of DB measures in PD and HC, as well as for their sensitivity to PD medication effects.

## **RESULTS**

Among the features differing between PD and HC, only a few tapping and **voice** features had good to excellent test-retest reliabilities and medium to large effect sizes. All other features performed poorly in this respect. Only a few features were sensitive to medication effects. The longitudinal analyses revealed significant alterations over time across a variety of features and in particular for the tapping task.

## **CONCLUSIONS**

These results indicate the need for further development of more standardized, sensitive, and reliable DB for application in self-administered remote studies in patients with PD. Motivational, learning, and other confounders may cause variations in performance that need to be considered in DB longitudinal applications.

**Accession number:** 34515645

**Copyright:** ©Mehran Sahandi Far, Simon B Eickhoff, Maria Goni, Juergen Dukart. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 13.09.2021.

**Correspondence author:** Sahandi Far, Mehran Institute of Neuroscience and Medicine, Brain & Behaviour (INM-7), Research Centre Jülich, Jülich, Germany. , Institute of Systems Neuroscience, Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Document type:** Journal Article, Research Support, Non-U.S. Gov't

**DOI:** <http://dx.doi.org/10.2196/26608>

**First available:** 2021-09-13

**Identifier (keyword):** Parkinson disease, **biomarkers**, diagnostic markers, health sciences, medical research, mobile phone, neurological disorders

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** **Biomarkers**; Cohort Studies; Gait; Humans; Parkinson Disease (major) -- diagnosis; Reproducibility of Results

**Notes:** Indexing method: Automated;; Publication model: Electronic;; Cited medium: Internet

**Publication date:** Sep 13, 2021

**Publication type:** Journal

**Publisher location:** CANADA

**Source attribution:** Medline, © Publisher specific

**Substance:** Substance Substance: Biomarkers; CAS: 0;

**Updates:** 2021-09-13 2021-09-14 2021-10-22 2021-10-27 2021-10-29

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Document 140

## **Machine learning accurately classifies neural responses to rhythmic **speech** vs. non-speech from 8-week-old infant EEG**

**Author:** Gibbon, Samuel 1 ; Attaheri, Adam 1 ; Ní Choisdealbha, Áine 1 ; Rocha, Sinead 1 ; Brusini, Perrine 1 ; Mead, Natasha 1 ; Boutris, Panagiotis 1 ; Olawole-Scott, Helen 1 ; Ahmed, Henna 1 ; Flanagan, Sheila 1 ; Mandke, Kanad 1 ; Keshavarzi, Mahmoud 2 ; Goswami, Usha 1

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**Publication info:** Brain and Language 220 Academic Press Inc. (Sep 2021)

**Abstract (summary):** Currently there are no reliable means of identifying infants at-risk for later language disorders. Infant neural responses to rhythmic stimuli may offer a solution, as neural tracking of rhythm is atypical in children with developmental language disorders. However, infant brain recordings are noisy. As a first step to developing accurate neural **biomarkers**, we investigate whether infant brain responses to rhythmic stimuli can be classified reliably using EEG from 95 eight-week-old infants listening to natural stimuli (repeated syllables or drumbeats). Both **Convolutional Neural Network (CNN)** and **Support Vector Machine (SVM)** approaches were employed. Applied to one infant at a time, the **CNN** discriminated syllables from drumbeats with a mean AUC of 0.87, against two levels of noise. The **SVM** classified with AUC 0.95 and 0.86 respectively, showing reduced performance as noise increased. Our proof-of-concept modelling opens the way to the development of clinical **biomarkers** for language disorders related to rhythmic entrainment.

**Accession number:** 2012894919

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**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Gibbon, Samuel Centre for Neuroscience in Education, Department of Psychology, University of Cambridge, United Kingdom.

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**Document type:** Article

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**First available:** 2021-06-30

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**Identifier (keyword):** Convolutional Neural Network, Developmental Language Disorders, EEG, Infancy, Machine Learning, Rhythm

**Language:** English

**Language of abstract:** English

**Number of references:** 58

**Publication date:** Sep 2021

**Publication type:** Journal

**Publisher:** Academic Press Inc.

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;biological marker;accuracy;algorithm;architecture;area under the curve;Article;artificial neural network;cesarean section;convolutional neural network;developmental language disorder;electroencephalogram;electroencephalography (major);female;functional magnetic resonance imaging;human;infant;latent period;learning;machine learning (major);male;nerve potential (major);noise;principal component analysis;psychophysiology;speech (major);stimulus;support vector machine;training

**Updates:** 2021-06-302021-12-17

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Document 141

## **Predicting acute suicidal ideation on Instagram using ensemble machine learning models**

**Author:** Lekkas, Damien 1 ; Klein, Robert J. 2 ; Jacobson, Nicholas C. 3

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**Publication info:** Internet Interventions 25 Elsevier B.V. (Sep 2021)

**Abstract (summary):** Introduction: Online social networking data (SN) is a contextually and temporally rich data stream that has shown promise in the prediction of suicidal thought and behavior. Despite the clear advantages of this digital medium, predictive modeling of acute suicidal ideation (SI) currently remains underdeveloped. SN data, in conjunction with robust machine learning algorithms, may offer a promising way forward. Methods: We applied an ensemble machine learning model on a

previously published dataset of adolescents on Instagram with a prior history of lifetime SI (N = 52) to predict SI within the past month. Using predictors that capture language use and activity within this SN, we evaluated the performance of our out-of-sample, cross-validated model against previous efforts and leveraged a model explainer to further probe relative predictor importance and subject-level phenomenology. Results: Linguistic and SN data predicted acute SI with an accuracy of 0.702 (sensitivity = 0.769, specificity = 0.654, AUC = 0.775). Model introspection showed a higher proportion of SN-derived predictors with substantial impact on prediction compared with linguistic predictors from structured interviews. Further analysis of subject-specific predictor importance uncovered potentially informative trends for future acute SI risk prediction. Conclusion: Application of ensemble learning methodologies to SN data for the prediction of acute SI may mitigate the complexities and modeling challenges of SI that exist within these time scales. Future work is needed on larger, more heterogeneous populations to fine-tune digital **biomarkers** and more robustly test external validity.

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**Author e-mail address:** Damien.Lekkas.GR@dartmouth.edu

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

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**Identifier (keyword):** Digital phenotyping, **Machine learning**, Social media, Suicidal ideation, Suicide prediction

**Language:** English

**Language of abstract:** English

**Number of references:** 57

**Publication date:** Sep 2021



**Publication type:** Journal

**Publisher:** Elsevier B.V.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;adolescent;adult;aphasia;area under the curve;Article;artificial neural network;burnout;decision making;decision tree;electronic health record;external validity;female;human;introspection;language;learning;learning algorithm;machine learning (major);major clinical study;male;mental disease;phenomenology;receiver operating characteristic;risk factor;sensitivity and specificity;social media (major);social network;structured interview;suicidal ideation (major);support vector machine;venous thromboembolism

**Updates:** 2021-07-192021-09-30

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Document 142

## **Exploring test-retest reliability and longitudinal stability of digital biomarkers for parkinson disease in the m-power data set: Cohort study**

**Author:** Far, Mehran Sahandi 1 ; Eickhoff, Simon B. 1 ; Goni, Maria 1 ; Dukart, Juergen 1

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**Publication info:** Journal of Medical Internet Research 23.9 JMIR Publications Inc. (Sep 2021)

**Abstract (summary):** Background: Digital biomarkers (DB), as captured using sensors embedded in modern smart devices, are a promising technology for home-based sign and symptom monitoring in Parkinson disease (PD). Objective: Despite extensive application in recent studies, test-retest reliability and longitudinal stability of DB have not been well addressed in this context. We utilized the large-scale m-Power data set to establish the test-retest reliability and longitudinal stability of gait, balance, voice, and tapping tasks in an unsupervised and self-administered daily life setting in patients with PD and healthy controls (HC). Methods: Intraclass correlation coefficients were computed to estimate the test-retest reliability of features that also differentiate between patients with PD and healthy volunteers. In addition, we tested for longitudinal stability of DB measures in PD and HC, as well as for their sensitivity to PD medication effects. Results: Among the features differing between PD and HC, only a few tapping and voice features had good to excellent test-retest reliabilities and medium to large effect sizes. All other features performed poorly in this respect. Only a few features were sensitive to medication effects. The longitudinal analyses revealed significant alterations over time across a variety of features and in particular for the tapping task. Conclusions: These results indicate the need for further development of more standardized, sensitive, and reliable

DB for application in self-administered remote studies in patients with PD. Motivational, learning, and other confounders may cause variations in performance that need to be considered in DB longitudinal applications.

**Accession number:** 2014675560

**Author e-mail address:** juergen.dukart@gmail.com

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**Correspondence author:** Dukart, Juergen Research Centre Jülich, Institute of Neuroscience and Medicine, Brain & Behaviour (INM-7), Wilhelm-Johnen-Strasse, Jülich, 52425, Germany.

**Database:** Embase®; 1947 to date (1947 - current)

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**First available:** 2021-09-27

**Identifier (keyword):** Biomarkers, Diagnostic markers, Health sciences, Medical research, Mobile phone, Neurological disorders, Parkinson disease

**Language:** English

**Language of abstract:** English

**Number of references:** 54

**Publication date:** Sep 2021

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**Publisher:** JMIR Publications Inc.

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**Subject:** Embase;MEDLINE;biological marker (major);mobile phone;sensor (major);adult;Article;body equilibrium;cohort analysis;confounding variable;controlled study;correlation coefficient;data analysis;effect size;feature extraction;female;finger tapping test;gait;human;intermethod comparison;learning;longitudinal study;male;middle aged;Parkinson disease -- diagnosis (major);task performance;test retest reliability (major);voice

**Updates:** 2021-09-272021-10-052021-10-25

## Automatic and objective speech analysis in Huntington's disease

**Author:** Adams, J. 1 ; Dorsey, E. 1 ; Coffey, M. 1 ; Pawlik, M. 1 ; Tarolli, C. 1 ; Schneider, R. 1 ; Najafi, B. 1 ; Zhou, H. 1 ; Vaziri, A. 1 ; Nguyen, H. 1

1 , Rochester, NY, United States

**Publication info:** Movement Disorder 36.SUPPL 1: S95-S96. John Wiley and Sons Inc. (Sep 2021)

**Abstract (summary):** Objective: To investigate the use of digital technology to assess speech in people with Huntington's disease (HD). Background: Dysarthria is common in Huntington's disease and changes in speech may be detected before the manifest of overt motor symptoms (1,2). Thus, there is potential for using speech biomarkers as an objective indicator of HD symptom onset, which may be useful in diseasemodifying therapies and clinical trials targeting individuals with premanifest and early manifest HD. Methods: 53 participants were included in the analysis (mean age=43.3±13.2 years). 9 participants were classified as prodromal-HD, 22 as manifest HD (UHDRS score=42.0±15.1), and 22 controls. Participants were asked to perform three speech assessment tests at their natural pace and voice: reading of the Rainbow Passage, counting from 1 to 50, and counting backwards from 50 by 3. Data were obtained using a voice recorder with a microphone clipped to the participant collar. Data were sampled at 44.1 kHz. Dysarthria was assessed as part of the UHDRS (average dysarthria score of HD (1.32±0.65), prodromal-HD (0.02±0.15), controls (0.0±0.0)). Acoustic and clinical metrics such as pitch, pitch variation, loudness, loudness variation, and power were extracted for analysis. Univariate analysis was used to compare across groups while adjusting for age, sex and education level. Significance was set at alpha=0.05 and Cohen's coefficient (d) was used to measure effect size. Results: Participants with HD exhibited significantly lower pitch and pitch variation, loudness, speech rate and backwards counting rate, but higher loudness variation and counting error than prodromal-HD patients (d ranges from 0.53-1.57) and controls (d=0.15-2.09), while the largest effect was observed in loudness variation (41% increase, p<0.001, d=1.57 and 58% increase, p<0.001, d=2.09, respectively). Prodromal-HD participants exhibited significantly lower power than controls (p=0.011, d=0.93). The extracted features were able to distinguish between groups with different UHDRS dysarthria scores of 0 (n=32), 1 (n=14), and ≥2 (n=7) (p<0.050, d=0.93-2.85). Conclusions: Digital technology can automatically assess speech performance in people with HD and can differentiate based on disease status and UHDRS dysarthria score. Development of objective and sensitive metrics to assess speech changes early in disease could be beneficial for novel therapies and clinical trials.

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**Conference end date:** 2021-09-22

**Conference location:** Virtual

**Conference start date:** 2021-09-17

**Conference title:** International Parkinson and Movement Disorder Society, MDS 2021

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Adams, J. , Rochester, NY, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1002/mds.28794>

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**Publisher location:** Netherlands

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**Subject:** Embase;adult;conference abstract;controlled study;digital technology;dysarthria;education;educational status (major);effect size;female;human;Huntington chorea (major);loudness;major clinical study;male;microphone;pitch;speech analysis (major);speech rate;Unified Huntington Disease Rating Scale;univariate analysis;voice

**Updates:** 2021-09-30

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Document 144

### **Acoustic speech markers for schizophrenia-spectrum disorders: a diagnostic and symptom-recognition tool**

**Author:** de Boer, J.N. 1 ; Voppel, A.E. 2 ; Brederoo, S.G. 2 ; Schnack, H.G. 3 ; Truong, K.P. 4 ; Wijnen, F.N.K. 5 ; Sommer, I.E.C. 2

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**Publication info:** Psychological medicine : 1-11. NLM (Medline). (Aug 4, 2021)

**Abstract (summary):** BACKGROUND: Clinicians routinely use impressions of **speech** as an element of mental status examination. In schizophrenia-spectrum disorders, descriptions of **speech** are used to assess the severity of psychotic symptoms. In the current study, we assessed the diagnostic value of acoustic **speech** parameters in schizophrenia-spectrum disorders, as well as its value in recognizing positive and negative symptoms. METHODS: **Speech** was obtained from 142 patients with a schizophrenia-spectrum disorder and 142 matched controls during a semi-structured interview on neutral topics. Patients were categorized as having predominantly positive or negative symptoms using the Positive and Negative Syndrome Scale (PANSS). Acoustic parameters were extracted with OpenSMILE, employing the extended Geneva Acoustic Minimalistic Parameter Set, which includes standardized analyses of pitch (F0), **speech** quality and pauses. **Speech** parameters were fed into a random forest algorithm with leave-ten-out cross-validation to assess their value for a schizophrenia-spectrum diagnosis, and PANSS subtype recognition. RESULTS: The **machine-learning speech** classifier attained an accuracy of 86.2% in classifying patients with a schizophrenia-spectrum disorder and controls on **speech** parameters alone. Patients with predominantly positive v. negative symptoms could be classified with an accuracy of 74.2%. CONCLUSIONS: Our results show that automatically extracted **speech** parameters can be used to accurately classify patients with a schizophrenia-spectrum disorder and healthy controls, as well as differentiate between patients with predominantly positive v. negatives symptoms. Thus, the field of **speech** technology has provided a standardized, powerful tool that has high potential for clinical applications in diagnosis and differentiation, given its ease of comparison and replication across samples.

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**Identifier (keyword):** Acoustic, biomarker, language, psychosis, speech

**Language:** English

**Language of abstract:** English

**Publication date:** Aug 4, 2021

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**Publisher:** NLM (Medline)

**Publisher location:** United Kingdom

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**Subject:** MEDLINE;biological marker (major);adult;article;classifier;controlled study;cross validation;diagnosis;diagnostic value;female;human;machine learning;major clinical study;male;negative syndrome (major);pitch;Positive and Negative Syndrome Scale;positive syndrome;random forest (major);schizophrenia (major);semi structured interview;voice parameter (major)

**Updates:** 2021-08-26

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Document 145

## **Screening major depressive disorder using vocal acoustic features in the elderly by sex**

**Author:** Lee, Subin 1 ; Suh, Seung Wan 2 ; Kim, Taehyun 3 ; Kim, Kayoung 3 ; Lee, Kyoung Hwan 3 ; Lee, Ju Ri 3 ; Han, Guehee 3 ; Hong, Jong Woo 3 ; Han, Ji Won 3 ; Lee, Kyogu 4 ; Kim, Ki Woong 5

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**Publication info:** Journal of Affective Disorders 291 : 15-23. Elsevier B.V. (Aug 1, 2021)

**Abstract (summary):** Background: Vocal acoustic features are potential biomarkers of elderly depression. Previous automated diagnostic tests for depression have employed unstandardized speech samples, and few studies have considered differences in voice reactivity. We aimed to develop a voice-based screening test for depression measuring vocal acoustic features of elderly

Koreans while they read a series of mood-inducing sentences (MIS). Methods: In this case-control study, we recruited 61 individuals with major depressive disorder and 143 healthy controls (mean age [SD]: 72 [6]; female, 70%) from the community-dwelling elderly population. Participants were asked to read MIS and their variation pattern of acoustic features represented by the correlation distance between two MIS were analyzed as input features using the univariate feature selection technique and subsequently classified by AdaBoost. Results: Acoustic features showing significant discriminatory performances were spectral and energy-related features for males (sensitivity 0.95, specificity 0.88, and accuracy 0.86) and prosody-related features for females (sensitivity 0.73, specificity 0.86, and accuracy 0.77). The correlation distance between negative and positive MIS was significantly shorter in the depressed group than in the healthy control ( $F = 18.574$ ,  $P < 0.001$ ). Limitations: Small sample size and relatively homogenous clinical profile of depression could limit the generalizability. Conclusions: While reading MIS, spectral and energy-related acoustic features for males and prosody-related features for females are good discriminators for major depressive disorder. These features may be used as **biomarkers** of depression in the elderly.

**Accession number:** 2012084521

**Author e-mail address:** kglee@snu.ac.kr, kwkimmd@snu.ac.kr

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**Correspondence author:** Lee, Kyogu Graduate School of Convergence Science and Technology, Seoul National University, 1 Gwanak-ro, Gwanak-gu, Seoul, 08826, South Korea.

Kim, Ki Woong Department of Neuropsychiatry, Seoul National University, College of Medicine, and Seoul National University Bundang Hospital, 82, Gumi-ro 173beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do, 13620, South Korea.

**Database:** Embase®; 1947 to date (1947 - current)

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**Embase document status:** Embase; In-Data-Review (MEDLINE in Embase)

**First available:** 2021-06-16

**Grant:** All authors have no financial relationships relevant to this article to disclose. None.

**Identifier (keyword):** aged, automated diagnostic system, depressive disorder, **speech** acoustics

**Language:** English

**Language of abstract:** English

**Number of references:** 69

**Publication date:** Aug 1, 2021

**Publication type:** Journal

**Publisher:** Elsevier B.V.

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**Subject:** Embase;MEDLINE;antidepressant agent -- drug therapy -- major depression;antidepressant agent -- special situation for pharmacovigilance -- aged;anxiolytic agent -- drug therapy -- major depression;anxiolytic agent -- special situation for pharmacovigilance -- aged;neuroleptic agent -- drug therapy -- major depression;neuroleptic agent -- special situation for pharmacovigilance -- aged;acoustics (major);aged;Article;case control study;cohort analysis;community dwelling person;controlled study;depression;feature selection;female;Geriatric Depression Scale;human;Korean (people);longitudinal study;major clinical study;major depression -- drug therapy -- antidepressant agent (major);major depression -- drug therapy -- anxiolytic agent (major);major depression -- drug therapy -- neuroleptic agent (major);male;mini international neuropsychiatric interview;Positive and Negative Affect Schedule;prospective study;psychopharmacotherapy;sensitivity and specificity;sex difference (major);speech (major);speech analysis;voice

**Updates:** 2021-06-162021-07-26

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Document 146

## **Detection of Minor and Major Depression through Voice as a Biomarker Using Machine Learning**

**Author:** Shin, Daun 1 ; Cho, Won Ik 2 ; Park, C Hyung Keun 3 ; Rhee, Sang Jin 4 ; Kim, Min Ji 4 ; Lee, Hyunju 1 ; Kim, Nam Soo 2 ; Ahn, Yong Min 5

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**Abstract (summary):** Both minor and major depression have high prevalence and are important causes of social burden worldwide; however, there is still no objective indicator to detect minor



depression. This study aimed to examine if **voice** could be used as a **biomarker** to detect minor and major depression. Ninety-three subjects were classified into three groups: the not depressed group (n = 33), the minor depressive episode group (n = 26), and the major depressive episode group (n = 34), based on current depressive status as a dimension. Twenty-one **voice** features were extracted from semi-structured interview recordings. A three-group comparison was performed through analysis of variance. Seven **voice** indicators showed differences between the three groups, even after adjusting for age, BMI, and drugs taken for non-psychiatric disorders. Among the **machine learning** methods, the best performance was obtained using the multi-layer processing method, and an AUC of 65.9%, sensitivity of 65.6%, and specificity of 66.2% were shown. This study further revealed **voice** differences in depressive episodes and confirmed that not depressed groups and participants with minor and major depression could be accurately distinguished through **machine learning**. Although this study is limited by a small sample size, it is the first study on **voice** change in minor depression and suggests the possibility of detecting minor depression through **voice**.

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Document 147

## **Deep learning-based automated speech detection as a marker of social functioning in late-life depression**

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**Publication info:** Psychological medicine 51.9: 1441-1450. NLM (Medline). (Jul 1, 2021)

**Abstract (summary):** BACKGROUND: Late-life depression (LLD) is associated with poor social functioning. However, previous research uses bias-prone self-report scales to measure social functioning and a more objective measure is lacking. We tested a novel wearable device to measure speech that participants encounter as an indicator of social interaction. METHODS: Twenty nine participants with LLD and 29 age-matched controls wore a wrist-worn device continuously for seven days, which recorded their acoustic environment. Acoustic data were automatically analysed using deep learning models that had been developed and validated on an independent speech dataset. Total speech activity and the proportion of speech produced by the device wearer were both detected whilst maintaining participants' privacy. Participants underwent a neuropsychological test battery and clinical and self-report scales to measure severity of depression, general and social functioning. RESULTS: Compared to controls, participants with LLD showed poorer self-reported social and general functioning. Total speech activity was much lower for participants with LLD than controls, with no overlap between groups. The proportion of speech produced by the participants was smaller for LLD than controls. In LLD, both speech measures correlated with attention and psychomotor speed performance but not with depression severity or self-reported social functioning. CONCLUSIONS:

Using this device, LLD was associated with lower levels of **speech** than controls and **speech** activity was related to psychomotor retardation. We have demonstrated that **speech** activity measured by wearable technology differentiated LLD from controls with high precision and, in this study, provided an objective measure of an aspect of real-world social functioning in LLD.

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**Identifier (keyword):** Ageing, **deep learning**, late-life depression, social functioning, **speech**, wearable technology

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**Subject:** MEDLINE;aged;aging;attention;case control study;electronic device;England;female;human;major depression;male;neuropsychological test;psychology (major);social adaptation;social interaction (major);**speech** (major);very elderly

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Document 148

**Digital biomarkers for neuromuscular disorders: A systematic scoping review**

**Author:** Youn, Bo-Young 1 ; Ko, Youme 2 ; Moon, Seunghwan 1 ; Lee, Jinhee 3 ; Ko, Seung-Gyu 2 ; Kim, Jee-Young 4

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**Abstract (summary):** Biomarkers play a vital role in clinical care. They enable early diagnosis and treatment by identifying a patient's condition and disease course and act as an outcome measure that accurately evaluates the efficacy of a new treatment or drug. Due to the rapid development of digital technologies, digital biomarkers are expected to grow tremendously. In the era of change, this scoping review was conducted to see which digital biomarkers are progressing in neuromuscular disorders, a diverse and broad-range disease group among the neurological diseases, to discover available evidence for their feasibility and reliability. Thus, a total of 10 studies were examined: 9 observational studies and 1 animal study. Of the observational studies, studies were conducted with amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy (DMD), and spinal muscular atrophy (SMA) patients. Non-peer reviewed poster presentations were not considered, as the articles may lead to erroneous results. The only animal study included in the present review investigated the mice model of ALS for detecting rest disturbances using a non-invasive digital biomarker.

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**Subject:** Embase;biological marker -- endogenous compound (major);acceleration;adult;amyotrophic lateral sclerosis;Article;Duchenne muscular dystrophy;female;gravity;heart rate variability;human;language;limb movement;male;middle aged;neuromuscular disease (major);nonhuman;physical activity;semantics;speech;speech rate;spinal muscular atrophy;standing;systematic review;upper limb;velocity;walking parameters

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Document 149

## **Artificial intelligence in neurodegenerative diseases: A review of available tools with a focus on machine learning techniques**

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**Abstract (summary):** Neurodegenerative diseases have shown an increasing incidence in the older population in recent years. A significant amount of research has been conducted to characterize these diseases. Computational methods, and particularly machine learning techniques, are now very useful tools in helping and improving the diagnosis as well as the disease monitoring process. In this paper, we provide an in-depth review on existing computational approaches used in the whole neurodegenerative spectrum, namely for Alzheimer's, Parkinson's, and Huntington's Diseases, Amyotrophic Lateral Sclerosis, and Multiple System Atrophy. We propose a taxonomy of the specific clinical features, and of the existing computational methods. We provide a detailed analysis of the various modalities and decision systems employed for each disease. We identify and present the

sleep disorders which are present in various diseases and which represent an important asset for onset detection. We overview the existing data set resources and evaluation metrics. Finally, we identify current remaining open challenges and discuss future perspectives.

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**Subject:** Embase;MEDLINE;biological marker -- endogenous compound;Alzheimer disease;amyotrophic lateral sclerosis;artificial intelligence (major);bradykinesia;brain depth stimulation;classification algorithm;convolutional neural network;degenerative disease -- diagnosis (major);differential diagnosis;diffuse Lewy body disease;disease classification;dyskinesia;freezing of gait;handwriting;human;Huntington chorea;machine learning (major);mild cognitive impairment;neuroimaging;nuclear magnetic resonance imaging;parasomnia;Parkinson disease;periodic limb movement disorder;positron emission tomography;priority journal;probabilistic neural network;progressive supranuclear palsy;restless legs syndrome;Review;Shy Drager syndrome;speech analysis;speech disorder;support vector machine;tremor

Document 150

## Uncovering the important acoustic features for detecting vocal fold paralysis with explainable machine learning

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**Publication info:** medRxiv : the preprint server for health sciences (Jun 24, 2021)

### Abstract (summary): OBJECTIVE

To detect unilateral vocal fold paralysis (UVFP) from voice recordings using an explainable model of machine learning.

### STUDY DESIGN

Case series - retrospective with a control group.

### SETTING

Tertiary care laryngology practice between 2009 to 2019.

### METHODS

Patients with confirmed UVFP through endoscopic examination (N=77) and controls with normal voices matched for age and sex (N=77) were included. Two tasks were used to elicit voice samples: reading the Rainbow Passage and sustaining phonation of the vowel "a". The 88 extended Geneva Minimalistic Acoustic Parameter Set (eGeMAPS) features were extracted as inputs for four machine learning models of differing complexity. SHAP was used to identify important features.

## RESULTS

The median bootstrapped Area Under the Receiver Operating Characteristic Curve (ROC AUC) score ranged from 0.79 to 0.87 depending on model and task. After removing redundant features for explainability, the highest median ROC AUC score was 0.84 using only 13 features for the vowel task and 0.87 using 39 features for the reading task. The most important features included intensity measures, mean MFCC1, mean F1 amplitude and frequency, and shimmer variability depending on model and task.

## CONCLUSION

Using the largest dataset studying UVFP to date, we achieve high performance from just a few seconds of **voice** recordings. Notably, we demonstrate that while similar categories of features related to **vocal** fold physiology were conserved across models, the models used different combinations of features and still achieved similar effect sizes. **Machine learning** thus provides a mechanism to detect UVFP and contextualize the accuracy relative to both model architecture and pathophysiology.

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**Correspondence author:** Low, Daniel M Program in Speech and Hearing Bioscience and Technology, Harvard Medical School, Boston, MA, USA. , Department of Brain and Cognitive Sciences, MIT, Cambridge, MA, USA. , McGovern Institute for Brain Research, MIT, Cambridge, MA, USA.

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**Identifier (keyword):** acoustic analysis, **biomarkers**, explainability, interpretability, **machine learning**, **speech**, **vocal** fold paralysis, **voice**

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Document 151

## **Validation of Visual and Auditory Digital Markers of Suicidality in Acutely Suicidal Psychiatric Inpatients: Proof-of-Concept Study**

**Author:** Galatzer-Levy, Isaac 1 ; Abbas, Anzar 2 ; Ries, Anja 3 ; Homan, Stephanie 3 ; Sels, Laura 4 ; Koesmahargyo, Vidya 2 ; Yadav, Vijay 2 ; Colla, Michael 5 ; Scheerer, Hanne 5 ; Vetter, Stefan 5 ; Seifritz, Erich 6 ; Scholz, Urte 5 ; Kleim, Birgit 3

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### **Abstract (summary): BACKGROUND**

Multiple symptoms of suicide risk have been assessed based on visual and auditory information, including flattened affect, reduced movement, and slowed **speech**. Objective quantification of such symptomatology from novel data sources can increase the sensitivity, scalability, and timeliness of suicide risk assessment.

## OBJECTIVE

We aimed to examine measurements extracted from video interviews using open-source **deep learning** algorithms to quantify facial, **vocal**, and movement behaviors in relation to suicide risk severity in recently admitted patients following a suicide attempt.

## METHODS

We utilized video to quantify facial, **vocal**, and movement markers associated with mood, emotion, and motor functioning from a structured clinical conversation in 20 patients admitted to a psychiatric hospital following a suicide risk attempt. Measures were calculated using open-source **deep learning** algorithms for processing facial expressivity, head movement, and **vocal** characteristics. Derived digital measures of flattened affect, reduced movement, and slowed **speech** were compared to suicide risk with the Beck Scale for Suicide Ideation controlling for age and sex, using multiple linear regression.

## RESULTS

Suicide severity was associated with multiple visual and auditory markers, including **speech** prevalence ( $\beta=-0.68$ ,  $P=.02$ ,  $r^2=0.40$ ), overall expressivity ( $\beta=-0.46$ ,  $P=.10$ ,  $r^2=0.27$ ), and head movement measured as head pitch variability ( $\beta=-1.24$ ,  $P=.006$ ,  $r^2=0.48$ ) and head yaw variability ( $\beta=-0.54$ ,  $P=.06$ ,  $r^2=0.32$ ).

## CONCLUSIONS

Digital measurements of facial affect, movement, and **speech** prevalence demonstrated strong effect sizes and linear associations with the severity of suicidal ideation.

**Accession number:** 34081022

**Copyright:** ©Isaac Galatzer-Levy, Anzar Abbas, Anja Ries, Stephanie Homan, Laura Sels, Vidya Koesmahargyo, Vijay Yadav, Michael Colla, Hanne Scheerer, Stefan Vetter, Erich Seifritz, Urte Scholz, Birgit Kleim. Originally published in the Journal of Medical Internet Research (<https://www.jmir.org>), 03.06.2021.

**Correspondence author:** Galatzer-Levy, Isaac Research and Development, AiCure, New York, NY, United States. , Psychiatry, New York University School of Medicine, New York, NY, United States.

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Document 152

## **Data mining of an acoustic **biomarker** in tongue cancers and its clinical validation**

**Author:** Xiao, Yudong 1 ; Wang, Tao 1 ; Deng, Wei 1 ; Yang, Le 1 ; Zeng, Bin 1 ; Lao, Xiaomei 1 ; Zhang, Sien 1 ; Liu, Xiangqi 1 ; Ouyang, Daiqiao 1 ; Liao, Guiqing 1 ; Liang, Yujie 1

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**Publication info:** Cancer Medicine 10.11: 3822-3835. John Wiley and Sons Inc. (Jun 2021)

**Abstract (summary):** The promise of **speech** disorders as **biomarkers** in clinical examination has been identified in a broad spectrum of neurodegenerative diseases. However, to the best of our knowledge, a validated acoustic marker with established discriminative and evaluative properties has not yet been developed for oral tongue cancers. Here we cross-sectionally collected a screening dataset that included acoustic parameters extracted from 3 sustained vowels /a/, /i/, /u/ and binary perceptual outcomes from 12 consonant-vowel syllables. We used a **support vector machine** with linear kernel function within this dataset to identify the formant centralization ratio (FCR) as a dominant predictor of different perceptual outcomes across gender and syllable. The Acoustic

analysis, Perceptual evaluation and Quality of Life assessment (APeQoL) was used to validate the FCR in 33 patients with primary resectable oral tongue cancers. Measurements were taken before (pre-op) and four to six weeks after (post-op) surgery. The **speech** handicap index (SHI), a **speech**-specific questionnaire, was also administered at these time points. Pre-op correlation analysis within the APeQoL revealed overall consistency and a strong correlation between FCR and SHI scores. FCRs also increased significantly with increasing T classification pre-operatively, especially for women. Longitudinally, the main effects of T classification, the extent of resection, and their interaction effects with time (pre-op vs. post-op) on FCRs were all significant. For pre-operative FCR, after merging the two datasets, a cut-off value of 0.970 produced an AUC of 0.861 (95% confidence interval: 0.785–0.938) for T<sub>3-4</sub> patients. In sum, this study determined that FCR is an acoustic marker with the potential to detect disease and related **speech** function in oral tongue cancers. These are preliminary findings that need to be replicated in longitudinal studies and/or larger cohorts.

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Liang, Yujie Department of Oral and Maxillofacial Surgery, Guanghua School of Stomatology, Guangdong Provincial Key Laboratory of Stomatology, Sun Yat-sen University, Guangzhou, China.

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**Identifier (keyword):** acoustic analysis, diagnostic tests, quality of life, **speechbiomarker**, **support vector machine**, tongue cancer

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Document 153

## Using i-vectors from voice features to identify major depressive disorder

**Author:** Di, Yazheng 1 ; Wang, Jingying 2 ; Li, Weidong 3 ; Zhu, Tingshao 1

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**Abstract (summary):** Background: Machine-learning methods using acoustic features in the diagnosis of major depressive disorder (MDD) have insufficient evidence from large-scale samples and clinical trials. This study aimed to evaluate the effectiveness of the promising i-vector method on a large sample of women with recurrent MDD diagnosed clinically, examine its robustness, and provide an explicit acoustic explanation of the i-vectors. Methods: We collected utterances edited from clinical interview speech records of 785 depressed and 1,023 healthy individuals. Then, we extracted Mel-frequency cepstral coefficient (MFCC) features and MFCC i-vectors from their utterances. To examine the effectiveness of i-vectors, we compared the performance of binary logistic regression between MFCC i-vectors and MFCC features and tested its robustness on different utterance durations. We also determined the correlation between MFCC features and MFCC i-vectors to analyze the acoustic meaning of i-vectors. Results: The i-vectors improved 7% and 14% of area under the curve (AUC) for MFCC features using different utterances. When the duration is >40 s, the classification results are stabilized. The i-vectors are consistently correlated to the maximum,

minimum, and deviations of MFCC features (either positively or negatively). Limitations: This study included only women. Conclusions: The i-vectors can improve 14% of the AUC on a large-scale clinical sample. This system is robust to utterance duration >40 s. This study provides a foundation for exploring the clinical application of **voice** features in the diagnosis of MDD.

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Zhu, Tingshao CAS Key Laboratory of Behavioral Science, Institute of Psychology, 16 Lincui Road, Chaoyang District, Beijing, 100101, China.

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**Subject:** Embase;MEDLINE;**biological marker** (major);acoustic analysis;adult;Article;**binary classification**;case control study;clinical effectiveness;clinical evaluation;constants and

coefficients;controlled study;correlation coefficient;cross validation;diagnostic test accuracy study;feature extraction;female;human;i vector method + (major);intermethod comparison;interview;logistic regression analysis;machine learning (major);major clinical study;major depression -- diagnosis (major);mel frequency cepstral coefficient +;mental patient;priority journal;psychiatric diagnosis;sensitivity and specificity;speech analysis;voice (major)

**Updates:** 2021-05-102021-05-24

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Document 154

## **Noninvasive Vocal Biomarker is Associated With Severe Acute Respiratory Syndrome Coronavirus 2 Infection**

**Author:** Maor, Elad 1 ; Tsur, Nir 2 ; Barkai, Galia 3 ; Meister, Ido 4 ; Makmel, Shmuel 4 ; Friedman, Eli 4 ; Aronovich, Daniel 5 ; Mevorach, Dana 5 ; Lerman, Amir 6 ; Zimlichman, Eyal 1 ; Bachar, Gideon 7

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**Publication info:** Mayo Clinic Proceedings: Innovations, Quality and Outcomes 5.3: 654-662. Elsevier B.V. (Jun 2021)

**Abstract (summary):** Objective: To investigate the association of voice analysis with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Patients and Methods: A vocal biomarker, a unitless scalar with a value between 0 and 1, was developed based on 434 voice samples. The biomarker training was followed by a prospective, multicenter, observational study. All subjects were tested for SARS-CoV-2, had their voice recorded to a smartphone application, and gave their informed consent to participate in the study. The association of SARS-CoV-2 infection with the vocal biomarker was evaluated. Results: The final study population included 80 subjects with a median age of 29 [range, 23 to 36] years, of whom 68% were men. Forty patients were positive for SARS-CoV-2. Infected patients were 12 times more likely to report at least one symptom (odds ratio, 11.8;  $P < .001$ ). The vocal biomarker was significantly higher among infected patients (OR, 0.11; 95% CI, 0.06 to 0.17 vs OR, 0.19; 95% CI, 0.12 to 0.3;  $P = .001$ ). The area under the receiver operating characteristic curve evaluating the association of the vocal biomarker with SARS-CoV-2 status was

72%. With a **biomarker** threshold of 0.115, the results translated to a sensitivity and specificity of 85% (95% CI, 70% to 94%) and 53% (95% CI, 36% to 69%), respectively. When added to a self-reported symptom classifier, the area under the curve significantly improved from 0.775 to 0.85. Conclusion: **Voice** analysis is associated with SARS-CoV-2 status and holds the potential to improve the accuracy of self-reported symptom-based screening tools. This pilot study suggests a possible role for **vocal biomarkers** in screening for SARS-CoV-2–infected subjects.

**Accession number:** 2013004358

**Author e-mail address:** Elad.Maor@Sheba.health.gov.il

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Maor, Elad Leviev Heart Center, Sheba Medical Center, Tel Hashomer, Derech Sheba 2, Ramat Gan, Israel.

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**Language:** English

**Language of abstract:** English

**Number of references:** 17

**Publication date:** Jun 2021

**Publication type:** Journal

**Publisher:** Elsevier B.V.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;**biological marker** (major);SARS coronavirus 2 nucleic acid test kit;smartphone;adult;algorithm;anosmia;area under the curve;Article;association;asthma;chronic



kidney failure; classifier; comorbidity; controlled study; coronavirus disease 2019 -- diagnosis (major); coughing; diabetes mellitus; diagnostic test accuracy study; dyspnea; female; fever; gastroesophageal reflux; heart failure -- diagnosis; human; hypertension; informed consent; lung congestion -- diagnosis; lung edema -- diagnosis; major clinical study; male; multicenter study; neurologic disease; non invasive procedure; obesity; observational study; pilot study; prospective study; pulmonary hypertension -- diagnosis; receiver operating characteristic; rhinorrhea; self report; sensitivity and specificity; severe acute respiratory syndrome -- diagnosis (major); Severe acute respiratory syndrome coronavirus 2 (major); smoking; symptom; telemedicine; viral respiratory tract infection -- diagnosis; vocal cord; voice analysis (major)

**Updates:** 2021-06-16 2021-06-25 2021-09-21

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Document 155

## Voice Analysis to Differentiate the Dopaminergic Response in People With Parkinson's Disease

**Author:** Jain, Anubhav 1 ; Abedinpour, Kian 2 ; Polat, Ozgur 1 ; Çalışkan, Mine Melodi 3 ; Asaei, Afsaneh 1 ; Pfister, Franz M. J. 4 ; Fietzek, Urban M. 5 ; Cernak, Milos 6

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**Publication info:** Frontiers in Human Neuroscience 15 Frontiers Media S.A. (May 31, 2021)

**Abstract (summary):** Humans' voice offers the widest variety of motor phenomena of any human activity. However, its clinical evaluation in people with movement disorders such as Parkinson's disease (PD) lags behind current knowledge on advanced analytical automatic speech processing methodology. Here, we use deep learning-based speech processing to differentially analyze voice recordings in 14 people with PD before and after dopaminergic medication using personalized Convolutional Recurrent Neural Networks (p-CRNN) and Phone Attribute Codebooks (PAC). p-CRNN yields an accuracy of 82.35% in the binary classification of ON and OFF motor states at a sensitivity/specificity of 0.86/0.78. The PAC-based approach's accuracy was slightly lower with 73.08% at a sensitivity/specificity of 0.69/0.77, but this method offers easier interpretation and understanding of the computational biomarkers. Both p-CRNN and PAC provide a differentiated view and novel insights into the distinctive components of the speech of persons with PD. Both methods

detect **voice** qualities that are amenable to dopaminergic treatment, including active **phonetic** and prosodic features. Our findings may pave the way for quantitative measurements of **speech** in persons with PD.

**Accession number:** 635264087

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**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

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Cernak, Milos Logitech Europe, École polytechnique fédérale de Lausanne - Quartier de l'Innovation, Lausanne, Switzerland.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document type:** Article

**DOI:** <http://dx.doi.org/10.3389/fnhum.2021.667997>

**Embase document status:** Embase

**First available:** 2021-06-16

**Identifier (keyword):** dopaminergic response, motor state, Parkinson's disease, **speech**, **voice**

**Language:** English

**Language of abstract:** English

**Number of references:** 29

**Publication date:** May 31, 2021

**Publication type:** Journal

**Publisher:** Frontiers Media S.A.

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**Subject:** Embase;**biological marker**;dopamine receptor stimulating agent (major);levodopa;electrode;microphone;adult;aged;Article;**binary classification**;bradykinesia;brain depth stimulation;cerebellar ataxia;clinical article;clinical trial;controlled study;**deep learning**;degenerative disease;disease duration;**dysarthria**;electroencephalography;female;human;image segmentation;**machine learning**;male;motor dysfunction;nerve cell plasticity;neuropsychological test;Parkinson disease (major);**phonetics**;quantitative analysis;**recurrent neural network**;sensitivity and specificity;signal

processing; speech analysis; speech disorder; speech perception; speech therapy; voice analysis  
(major)

**Substance:** Substance Substance: levodopa; CAS: 59-92-7;

**Updates:** 2021-06-16 2021-12-06

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Document 156

## **Amyloid beta associations with connected speech in cognitively unimpaired adults**

**Author:** Mueller, Kimberly D 1 ; Van Hulle, Carol A 2 ; Kosciak, Rebecca L 3 ; Jonaitis, Erin 4 ; Peters, Cassandra C 5 ; Betthausen, Tobey J 2 ; Christian, Bradley 6 ; Chin, Nathaniel 7 ; Hermann, Bruce P 8 ; Johnson, Sterling 9

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**Publication info:** Alzheimer's & dementia (Amsterdam, Netherlands) 13.1: e12203. (May 27, 2021)

## **Abstract (summary): INTRODUCTION**

Connected **speech** and language (CSL) decline has been associated with early cognitive decline, but associations between CSL and Alzheimer's disease (AD) **biomarkers** remain a gap in the literature. Our goal was to examine associations with amyloid beta (A $\beta$ ) and longitudinal CSL trajectories in cognitively unimpaired adults at increased AD risk.

## **METHODS**

Using data from the Wisconsin Registry for Alzheimer's Prevention, CSL measures were automatically extracted from **digitally** recorded picture descriptions. Positron emission tomography determined A $\beta$  status. Linear mixed effects models assessed the interaction between age and A $\beta$  on CSL trajectories.

## **RESULTS**

Participants who were A $\beta$  positive experienced more rapid decline on specific word content, when controlling for age, sex, and literacy. There were no differences between groups in lexical diversity measures over time.

## **DISCUSSION**

These results indicate that declines in connected **speech** may be related to preclinical AD. CSL may be a promising, inexpensive, and easy-to-collect **digital** cognitive marker for AD studies.

**Accession number:** 34095435

**Copyright:** © 2021 The Authors. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring published by Wiley Periodicals, LLC on behalf of Alzheimer's Association.

**Correspondence author:** Mueller, Kimberly D Department of Communication Sciences and Disorders University of Wisconsin-Madison Madison Wisconsin USA. , Wisconsin Alzheimer's Disease Research Center University of Wisconsin School of Medicine and Public Health Madison Wisconsin USA. , Wisconsin Alzheimer's Institute University of Wisconsin School of Medicine and Public Health Madison Wisconsin USA. , Division of Geriatrics and Gerontology Department of Medicine University of Wisconsin School of Medicine & Public Health Madison Wisconsin USA.

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**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1002/dad2.12203>

**First available:** 2021-06-07

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R01 AG027161. NIA NIH HHS. United States.

RF1 AG027161. NIA NIH HHS. United States.

**Identifier (keyword):** Alzheimer's disease, Mild Cognitive Impairment, PET imaging, Pittsburgh Compound-B; **speech**, computational linguistics, connected **speech**, dementia, discourse, language, picture description, preclinical Alzheimer's disease

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Aside from external funding listed in the acknowledgments, no other authors have disclosures to report.;; Publication model: Electronic-eCollection;; Cited medium:Print

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Document 157

### **Automated, multiparametric monitoring of respiratory **biomarkers** and vital signs in clinical and home settings for COVID-19 patients**

**Author:** Ni, Xiaoyue 1 ; Ouyang, Wei 2 ; Jeong, Hyoyoung 2 ; Kim, Jin-Tae 2 ; Tzaveils, Andreas 3 ; Mirzazadeh, Ali 4 ; Wu, Changsheng 2 ; Lee, Jong Yoon 5 ; Keller, Matthew 6 ; Mummidisetty, Chaithanya K 7 ; Patel, Manish 8 ; Shawen, Nicholas 7 ; Huang, Joy 9 ; Chen, Hope 9 ; Ravi, Sowmya 10 ; Chang, Jan-Kai 11 ; Lee, KunHyuck 12 ; Wu, Yixin 12 ; Lie, Ferrona 2 ; Kang, Youn J 2 ; Kim, Jong Uk 13 ; Chamorro, Leonardo P 14 ; Banks, Anthony R 2 ; Bharat, Ankit 15 ; Jayaraman, Arun 7 ; Xu, Shuai 16 ; Rogers, John A 17

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Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208, Department of Biomedical Engineering, Northwestern University, Evanston, IL 60208, Medical Scientist Training Program, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611 4 College of Computing, Georgia Institute of Technology, Atlanta, GA 30332 5 Sibel Inc., Niles, IL 60714 6 Sonica Health, Niles, IL 60714 7 Max Nader Lab for Rehabilitation Technologies and Outcomes Research, Center for Bionic Medicine, Shirley Ryan AbilityLab, Chicago, IL 60611 8 Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208, College of Medicine, University of Illinois at Chicago, Chicago, IL 60612 9 Feinberg School of Medicine, Northwestern University, Chicago, IL 60611 10 Division of Thoracic Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611 11 Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208, Wearifi Inc., Evanston, IL 60201 12 Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208, Department of Materials Science and Engineering, Northwestern University, Evanston, IL 60208 13 School of Chemical Engineering, Sungkyunkwan University, Suwon, 16419, Republic of Korea, Republic of Korea 14 Department of Mechanical Science and Engineering, University of Illinois at Urbana-Champaign, Champaign, IL 61801 15 Department of Surgery, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611 16 Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208; stevexu@northwestern.edu, Department of Dermatology, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611 jrogers@northwestern.edu 17 Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208; stevexu@northwestern.edu, Department of Biomedical Engineering, Northwestern University, Evanston, IL 60208, Department of Materials Science and Engineering, Northwestern University, Evanston, IL 60208, Department of Mechanical Engineering, Northwestern University, Evanston, IL 60208, Department of Chemistry, Northwestern University, Evanston, IL 60208, Department of Electrical Engineering and Computer Science, Northwestern University, Evanston, IL 60208, Department of Neurological Surgery, Northwestern University, Evanston, IL 60208 jrogers@northwestern.edu

**Publication info:** Proceedings of the National Academy of Sciences of the United States of America 118.19 (May 11, 2021)

**Abstract (summary):** Capabilities in continuous monitoring of key physiological parameters of disease have never been more important than in the context of the global COVID-19 pandemic. Soft, skin-mounted electronics that incorporate high-bandwidth, miniaturized motion sensors enable digital, wireless measurements of mechanoacoustic (MA) signatures of both core vital signs (heart rate, respiratory rate, and temperature) and underexplored **biomarkers** (coughing count) with high fidelity and immunity to ambient noises. This paper summarizes an effort that integrates such MA sensors with a cloud data infrastructure and a set of analytics approaches based on digital filtering and **convolutional neural networks** for monitoring of COVID-19 infections in sick and healthy individuals in the hospital and the home. Unique features are in quantitative measurements of coughing and other **vocal** events, as indicators of both disease and infectiousness. Systematic imaging studies demonstrate correlations between the time and intensity of coughing, speaking, and laughing and the total droplet production, as an approximate indicator of the probability for disease spread. The sensors, deployed on COVID-19 patients along with healthy controls in both inpatient and home settings, record coughing frequency and intensity continuously, along with a collection of other

biometrics. The results indicate a decaying trend of coughing frequency and intensity through the course of disease recovery, but with wide variations across patient populations. The methodology creates opportunities to study patterns in biometrics across individuals and among different demographic groups.

**Accession number:** 33893178

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**Identifier (keyword):** COVID-19, **biomarkers**, digital health, respiratory disease, wearable electronics

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** **Biomarkers**; COVID-19 -- physiopathology (major); Heart Rate (major); Humans; Monitoring, Physiologic; Respiratory Rate (major); Respiratory Sounds (major); SARS-CoV-2 (major); Wireless Technology (major)

**Notes:** Competing interest statement: X.N., H.J., J.Y.L., K.L., A.J., S.X., and J.A.R. report inventorships and potential royalties in patents assigned to Northwestern University. M.K. and J.Y.L. are employees of a small private company with a commercial interest in the technology. A.R.B., S.X.,

and J.A.R. report equity ownership in a small private company with a commercial interest in the technology.; Publication model: Print;; Cited medium:Internet

**Publication date:** May 11, 2021

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**Substance:** Substance Substance: Biomarkers; CAS: 0;

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Document 158

## **A Study of Novel Exploratory Tools, Digital Technologies, and Central Nervous System Biomarkers to Characterize Unipolar Depression**

**Author:** Sverdlov, Oleksandr 1 ; Curcic, Jelena 2 ; Hannesdottir, Kristin 3 ; Gou, Liangke 1 ; De Luca, Valeria 2 ; Ambrosetti, Francesco 2 ; Zhang, Bingsong 4 ; Praestgaard, Jens 3 ; Vallejo, Vanessa 2 ; Dolman, Andrew 3 ; Gomez-Mancilla, Baltazar 2 ; Biliouris, Konstantinos 3 ; Deurinck, Mark 2 ; Cormack, Francesca 5 ; Anderson, John J. 6 ; Bott, Nicholas T. 7 ; Peremen, Ziv 8 ; Issachar, Gil 8 ; Laufer, Offir 8 ; Joachim, Dale 9 ; Jagesar, Raj R. 10 ; Jongs, Niels 10 ; Kas, Martien J. 10 ; Zhuparris, Ahnjili 11 ; Zuiker, Rob 11 ; Recourt, Kasper 11 ; Zuilhof, Zoë 11 ; Cha, Jang-Ho 3 ; Jacobs, Gabriel E. 12

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**Publication info:** Frontiers in Psychiatry 12 Frontiers Media S.A. (May 6, 2021)

**Abstract (summary):** Background: Digital technologies have the potential to provide objective and precise tools to detect depression-related symptoms. Deployment of digital technologies in clinical research can enable collection of large volumes of clinically relevant data that may not be captured using conventional psychometric questionnaires and patient-reported outcomes. Rigorous



methodology studies to develop novel **digital** endpoints in depression are warranted. Objective: We conducted an exploratory, cross-sectional study to evaluate several **digital** technologies in subjects with major depressive disorder (MDD) and persistent depressive disorder (PDD), and healthy controls. The study aimed at assessing utility and accuracy of the **digital** technologies as potential diagnostic tools for unipolar depression, as well as correlating **digital biomarkers** to clinically validated psychometric questionnaires in depression. Methods: A cross-sectional, non-interventional study of 20 participants with unipolar depression (MDD and PDD/dysthymia) and 20 healthy controls was conducted at the Centre for Human Drug Research (CHDR), the Netherlands. Eligible participants attended three in-clinic visits (days 1, 7, and 14), at which they underwent a series of assessments, including conventional clinical psychometric questionnaires and **digital** technologies. Between the visits, there was at-home collection of data through mobile applications. In all, seven **digital** technologies were evaluated in this study. Three technologies were administered via mobile applications: an interactive tool for the self-assessment of mood, and a cognitive test; a passive behavioral monitor to assess social interactions and global mobility; and a platform to perform **voice** recordings and obtain **vocal biomarkers**. Four technologies were evaluated in the clinic: a neuropsychological test battery; an eye motor tracking system; a standard high-density electroencephalogram (EEG)-based technology to analyze the brain network activity during cognitive testing; and a task quantifying bias in emotion perception. Results: Our data analysis was organized by technology – to better understand individual features of various technologies. In many cases, we obtained simple, parsimonious models that have reasonably high diagnostic accuracy and potential to predict standard clinical outcome in depression. Conclusion: This study generated many useful insights for future methodology studies of **digital** technologies and proof-of-concept clinical trials in depression and possibly other indications.

**Accession number:** 635070696

**Author e-mail address:** alex.sverdlov@novartis.com

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Sverdlov, Oleksandr Novartis Pharmaceuticals Corporation, East Hanover, NJ, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Device trade name:** Device trade name Name: BeHapp; Manufacturer: Undefined;

Name: Cognition Kit; Manufacturer: Undefined;

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Name: Neurocart; Manufacturer: Undefined;

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**Identifier (keyword):** digitalbiomarkers, major depression, mobile health, novel endpoints, variable selection

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**Subject:** Embase;biological marker (major);BeHapp +;Cognition Kit +;EIMindA BNA +;eye movement monitor;mobile health application;Neurocart +;Neurotrack +;Sonde Health +;adult;Article;brain function (major);clinical article;cognition assessment;controlled study;cross-sectional study;depression -- diagnosis;diagnostic accuracy;diagnostic test accuracy study;digital technology (major);dysthymia -- diagnosis;electroencephalogram;emotional bias task +;exploratory research;female;human;major depression -- diagnosis (major);male;mood;Netherlands;neuropsychological test;persistent depressive disorder + -- diagnosis;predictive value;questionnaire;receiver operating characteristic;sensitivity and specificity;social interaction;voice analysis

**Updates:** 2021-05-272021-11-01

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Document 159

## Computer Vision and Voice Analysis for Diagnostic Assessment of PTSD, Depression, and Neurocognitive Functioning

**Author:** Schultebrucks, Katharina 1 ; Galatzer-Levy, Isaac 2

1 Columbia University Medical Center 2 AiCure

**Publication info:** Biological Psychiatry, suppl. Supplement 89.9: S19. Elsevier Inc. (May 1, 2021)

**Abstract (summary):** Background: The clinical and diagnostic assessment of psychiatric diagnosis and neurocognitive functioning is burdensome, time-consuming, and cost-intensive. Direct measurement and quantification of visual and auditory signs provide a promising alternative through the application of machine learning (ML) based on accessible and passively collected data sources. We investigated whether computer vision, semantic, and acoustic analysis based on ML can be used to accurately assess Posttraumatic Stress Disorder (PTSD) and Major Depressive Disorder (MDD) and cognitive functioning. Methods: We used computer vision and voice analysis. We extracted facial, voice, speech, and movement characteristics from an unstructured clinical interview (N=81), one month after admission to a Level-1 Trauma Unit following a life-threatening traumatic event. Digital markers were used as inputs to classify PTSD and MDD status and to identify predictive signals of cognitive functioning. Cross-validation procedures were used to evaluate the predictive performance. Results: Video- and audio-based markers were able to accurately discriminate PTSD status (AUC=0.90, precision=0.83, recall=0.84, and f1-score=0.83) and depression status (AUC=0.86, precision=0.83, recall=0.82, and f1-score=0.82). Additionally, digital markers accounted for large variance in cognitive functioning (motor coordination: R2=0.54; processing speed: R2=0.42; emotional bias: R2=0.54; sustained attention: R2=0.50; controlled attention: R2=0.45; cognitive flexibility: R2=0.56; cognitive inhibition: R2=0.69; executive functioning: R2=0.60). Conclusions: Digital markers identified in direct clinical observation during posttraumatic free speech can be used to classify PTSD and MDD status. Additionally, automated measurement of reliable proxies for cognitive functioning is a very promising high-priority research topic. Digital biomarkers could improve the scalability of clinical assessments using low burden, passive patient evaluations. Supported By: NIMH K01MH102415 (Isaac Galatzer-Levy); DFG SCHU 3259/1-1 (Katharina Schultebrucks) Keywords: Computer Vision, Digital Biomarkers, PTSD - Posttraumatic Stress Disorder, Neurocognitive Functioning, Depression

**Accession number:** 2011560587

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**Conference start date:** 2021-04-24

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**Subject:** Embase;biological marker;adult;attention;clinical assessment;clinical evaluation;clinical observation;cognitive flexibility;computer vision (major);conference abstract;controlled study;cross validation;diagnosis;emotional bias;executive function;face;female;human;interview;major clinical study;major depression;male;motor coordination;posttraumatic stress disorder (major);processing speed;recall;speech;videorecording;voice analysis (major)

**Updates:** 2021-04-12

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Document 160

## **Validation of Visual and Auditory Digital Markers of Suicidality in Acutely Suicidal Psychiatric In-Patients**

**Author:** Ries, Anja 1 ; Abbas, Anzar 2 ; Homan, Stephanie 1 ; Koesmahargyo, Vidya 2 ; Yadav, Vijay 2 ; Colla, Michael 3 ; Scheerer, Hanne 3 ; Vetter, Stefan 3 ; Seifritz, Erich 3 ; Scholz, Urte 4 ; Galatzer-Levy, Isaac 2 ; Kleim, Birgit 1

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**Publication info:** Biological Psychiatry, suppl. Supplement 89.9: S19-S20. Elsevier Inc. (May 1, 2021)

**Abstract (summary):** Background: Multiple symptoms of suicide risk are assessed based on visual and auditory information including flattened affect, reduced movement, and slowed speech. Objective quantification of such symptomatology from unstructured data sources can increase the sensitivity,

scalability, and timeliness of suicide risk assessment. Methods: In the current study we utilized video to quantify facial, **vocal**, and movement markers associated with mood, emotion, and motor functioning from an open-ended clinical conversation in n = 20 patients admitted to a psychiatric hospital following a suicide risk attempt. Measures were calculated using open-source **deep learning** algorithms for processing facial expressivity, head movement, and **vocal** characteristics. Derived digital measures of flattened affect, reduced movement, and slowed **speech** were compared to suicide severity using the Beck Suicide Scale (BSS), controlling for age and gender using multiple linear regression. Results: Suicide severity was associated with multiple visual and auditory markers including **speech** prevalence ( $\beta = -0.68$ ;  $p < .01$ ,  $r^2 = .40$ ), overall expressivity ( $\beta = -0.46$ ;  $p = .10$ ,  $r^2 = .27$ ), and head movement, measured as head pitch variability ( $\beta = -1.24$ ;  $p < .01$ ,  $r^2 = .48$ ) and head yaw variability ( $\beta = -0.54$ ;  $p < .05$ ,  $r^2 = .32$ ). Conclusions: Digital measurements of flattened affect, movement, and **speech** prevalence demonstrated significant linear associations with suicide severity. Supported By: Swiss National Science Foundation Keywords: Suicide, Suicide Risk Factors, Digital Biomarkers, **Deep Learning**, Visual and Auditory Markers

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**Subject:** Embase;biological marker;adult;algorithm (major);clinical article;conference abstract;controlled study;conversation;deep learning;face;female;gender;genetic marker;head movement;hospital patient (major);human;male;mental hospital;mood;motor performance;pitch;prevalence;quantitative analysis;risk factor;speech;suicide (major);videorecording

**Updates:** 2021-04-12

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Document 161

## Using Computerized Human Language Technology to Generate Biomarkers for Disturbances in Language

**Author:** Krell, Rony 1 ; Tang, Wenqing 1 ; Hänsel, Katrin 2 ; Sobolev, Michael 2 ; Cho, Sunghye 3 ; Berretta, Sarah 4 ; Mehta, Aarush 4 ; Liberman, Mark 3 ; Tang, Sunny 5

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**Publication info:** Biological Psychiatry, suppl. Supplement 89.9: S375. Elsevier Inc. (May 1, 2021)

**Abstract (summary):** Background: Computerized human language technology (HLT), including automated analysis of acoustic and lexical features, presents a promising opportunity to identify scalable biomarkers for psychiatric disorders, particularly psychotic disorders. It is not understood how individual dimensions of speech disturbance, like poverty or perseveration, can be modeled by HLT-derived features. Methods: We identified 20 speech samples from YouTube videos of clinical interviews depicting individuals identified as having psychotic disorders. Three experts provided consensus ratings on the Scale for the Assessment of Thought Language and Communication Disorders (TLC) and the inflection and latency items from the Scale for the Assessment of Negative Symptoms (SANS). Twenty-four NLP measures were derived from each sample, including semantic, coherence, acoustic, and text-aligned features. A Least Absolute Shrinkage and Selection Operator (LASSO) regression model was trained on 80% of the data using 10-fold cross-validation to predict clinical language ratings. Results: In the test sample, LASSO models resulted in positive R2 values for four clinical measures: poverty of speech (R2=0.57), perseveration (R2=0.52), vocal inflection (R2=0.20), and latency (R2=0.53). Predictors included coherence, total words spoken, speaking rate, and incomplete words, but sometimes loaded in opposite directions for different clinical parameters. E.g., A coherence measure was positively correlated with poverty of speech, but negatively correlated with perseveration. Conclusions: A combination of acoustic and lexical HLT-derived features predicted clinical ratings of speech disturbance. However, different dimensions of speech disturbance, like poverty of speech versus perseveration, should be considered as separate entities and not aggregated into a single dimension of disordered language for these purposes. Supported By: NARSAD (SXT) Keywords: Natural Language Processing (NLP), Biomarkers, Schizophrenia, Speech, Computational Modeling

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**Subject:** Embase;biological marker (major);adult;computer model;conference abstract;consensus;controlled study;cross validation;human;interview;language disability (major);natural language processing;negative syndrome;perseveration;poverty;speech analysis;speech disorder;speech rate;validation process;videorecording

**Updates:** 2021-04-12

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Document 162

## **Visual and Auditory Markers of Major Depressive Disorder Treatment Response to Serotonin Reuptake Inhibitors: Evidence for Changes in Motor Functioning as an Index of Antidepressant Response**

**Author:** Galatzer-Levy, Isaac 1 ; Abbas, Anzar 1 ; Yadav, Vijay 1 ; Koesmahargyo, Vidya 1 ; Sauder, Colin 2

1 AiCure 2 Adams Clinical

**Publication info:** Biological Psychiatry, suppl. Supplement 89.9: S20. Elsevier Inc. (May 1, 2021)

**Abstract (summary):** Background: Multiple **machine learning**-based visual and auditory digital **markers** have demonstrated associations between Major Depressive Disorder (MDD) status and severity. The current study examines if such measurements can quantify response to antidepressant treatment (ADT) with selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine uptake inhibitors (SNRIs). Given the role of serotonin in movement/motor functioning via expression in the motor cortex, we hypothesized that measures reflecting motor activity would be responsive to SSRI-based ADT. Methods: Visual and auditory **markers** were acquired through an automated smartphone task that measures facial, **vocal**, and head movement characteristics across four weeks of treatment (with timepoints at baseline, 2 weeks, and 4 weeks) on ADT (n = 12). The Montgomery-Asberg Depression Rating Scale (MADRS) was collected concordantly through clinical interviews to confirm diagnosis and assess changes in MDD severity. Results: Patient responses to ADT demonstrated clinically and statistically significant changes in the MADRS  $F(2,34) = 51.62, p < .0001$ . Additionally, patients demonstrated significant increases in multiple digital **markers** including facial expressivity [ $F(2,28) = 39.27, p < .0001$ ], head movement [ $F(2,26) = 8.90, p = 0.007$ ], and rate of **speech** [ $F(2,26) = 5.77, p = 0.008$ ]. Conclusions: Multiple digital **markers** related to motor functioning demonstrated robust antidepressant treatment effects on SSRIs. Theoretical implications for improved sensitivity and scalability of MDD treatment response will be discussed. Keywords: Antidepressant Response, Digital Phenotyping, Major Depressive Disorder (MDD)

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**Subject:** Embase;serotonin;serotonin noradrenalin reuptake inhibitor (major);adult;clinical article;conference abstract;controlled study;drug combination;drug therapy;face;female;head movement;human;interview;major depression (major);male;Montgomery Asberg Depression Rating Scale;motor cortex;motor performance (major);phenotype;quantitative analysis;smartphone;speech;theoretical study

**Substance:** Substance Substance: serotonin; CAS: 50-67-9;

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Document 163

**Speech analysis using artificial intelligence as a peri-operative evaluation: A case report of a patient with temporal lobe epilepsy secondary to tuberous sclerosis complex who underwent epilepsy surgery**

**Author:** Niimi, Keiko 1 ; Fujimoto, Ayataka 2 ; Kano, Yoshinobu 3 ; Otsuki, Yoshiro 4 ; Enoki, Hideo 5 ; Okanishi, Tohru 5

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**Publication info:** Brain Sciences 11.5 MDPI AG. (May 2021)

**Abstract (summary):** Background: Improved conversational fluency is sometimes identified postoperatively in patients with epilepsy, but improvements can be difficult to assess using tests such as the intelligence quotient (IQ) test. Evaluation of pre- and postoperative differences might be considered subjective at present because of the lack of objective criteria. Artificial intelligence (AI) could possibly be used to make the evaluations more objective. The aim of this case report is thus to

analyze the **speech** of a young female patient with epilepsy before and after surgery. Method: The **speech** of a nine-year-old girl with epilepsy secondary to tuberous sclerosis complex is recorded during interviews one month before and two months after surgery. The recorded **speech** is then manually transcribed and annotated, and subsequently automatically analyzed using **AI** software. IQ testing is also conducted on both occasions. The patient remains seizure-free for at least 13 months postoperatively. Results: There are decreases in total interview time and subjective case **markers** per second, whereas there are increases in morphemes and objective case **markers** per second. Postoperatively, IQ scores improve, except for the Perceptual Reasoning Index. Conclusions: **AI** analysis is able to identify differences in **speech** before and after epilepsy surgery upon an epilepsy patient with tuberous sclerosis complex.

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**Identifier (keyword):** **Artificial intelligence**, Epilepsy, Intelligence quotient, **Speech** analysis, Surgery

**Language:** English

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**Publisher location:** Switzerland

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**Subject:** Embase;electrocardiograph;angiomyolipoma;Article;**artificial intelligence** (major);brain dysfunction;case report;child;clinical article;electroencephalography;epilepsy (major);epileptic

patient;female;fluid-attenuated inversion recovery imaging;human;image quality;intelligence quotient;interview;lobectomy;machine learning;neuropathology;nuclear magnetic resonance imaging;postoperative care;preoperative care;preoperative evaluation;school child;seizure;speech analysis (major);support vector machine;temporal lobe epilepsy (major);tuberous sclerosis (major)

**Updates:** 2021-05-172021-06-18

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Document 164

## Characterizing expressive language deficit patterns in primary progressive aphasia using NLP

**Author:** Lukic, Sladjana 1 ; Fan, Zekai 1 ; Welch, Ariane E. 1 ; Miller, Zachary 1 ; Miller, Bruce L. 1 ; Wilson, Stephen M. 2 ; Tempini, Maria Luisa Gorno 1

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**Publication info:** Neurology 96.15 SUPPL 1 Lippincott Williams and Wilkins. (May 2021)

**Abstract (summary):** Objective: We aimed to investigate spontaneous production in the three PPA variants and normal controls and to identify linguistic markers that classify the variants, using NLP. Background: Expressive language impairments are frequently described clinical features associated with the three variants of primary progressive aphasia (PPA): nonfluent/agrammatic PPA, logopenic variant PPA, and semantic variant PPA. The limited scope of currently available standardized tasks limits the timely and accurate detection of deficits in the three PPA variants. Design/Methods: We obtained spontaneous speech samples from 120 participants with PPA, and 25 normal controls. Participants were asked to describe a black and white drawing of a picnic scene while three minutes of speech were recorded, transcribed, and later analyzed for content using NLP. Two types of features are extracted from statistically-tagged transcripts: (1) morpho-syntax knowledge: types of pronouns (e.g., subjective/possessive), verb tenses (e.g., present, past, be + progressive "-ing"), sentence forms (e.g., coordination/subordination), and (2) thematic knowledge: arguments and adjuncts (e.g., the man is flying [a kite] [at the beach] ). To account for variation in lengths of speech produced by participants, these features are divided by total number of non-stop words, evaluated as a metric for classifying three PPA variants using a Support Vector Machine (SVM) classifier. Results: The SVM analyses revealed that the nonfluent/agrammatic patients are classified by the morphosyntactic features with 88% accuracy, and showed reduction in production of verbs, verb tenses and sentence forms. All three PPA variants are classified by the arguments and adjuncts features with over 75% accuracy, with nfvPPA participants producing a lower proportion of arguments compared to adjuncts. No differences in producing arguments and adjuncts were found for logopenic or semantic PPA patients. Conclusions: Our findings highlight specific expressive language deficit patterns in the three PPA variants using an automated analysis of expressive language.

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**Correspondence author:** Lukic, Sladjana Department of Neurology, Memory and Aging Center, University of California, San Francisco, CA, United States.

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**Subject:** Embase;morphine;adult;clinical feature;conference abstract;controlled study;drawing;flying;genetic transcription;human;language disability (major);major clinical study;male;seashore;semantic dementia (major);speech analysis;support vector machine

**Substance:** Substance Substance: morphine; CAS: 52-26-657-27-2;

**Updates:** 2021-09-14

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Document 165

**Unobtrusive Sensing Technology for Quantifying Stress and Well-Being Using Pulse, Speech, Body Motion, and Electrodermal Data in a Workplace Setting: Study Concept and Design**

**Author:** Izumi, Keisuke 1 ; Minato, Kazumichi 2 ; Shiga, Kiko 2 ; Sugio, Tatsuki 2 ; Hanashiro, Sayaka 2 ; Cortright, Kelley 2 ; Kudo, Shun 2 ; Fujita, Takanori 3 ; Sado, Mitsuhiro 4 ; Maeno, Takashi 5 ; Takebayashi, Toru 6 ; Mimura, Masaru 2 ; Kishimoto, Taishiro 7

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**Publication info:** *Frontiers in Psychiatry* 12 Frontiers Media S.A. (Apr 28, 2021)

**Abstract (summary):** Introduction: Mental disorders are a leading cause of disability worldwide. Depression has a significant impact in the field of occupational health because it is particularly prevalent during working age. On the other hand, there are a growing number of studies on the relationship between “well-being” and employee productivity. To promote healthy and productive workplaces, this study aims to develop a technique to quantify stress and well-being in a way that does not disturb the workplace. Methods and analysis: This is a single-arm prospective observational study. The target population is adult (>20 years old) workers at companies that often engage in desk work; specifically, a person who sits in front of a computer for at least half their work hours. The following data will be collected: (a) participants' background characteristics; (b) participants' biological data during the 4-week observation period using sensing devices such as a camera built into the computer (pulse wave data extracted from the facial video images), a microphone built into their work computer (voice data), and a wristband-type wearable device (electrodermal activity data, body motion data, and body temperature); (c) stress, well-being, and depression rating scale assessment data. The analysis workflow is as follows: (1) primary analysis, comprised of using software to digitalize participants' vital information; (2) secondary analysis, comprised of examining the relationship between the quantified vital data from (1), stress, well-being, and depression; (3) tertiary analysis, comprised of generating machine learning algorithms to estimate stress, well-being, and degree of depression in relation to each set of vital data as well as multimodal vital data. Discussion: This study will evaluate digital phenotype regarding stress and well-being of white-collar workers over a 4-week period using persistently obtainable biomarkers such as heart rate, acoustic characteristics, body motion, and electrodermal activity. Eventually, this study will lead to the development of a machine learning algorithm to determine people's optimal levels of stress and well-being. Ethics and dissemination: Collected data and study results will be disseminated widely through conference

presentations, journal publications, and/or mass media. The summarized results of our overall analysis will be supplied to participants. Registration: UMIN000036814

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**Author e-mail address:** taishiro-k@mti.biglobe.ne.jp

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**Correspondence author:** Kishimoto, Taishiro Medical AI Center, Keio University, Tokyo, Japan.

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**Identifier (keyword):** adult psychiatry, depression, mental health, occupational & industrial medicine, protocols, stress, wearabe sensors, well-being

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**Subject:** Embase;biological marker;computer;wearable sensor (major);adult;Article;body movement (major);controlled study;depression (major);depression rating scale assessment +;electrodermal response (major);human;Likert scale;limit of quantitation;observational study;phenotype;physiological stress (major);population research;prospective study;psychological rating scale;pulse wave (major);sample size;self report;speech (major);wellbeing (major);working time;workplace

**Updates:** 2021-05-262021-10-25

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Document 166

## **Voice for Health: The Use of Vocal Biomarkers from Research to Clinical Practice**

**Author:** Fagherazzi, Guy 1 ; Fischer, Aurélie 1 ; Ismael, Muhannad 2 ; Despotovic, Vladimir 3

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**Publication info:** Digital biomarkers 5.1: 78-88. (Apr 16, 2021)

**Abstract (summary):** Diseases can affect organs such as the heart, lungs, brain, muscles, or vocal folds, which can then alter an individual's voice. Therefore, voice analysis using artificial intelligence opens new opportunities for healthcare. From using vocal biomarkers for diagnosis, risk prediction, and remote monitoring of various clinical outcomes and symptoms, we offer in this review an overview of the various applications of voice for health-related purposes. We discuss the potential of this rapidly evolving environment from a research, patient, and clinical perspective. We also discuss the key challenges to overcome in the near future for a substantial and efficient use of voice in healthcare.

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**Correspondence author:** Fagherazzi, Guy Deep Digital Phenotyping Research Unit, Department of Population Health, Luxembourg Institute of Health, Strassen, Luxembourg.

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Document 167

## **Screening major depressive disorder using vocal acoustic features in the elderly by sex**

**Author:** Suh, Seung Wan 1 ; Lee, Subin 2 ; Lee, Kyogu 3 ; Kim, Ki Woong 4

1 Department of Psychiatry, Kangdong Sacred Heart Hospital, South Korea 2 Department of Music and Audio Research Group, Seoul National University, South Korea 3 Department of Graduate School of Convergence Science and Technology, Seoul National University, South Korea 4 Department of Psychiatry, Seoul National University, Bundang Hospital, South Korea

**Publication info:** Asia-Pacific Psychiatry 13.SUPPL 1 Wiley-Blackwell. (Apr 2021)

**Abstract (summary):** Purpose: Vocal acoustic features are potential biomarkers of elderly depression. Previous automated diagnostic tests for depression have employed unstandardized speech samples, and few studies have considered differences in voice reactivity. We aimed to develop a voicebased screening test for depression measuring vocal acoustic features of elderly Koreans while they read a series of mood-inducing sentences (MIS). Materials and method: In this case-control study, we recruited 61 individuals with major depressive disorder and 143 healthy controls (mean age [SD]: 72 [6]; female, 70%) from the communitydwelling elderly population. Participants were asked to read MIS and their variation pattern of acoustic features represented by



the correlation distance between two MIS were analyzed as input features using the univariate feature selection technique and subsequently classified by AdaBoost. Results: Acoustic features showing significant discriminatory performances were spectral and energy-related features for males (sensitivity 0.95, specificity 0.88, and accuracy 0.86) and prosody-related features for females (sensitivity 0.73, specificity 0.86, and accuracy 0.77). The correlation distance between negative and positive MIS was significantly shorter in the depressed group than in the healthy control ( $F = 18.574$ ,  $P < 0.001$ ). Conclusion: While reading MIS, spectral and energy-related acoustic features for males and prosody-related features for females are good discriminators for major depressive disorder. These features may be used as **biomarkers** of depression in the elderly.

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**Correspondence author:** Suh, Seung Wan Department of Psychiatry, Kangdong Sacred Heart Hospital, South Korea.

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**Subject:** Embase;biological marker;aged;case control study;conference abstract;controlled study;feature selection;female;human;Korean (people);major clinical study;major depression (major);male;mood;reading;screening test;sensitivity and specificity

**Updates:** 2021-04-26

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Document 168

## **Advances in Parkinson's Disease detection and assessment using voice and speech: A review of the articulatory and phonatory aspects**

**Author:** Moro-Velazquez, Laureano 1 ; Gomez-Garcia, Jorge A. 2 ; Arias-Londoño, Julian D. 3 ; Dehak, Najim 1 ; Godino-Llorente, Juan I. 2

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**Publication info:** Biomedical Signal Processing and Control 66 Elsevier Ltd. (Apr 2021)

**Abstract (summary):** Parkinson's Disease (PD) affects speech in the form of dysphonia and hypokinetic dysarthria. Multiple studies have evaluated PD's influence on different aspects of speech, showing differences between speakers with and without PD. Most recent studies are focused on the proposal of new automatic and objective tools to help in the diagnosis and severity assessment. This comprehensive review identifies the most common features and machine learning techniques employed in automatically detecting and assessing the severity of PD using phonatory and articulatory aspects of speech and voice. We discuss their discriminant properties and literature findings as well as identify common methodological issues that can potentially bias results. The objective is to provide a broad overview of these methods, their advantages and disadvantages, and to identify the most promising methodologies to be explored in future works. We conclude that there is clear evidence that the articulatory and phonatory aspects of speech and voice are relevant for the automatic detection and severity assessment of PD. However, there is no standard methodology sufficiently validated in a clinical trial, and further research is required, especially to develop larger corpora and identify new objective biomarkers.

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**Author e-mail address:** laureano@jhu.edu

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**Identifier (keyword):** Articulation, Automatic assessment, Automatic detection, Parkinson's disease, Phonation, Voice and speech

**Language:** English

**Language of abstract:** English

**Number of references:** 208

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**Publication type:** Journal

**Publisher:** Elsevier Ltd

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**Subject:** Embase;biological marker;Article;automation;disease severity assessment;human;kinematics;machine learning;methodology;Parkinson disease (major);phonation (major);phoneme;priority journal;speech articulation (major);voice (major)

**Updates:** 2021-02-042021-05-212021-10-22

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Document 169

## **Identification of robust and interpretable brain signatures of autism and clinical symptom severity using a dynamic time-series deep neural network**

**Author:** Supekar, K. 1 ; Ryali, S. 1 ; Yuan, R. 1 ; Kumar, D. 1 ; De Los Angeles, C. 1 ; Menon, V. 1

1 Psychiatry and Behavioral Sciences, Stanford University, Stanford, United States

**Publication info:** European Psychiatry, suppl. Supplement 1 64 : S145. Cambridge University Press. (Apr 2021)

**Abstract (summary):** Introduction: Autism spectrum disorder (ASD) is among the most common and pervasive neurodevelopmental disorders. Yet, despite decades of research, the neurobiology of ASD is still poorly understood, as inconsistent findings preclude the identification of robust and interpretable neurobiological markers and predictors of clinical symptoms. Objectives: Identify robust and interpretable dynamic brain markers that distinguish children with ASD from typically developing (TD) children and predict clinical symptom severity. Methods: We leverage multiple functional brain imaging cohorts (ABIDE, Stanford; N = 1004) and exciting recent advances in explainable artificial intelligence (xAI), to develop a novel multivariate time series deep neural network model that extracts informative brain dynamics features that accurately distinguish between ASD and TD children, and predict clinical symptom severity. Results: Our model achieved consistently high classification accuracies in cross-validation analysis of data from the ABIDE cohort. Crucially, despite the differences in symptom profiles, age, and data acquisition protocols, our model also accurately classified data from an independent Stanford cohort without additional training. xAI analyses revealed that brain features associated with the default mode network, and the human voice/face processing and communication systems, most clearly distinguished ASD from TD children in both cohorts. Furthermore, the posterior cingulate cortex emerged as robust predictor of the severity of social and communication deficits in ASD in both cohorts. Conclusions: Our findings, replicated across two independent cohorts, reveal robust and neurobiologically interpretable brain features that detect ASD and predict core phenotypic features of ASD, and have the potential to transform our understanding of the etiology and treatment of the disorder.

**Accession number:** 639617595

**Conference end date:** 2021-04-13

**Conference location:** Virtual

**Conference start date:** 2021-04-10

**Conference title:** 29th European Congress of Psychiatry, EPA 2021

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**Correspondence author:** Supekar, K. Psychiatry and Behavioral Sciences, Stanford University, Stanford, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1192/j.eurpsy.2021.397>

**Embase document status:** Embase

**First available:** 2022-11-30

**Identifier (keyword):** autism, **biomarkers**, brain dynamics, fMRI

**Language:** English

**Language of abstract:** English

**Publication date:** Apr 2021

**Publication type:** Journal

**Publisher:** Cambridge University Press

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;**biological marker** (major);**artificial intelligence**;autism (major);child;cohort analysis;conference abstract;controlled study;**cross validation**;**deep neural network** (major);default mode network;facial recognition;female;functional magnetic resonance imaging (major);functional neuroimaging;human;major clinical study;male;posterior cingulate (major);time series analysis (major);**voice**

**Updates:** 2022-11-30

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Document 170

## **A Deep Learning Approach to Diagnosing Multiple Sclerosis from Smartphone Data**

**Author:** Schwab, Patrick; Karlen, Walter

**Publication info:** IEEE journal of biomedical and health informatics 25.4: 1284-1291. (Apr 2021)

**Abstract (summary):** Multiple sclerosis (MS) affects the central nervous system with a wide range of symptoms. MS can, for example, cause pain, changes in mood and fatigue, and may impair a person's movement, **speech** and visual functions. Diagnosis of MS typically involves a combination of complex clinical assessments and tests to rule out other diseases with similar symptoms. New technologies, such as smartphone monitoring in free-living conditions, could potentially aid in objectively assessing the symptoms of MS by quantifying symptom presence and intensity over long periods of time. Here, we present a **deep-learning** approach to diagnosing MS from smartphone-derived digital **biomarkers** that uses a novel combination of a multilayer **perceptron** with neural soft attention to improve learning of patterns in long-term smartphone monitoring data. Using data from a cohort of 774 participants, we demonstrate that our **deep-learning** models are able to distinguish between people with and without MS with an area under the receiver operating characteristic curve of 0.88 (95% CI: 0.70, 0.88). Our experimental results indicate that digital **biomarkers** derived from smartphone data could in the future be used as additional diagnostic criteria for MS.

**Accession number:** 32877343

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Document type:** Journal Article, Research Support, Non-U.S. Gov't

**DOI:** <http://dx.doi.org/10.1109/JBHI.2020.3021143>

**First available:** 2020-09-03

**Language:** English

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**Medline document status:** MEDLINE

**MeSH:** Deep Learning (major);Fatigue;Humans;Multiple Sclerosis (major) -- diagnosis;Neural Networks, Computer;Smartphone

**Notes:** Indexing method: Automated;; Publication model: Print-Electronic;; Cited medium:Internet

**Publication date:** Apr 2021

**Publication type:** Journal

**Publisher location:** UNITED STATES

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Document 171

## **Remote Digital Measurement of Facial and Vocal Markers of Major Depressive Disorder Severity and Treatment Response: A Pilot Study**

**Author:** Abbas, Anzar 1 ; Sauder, Colin 2 ; Yadav, Vijay 1 ; Koesmahargyo, Vidya 1 ; Aghjayan, Allison 3 ; Marecki, Serena 3 ; Evans, Miriam 3 ; Galatzer-Levy, Isaac R 4

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**Publication info:** Frontiers in digital health 3 : 610006. (Mar 31, 2021)

**Abstract (summary):** Objectives: Multiple machine learning-based visual and auditory digital markers have demonstrated associations between major depressive disorder (MDD) status and

severity. The current study examines if such measurements can quantify response to antidepressant treatment (ADT) with selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine uptake inhibitors (SNRIs). Methods: Visual and auditory markers were acquired through an automated smartphone task that measures facial, **vocal**, and head movement characteristics across 4 weeks of treatment (with time points at baseline, 2 weeks, and 4 weeks) on ADT (n = 18). MDD diagnosis was confirmed using the Mini-International Neuropsychiatric Interview (MINI), and the Montgomery-Åsberg Depression Rating Scale (MADRS) was collected concordantly to assess changes in MDD severity. Results: Patient responses to ADT demonstrated clinically and statistically significant changes in the MADRS [F (2, 34) = 51.62, p <0.0001]. Additionally, patients demonstrated significant increases in multiple digital markers including facial expressivity, head movement, and amount of **speech**. Finally, patients demonstrated significantly decreased frequency of fear and anger facial expressions. Conclusion: Digital markers associated with MDD demonstrate validity as measures of treatment response.

**Accession number:** 34713091

**Copyright:** Copyright © 2021 Abbas, Sauder, Yadav, Koesmahargyo, Aghjayan, Marecki, Evans and Galatzer-Levy.

**Correspondence author:** Abbas, Anzar AiCure, New York, NY, United States.

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**Date created:** 2021-10-29

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**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.3389/fdgth.2021.610006>

**First available:** 2021-10-29

**Identifier (keyword):** Montgomery-Åsberg Depression Rating Scale, antidepressant treatment, computer vision, digital **biomarker**, digital phenotyping, **machine learning**, major depressive disorder

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** At the time of the study, AAb, VY, VK and IG-L were employees of AiCure and held stock options in AiCure. CS, AAg, SM, and ME were employees of Adams Clinical, and CS was also an employee of Karuna Therapeutics. The authors declare that the study was jointly funded by AiCure, LLC and Adams Clinical, both of which may benefit from research reported in the manuscript and were involved in study design and execution. Adams Clinical conducted patient recruitment, enrollment, and clinical assessments. AiCure developed methods for digital phenotyping and provided software tools for remote collection of video data used. Both AiCure and Adams Clinical were involved

in subsequent data analysis, interpretation, and presentation of findings.; Publication model: Electronic-eCollection;; Cited medium:Internet

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**Publication type:** Journal

**Publisher location:** SWITZERLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2021-10-292021-10-30

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Document 172

## Processing of Degraded Speech in Brain Disorders

**Author:** Jiang, Jessica 1 ; Benhamou, Elia 1 ; Waters, Sheena 2 ; Johnson, Jeremy C S 1 ; Volkmer, Anna 3 ; Weil, Rimona S 1 ; Marshall, Charles R 4 ; Warren, Jason D 1 ; Hardy, Chris J D 1

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**Publication info:** Brain sciences 11.3 (Mar 20, 2021)

**Abstract (summary):** The speech we hear every day is typically "degraded" by competing sounds and the idiosyncratic vocal characteristics of individual speakers. While the comprehension of "degraded" speech is normally automatic, it depends on dynamic and adaptive processing across distributed neural networks. This presents the brain with an immense computational challenge, making degraded speech processing vulnerable to a range of brain disorders. Therefore, it is likely to be a sensitive marker of neural circuit dysfunction and an index of retained neural plasticity. Considering experimental methods for studying degraded speech and factors that affect its processing in healthy individuals, we review the evidence for altered degraded speech processing in major neurodegenerative diseases, traumatic brain injury and stroke. We develop a predictive coding framework for understanding deficits of degraded speech processing in these disorders, focussing on the "language-led dementias"-the primary progressive aphasias. We conclude by considering prospects for using degraded speech as a probe of language network pathophysiology, a diagnostic tool and a target for therapeutic intervention.

**Accession number:** 33804653



**Correspondence author:** Jiang, Jessica Dementia Research Centre, Department of Neurodegenerative Disease, UCL Queen Square Institute of Neurology, London WC1N 3BG, UK.

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**Document status:** Revised

**Document type:** Journal Article, Review

**DOI:** <http://dx.doi.org/10.3390/brainsci11030394>

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PA23\_Hardy. Action on Hearing Loss. United Kingdom.

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The Wolfson Foundation.

Guarantors of Brain Clinical Research Training Fellowship. Association of British Neurologists.

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PR/ylr/18575. University College London Leonard Wolfson Experimental Neurology Centre.

205167/Z/16/Z. Wellcome Trust. United Kingdom.

National Institute for Health Research Development Skills Enhancement Award.

BRC302/NS/RW/101410. UCLH Biomedical Research Centre.

PA23. RNID. United Kingdom.

Frontotemporal Dementia Research Studentship in Memory of David Blechner. National Brain Appeal.

**Identifier (keyword):** Alzheimer's disease, Parkinson's disease, degraded **speech** processing, dementia, perceptual learning, predictive coding, primary progressive aphasia

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Electronic;; Cited medium:Print

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**Updates:** 2021-04-052021-04-052021-04-072021-04-082021-04-112021-04-132022-03-232023-02-22

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Document 173

## **X-Vectors: New Quantitative Biomarkers for Early Parkinson's Disease Detection From Speech**

**Author:** Jeancolas, Laetitia 1 ; Petrovska-Delacrétaz, Dijana 2 ; Mangone, Graziella 3 ; Benkelfat, Badr-Eddine 2 ; Corvol, Jean-Christophe 3 ; Vidailhet, Marie 3 ; Lehericy, Stéphane 4 ; Benali, Habib 5

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**Publication info:** Frontiers in Neuroinformatics 15 Frontiers Media S.A. (Feb 19, 2021)

**Abstract (summary):** Many articles have used **voice** analysis to detect Parkinson's disease (PD), but few have focused on the early stages of the disease and the gender effect. In this article, we have adapted the latest speaker recognition system, called x-vectors, in order to detect PD at an early stage using **voice** analysis. X-vectors are embeddings extracted from **Deep Neural Networks (DNNs)**, which provide robust speaker representations and improve speaker recognition when large amounts of training data are used. Our goal was to assess whether, in the context of early PD detection, this technique would outperform the more standard classifier MFCC-GMM (Mel-Frequency Cepstral Coefficients—Gaussian Mixture Model) and, if so, under which conditions. We recorded 221 French speakers (recently diagnosed PD subjects and healthy controls) with a high-quality microphone and via the telephone network. Men and women were analyzed separately in order to have more precise models and to assess a possible gender effect. Several experimental and methodological aspects were tested in order to analyze their impacts on classification performance. We assessed the impact

of the audio segment durations, data augmentation, type of dataset used for the neural network training, kind of **speech** tasks, and back-end analyses. X-vectors technique provided better classification performances than MFCC-GMM for the text-independent tasks, and seemed to be particularly suited for the early detection of PD in women (7–15% improvement). This result was observed for both recording types (high-quality microphone and telephone).

**Accession number:** 634383867

**Author e-mail address:** laetitia.jeancolas@icm-institute.org

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**Correspondence author:** Jeancolas, Laetitia Paris Brain Institute—ICM, Centre de NeuroImagerie de Recherche—CENIR, Paris, France.

Jeancolas, Laetitia Laboratoire SAMOVAR, Télécom SudParis, Institut Polytechnique de Paris, Palaiseau, France.

**Database:** Embase®; 1947 to date (1947 - current)

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**Identifier (keyword):** automatic detection, **deepneural networks**, early detection, MFCC, Parkinson's disease, telediagnosis, **voice** analysis, x-vectors

**Language:** English

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**Number of references:** 85

**Publication date:** Feb 19, 2021

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**Subject:** Embase;biological marker (major);levodopa;adult;Article;bootstrapping;computer model;controlled study;convolutional neural network;deep neural network;diagnostic test accuracy study;early diagnosis (major);expectation-maximization algorithm;facial recognition>false positive result;female;Hoehn and Yahr scale;human;machine learning (major);major clinical study;male;middle aged;nuclear magnetic resonance;Parkinson disease -- diagnosis (major);program efficacy;sensitivity and specificity;speech analysis (major);speech sound disorder;speech test;time delay neural network;Unified Parkinson Disease Rating Scale;voice analysis;voice recognition;X vector + (major)

**Substance:** Substance Substance: levodopa; CAS: 59-92-7;

**Updates:** 2021-03-152021-04-28

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Document 174

## Laryngotracheal Mucosal Surface Expression of Candidate Biomarkers in Idiopathic Subglottic Stenosis

**Author:** Liu, Melissa M. 1 ; Motz, Kevin M. 1 ; Murphy, Michael K. 2 ; Yin, Linda X. 3 ; Ding, Dacheng 1 ; Gelbard, Alexander 4 ; Hillel, Alexander T. 5

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**Publication info:** Laryngoscope 131.2: 342-349. John Wiley and Sons Inc. (Feb 2021)

**Abstract (summary):** Objectives: Idiopathic subglottic stenosis (iSGS) is an inflammatory process leading to fibrosis and narrowing of the laryngotracheal airway. There is variability in patient response to surgical intervention, but the mechanisms underlying this variability are unknown. In this pilot study,

we measure expression of candidate targets at the mucosal surface of the subglottis in iSGS patients. We aim to identify putative **biomarkers** for iSGS that provide insights into the molecular basis of disease progression, yield a gene signature for the disease, and/or predict a response to therapy. Study Design: In vitro comparative study of human cells. Methods: Levels of candidate transcripts and proteins were measured in healthy and stenotic laryngotracheal tissue specimens taken from the mucosal surface in 16 iSGS patients undergoing endoscopic balloon dilation. Pre- and post-operative pulmonary function test and patient reported **voice** and breathing outcomes were also assessed. Unsupervised clustering was used to define patient subgroups based on expression profile. Results: Pulmonary function and **voice** and breathing outcome metrics demonstrated significant post-operative improvement. Transcript levels of  $\alpha$ SMA, CCL2, COL1A1, COL3A1, FN1, IFNG, and TGFB1 and protein levels of CCL2, IFNG, and IL-6 were significantly upregulated in stenotic as compared to healthy tissues. Marked heterogeneity was observed in the patterns of expression of candidate markers across individuals and tissue types. Patient subgroups defined by expression profile did not show a statistically significant difference in dilation interval. Conclusion: Pro-inflammatory and pro-fibrotic pathways are significantly upregulated along the mucosal surface of stenotic laryngotracheal tissues, and CCL2 and IFNG merit further investigation as potential iSGS **biomarkers**. Level of Evidence: 4 Laryngoscope, 131:342–349, 2021.

**Accession number:** 2004838618

**Author e-mail address:** ahillel@jhmi.edu

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**Correspondence author:** Hillel, Alexander T. Department of Otolaryngology-Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, United States.

Hillel, Alexander T. The North American Airway Collaborative, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2021-02-10

**Device company:** Device company Device trade name: Undefined; Manufacturer: Boston Scientific; Country: United States;

Device trade name: Undefined; Manufacturer: ConMed; Country: United States;

**Device trade name:** Device trade name Name: CBA Flex Set; Manufacturer: Becton Dickinson Biosciences; Country: United States;

Name: iScript; Manufacturer: Biorad; Country: United States;

Name: MicroLoop Spirometer; Manufacturer: Undefined;

Name: NanoDrop; Manufacturer: Thermo; Country: United States;

Name: RNeasy Mini Kit; Manufacturer: Qiagen; Country: United States;

Name: StepOnePlus; Manufacturer: Thermo; Country: United States;

Name: Surgifoam; Manufacturer: Ethicon; Country: United States;

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1002/lary.28712>

**Embase document status:** Embase; MEDLINE

**First available:** 2020-05-25

**Grant:** ACS. American College of Surgeons.

ALROS. American Laryngological, Rhinological and Otological Society.

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and Conflicts of Interest: Research in this publication was supported by National Institute on Deafness and Other Communication Disorders (NIDCD) of the National Institutes of Health (NIH) under grants 1K23DC014082 (a.t.h.) and 1R21DC01722501 (a.t.h.). The North American Airway Collaborative is supported through the Patient Centered Outcomes Research Institute (PCORI) grant number 1409-22214 (a.g.). This study was also supported by the Triological Society and American College of Surgeons (ACS) (a.t.h.). The content is solely the responsibility of the authors and does not represent the official views of the NIH, TRIO, the ACS, or PCORI. The authors have no other funding, financial relationships, or conflicts of interest to disclose.

**Identifier (keyword):** dilation, gene expression, Idiopathic subglottic stenosis, protein expression

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**Language of abstract:** English

**Number of references:** 27

**Publication date:** Feb 2021

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc

**Publisher location:** United States

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**Subject:** Embase;MEDLINE;alpha smooth muscle actin -- endogenous compound;biological marker -  
- endogenous compound (major);collagen type 1 -- endogenous compound;collagen type 1A1 + --  
endogenous compound;collagen type 1A3 + -- endogenous compound;gamma interferon --  
endogenous compound;gelatin sponge -- endogenous compound;gelfoam -- endogenous  
compound;interleukin 13 -- endogenous compound;interleukin 17 -- endogenous  
compound;interleukin 4 -- endogenous compound;interleukin 6 -- endogenous compound;lidocaine --  
endogenous compound;lidocaine -- topical drug administration;monocyte chemotactic protein 1 --  
endogenous compound;transforming growth factor beta1 -- endogenous compound;triamcinolone --  
endogenous compound;triamcinolone -- parenteral drug administration;unclassified drug;balloon

catheter;biopsy brush;CBA Flex Set +;endotracheal tube;genetic analyzer;immunoassay analyzer;iScript +;laryngoscope;MicroLoop Spirometer +;operating room;polymerase chain reaction system;RNeasy Mini Kit +;spectrophotometer;spirometer;Surgifoam +;adult;area under the curve;Article;balloon dilatation;breathing;brush biopsy;clinical article;cohort analysis;comparative study;controlled clinical trial;controlled study;disease exacerbation;endoscopy;female;forced expiratory volume;forced vital capacity;gene expression (major);gene expression profiling;general anesthesia;genetic transcription;human;human cell;human tissue;idiopathic disease -- therapy (major);in vitro study;larynx mucosa (major);larynx stenosis;lung function;lung function test;middle aged;oxygen saturation;patient-reported outcome;pilot study;postoperative period;prediction;priority journal;protein isolation;quality of life assessment;real time polymerase chain reaction;RNA translation;subglottic stenosis -- therapy (major);submucosal drug administration;trachea mucosa (major);trachea stenosis;treatment response;unsupervised machine learning;upregulation;vocal cord;voice;voice handicap index 10 +;Voice Related Quality of Life Survey +

**Substance:** Substance Substance: gamma interferon; CAS: 82115-62-6; Substance: gelatin sponge; CAS: 69235-27-4; Substance: interleukin 13; CAS: 148157-34-0; Substance: lidocaine; CAS: 137-58-624847-67-456934-02-273-78-9; Substance: triamcinolone; CAS: 124-94-7;

**Updates:** 2020-05-252021-01-202021-02-012021-02-10

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Document 175

## Part of **Speech** Production in Patients With Primary Progressive Aphasia: An Analysis Based on Natural Language Processing

**Author:** Themistocleous, Charalambos 1 ; Webster, Kimberly 2 ; Afthinos, Alexandros 1 ; Tsapkini, Kyrana 3

1 Department of Neurology, Johns Hopkins School of Medicine, MD, Baltimore, United States 2 Department of Otolaryngology, Johns Hopkins Medicine 3 Department of Neurology, Johns Hopkins School of Medicine, MD, Baltimore, United States, Department of Cognitive Science, Johns Hopkins University

**Publication info:** American journal of speech-language pathology 30.1: 466-480. NLM (Medline). (Feb 11, 2021)

**Abstract (summary):** Background Primary progressive aphasia (PPA) is a neurodegenerative disorder characterized by a progressive decline of language functions. Its symptoms are grouped into three PPA variants: nonfluent PPA, logopenic PPA, and semantic PPA. Grammatical deficiencies differ depending on the PPA variant. Aims This study aims to determine the differences between PPA variants with respect to part of **speech** (POS) production and to identify morphological **markers** that classify PPA variants using **machine learning**. By fulfilling these aims, the overarching goal is to provide objective measures that can facilitate clinical diagnosis, evaluation, and prognosis. Method

and Procedure Connected **speech** productions from PPA patients produced in a picture description task were transcribed, and the POS class of each word was estimated using natural language processing, namely, POS tagging. We then implemented a twofold analysis: (a) linear regression to determine how patients with nonfluent PPA, semantic PPA, and logopenic PPA variants differ in their POS productions and (b) a supervised classification analysis based on POS using **machine learning** models (i.e., random forests, decision trees, and **support vector machines**) to subtype PPA variants and generate feature importance (FI). Outcome and Results Using an automated analysis of a short picture description task, this study showed that content versus function words can distinguish patients with nonfluent PPA, semantic PPA, and logopenic PPA variants. Verbs were less important as distinguishing features of patients with different PPA variants than earlier thought. Finally, the study showed that among the most important distinguishing features of PPA variants were elaborative **speech** elements, such as adjectives and adverbs.

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**Grant:** R01 AG068881. , NIA. National Institute on Aging.

R01 DC014475. , NIDCD. National Institute on Deafness and Other Communication Disorders.

**Language:** English

**Language of abstract:** English

**Publication date:** Feb 11, 2021

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**Publisher:** NLM (Medline)

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**Subject:** MEDLINE;human;language;natural language processing;**primary progressive aphasia** -- diagnosis (major);semantics;**speech** (major)

**Updates:** 2020-07-282021-02-242021-07-13



## **Multilingual automation of transcript preprocessing in Alzheimer's disease detection**

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1 Department of Software and IT Engineering, École de technologie supérieure, Montreal, QC, Canada frederic.abiven.1@ens.etsmtl.ca

**Publication info:** Alzheimer's and Dementia: Translational Research and Clinical Interventions 7.1 John Wiley and Sons Inc. (2021)

**Abstract (summary):** Introduction: Analyzing linguistic functions can improve early detection of Alzheimer's disease (AD). To date, no studies have focused on creating a universal pipeline for clinical transcript preprocessing. Methods: This article presents a simple and efficient method for processing linguistic and **phonetic** data, sequencing subproblems of cleaning, normalization, and measure extraction tasks. Because some of these tasks are language- and context- dependent, they were designed to be easily configurable, thus increasing their scalability when dealing with new corpora. Results: Results show improved performances over previous studies in this time-consuming preprocessing task. Moreover, our findings showed that some discursive **markers** extracted from transcripts revealed a significant correlation (>0.5) with cognitive impairment severity. Discussion: This article contributes to the literature on AD by presenting an efficient pipeline that allows speeding up the transcripts preprocessing task. We further invite other researchers to contribute to this work to help improve the quality of this pipeline (<https://github.com/LINCS-lab/usAge>).

**Accession number:** 2014923457

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**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Abiven, Frédéric Department of Software and IT Engineering, École de technologie supérieure, Montreal, QC, Canada.

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**Identifier (keyword):** Alzheimer's disease, discursive markers, early detection, linguistic features, phonetic features, pipeline, transcript preprocessing

**Language:** English

**Language of abstract:** English

**Number of references:** 13

**Publication date:** 2021

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;Alzheimer disease (major);Article;automation (major);cognitive defect;cross validation;feature selection;human;multilingualism (major);phonetics

**Updates:** 2022-02-162022-05-04

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Document 177

## **Automatic Subtyping of Individuals with Primary Progressive Aphasia**

**Author:** Themistocleous, Charalambos 1 ; Ficek, Bronte 1 ; Webster, Kimberly 1 ; den Ouden, Dirk-Bart 2 ; Hillis, Argye E 1 ; Tsapkini, Kyrana 1

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**Publication info:** Journal of Alzheimer's disease : JAD 79.3: 1185-1194. (2021)

### **Abstract (summary): BACKGROUND**

The classification of patients with primary progressive aphasia (PPA) into variants is time-consuming, costly, and requires combined expertise by clinical neurologists, neuropsychologists, speech pathologists, and radiologists.

## **OBJECTIVE**

The aim of the present study is to determine whether acoustic and linguistic variables provide accurate classification of PPA patients into one of three variants: nonfluent PPA, semantic PPA, and logopenic PPA.

## METHODS

In this paper, we present a **machine learning** model based on **deep neural networks (DNN)** for the subtyping of patients with PPA into three main variants, using combined acoustic and linguistic information elicited automatically via acoustic and linguistic analysis. The performance of the **DNN** was compared to the classification accuracy of Random Forests, **Support Vector Machines**, and Decision Trees, as well as to expert clinicians' classifications.

## RESULTS

The **DNN** model outperformed the other **machine learning** models as well as expert clinicians' classifications with 80% classification accuracy. Importantly, 90% of patients with nfvPPA and 95% of patients with lvPPA was identified correctly, providing reliable subtyping of these patients into their corresponding PPA variants.

## CONCLUSION

We show that the combined **speech** and language **markers** from connected **speech** productions can inform variant subtyping in patients with PPA. The end-to-end automated **machine learning** approach we present can enable clinicians and researchers to provide an easy, quick, and inexpensive classification of patients with PPA.

**Accession number:** 33427742

**Correspondence author:** Themistocleous, Charalambos Johns Hopkins School of Medicine, Baltimore, MD, USA.

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**Document type:** Journal Article, Research Support, N.I.H., Extramural, Research Support, Non-U.S. Gov't

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**Grant:** P30 AG066507. NIA NIH HHS. United States.

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**Identifier (keyword):** Classification, machine learning, natural language processing, primary progressive aphasia

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Acoustics;Aged;Aphasia, Primary Progressive -- classification (major);Aphasia, Primary Progressive -- diagnosis;Decision Trees;Female;Humans;Linguistics;Machine Learning;Male;Models, Theoretical;Neural Networks, Computer;Primary Progressive Nonfluent Aphasia -- classification;Primary Progressive Nonfluent Aphasia -- diagnosis;Reproducibility of Results;Support Vector Machine

**Notes:** Publication model: Print;; Cited medium:Internet

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**Publication type:** Journal

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Document 178

## **Estimation of forced vital capacity using speech acoustics in patients with ALS**

**Author:** Stegmann, Gabriela M. 1 ; Hahn, Shira 1 ; Duncan, Cayla J. 2 ; Rutkove, Seward B. 3 ; Liss, Julie 1 ; Shefner, Jeremy M. 4 ; Berisha, Visar 1

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**Publication info:** Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 22.S1: 14-21. Taylor and Francis Ltd. (2021)

**Abstract (summary):** In this study, we present and provide validation data for a tool that predicts forced vital capacity (FVC) from **speech** acoustics collected remotely via a mobile app without the need for any additional equipment (e.g. a spirometer). We trained a **machine learning** model on a sample of healthy participants and participants with amyotrophic lateral sclerosis (ALS) to learn a mapping from **speech** acoustics to FVC and used this model to predict FVC values in a new sample from a different study of participants with ALS. We further evaluated the cross-sectional accuracy of the model and its sensitivity to within-subject change in FVC. We found that the predicted and observed FVC values in the test sample had a correlation coefficient of .80 and mean absolute error between .54 L and .58 L (18.5% to 19.5%). In addition, we found that the model was able to detect longitudinal decline in FVC in the test sample, although to a lesser extent than the observed FVC values measured using a spirometer, and was highly repeatable (ICC = 0.92–0.94), although to a lesser extent than the actual FVC (ICC = .97). These results suggest that sustained **phonation** may be a useful surrogate for VC in both research and clinical environments.

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**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Shefner, Jeremy M. Barrow Neurological Institute, 240 West Thomas Road, Phoenix, AZ, 85013, United States.

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**Grant:** This work was supported by NIH SBIR [1R43DC017625-01], NSF SBIR [1853247], NIH R01 [5R01DC006859-13], ALS Finding a Cure Grant, and a grant from the Dignity Health ASU Research Collaboration.

**Identifier (keyword):** **biomarker**, Clinical trial, respiratory function, **speech** analysis, ventilation

**Language:** English

**Language of abstract:** English

**Number of references:** 20

**Publication date:** 2021

**Publication type:** Journal

**Publisher:** Taylor and Francis Ltd.

**Publisher location:** United Kingdom

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;biological marker (major);spirometer;adult;amyotrophic lateral sclerosis (major);Article;cognitive defect;controlled study;correlation coefficient;cross-sectional study;female;forced vital capacity (major);grip strength;human;impedance;machine learning;male;measurement accuracy;mobile application;myography;outcome assessment;phonation;speech analysis (major);speech and language assessment;spirometry

**Updates:** 2021-08-102021-08-272021-10-15

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Document 179

### **Protocol for a remote data collection speech analysis study in people at risk for Alzheimer's disease dementia: The SPeAk study**

**Author:** Gregory, Sarah 1 ; Linz, Nicklas 2 ; Langel, Kai 3 ; Pullen, Hannah 1 ; König, Alexandra 4 ; Luz, Saturnino 5 ; Harrison, Professor John 6 ; Universiteit, Vrije 7 ; Ritchie, Professor Craig 1

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**Publication info:** Brain and Neuroscience Advances 5 : 205-206. SAGE Publications Ltd. (Jan 2021 - Dec 2021)

**Abstract (summary):** Introduction: Speech and language analysis is an emerging area of research in the identification of Alzheimer's disease (AD) biomarkers (Boschi et al, 2017). Such biomarkers include failure to stop autocorrect errors when reading aloud, which correlates with A $\beta$ 1-42 (Gollan et al, 2020). This study aims to develop algorithms to identify speech biomarkers in the data that are predictive of CSF AD biomarkers. Secondary and exploratory objectives are to assess ceiling performance and test-retest reliability of the phone administered cognitive assessments, to explore participant acceptability and to conduct conversational analysis. Methods: Participants must have previously enrolled in the EPAD LCS or CHARIOT Pro sub-study at the Edinburgh Dementia Prevention site and agreed to be contacted about future research. Consent will be recorded using a secure online form. We will collect demographic information (age, sex, education, living status and medication). Participants will initially engage in two conversational tasks followed by immediate and delayed list learning, digit span, semantic and phonemic fluency. Participants will repeat the cognitive testing at 3 months with an automated tester. Participants will receive acceptability questionnaires after each appointment. Participants will be randomised 1:1 to receive results after each visit or only

at study completion. Approach for statistical analysis: Algorithm development will extract the following features: classical cognitive outcome variables, novel or qualitative outcome variables based on produced language and low-level **speech** descriptors such as **speech** rate. A combination of predictive statistical and **machine learning** models will be used, with participants' **biomarker** status (from EPAD LCS) as a target variable. Models will be constructed with task specific features and using aggregated variables spanning multiple cognitive tasks. Ceiling and test-retest reliability will be analysed with ANOVA and repeated measures correlation. Frequency statistics, paired t-tests and qualitative analysis will be used for acceptability questionnaires. Exploratory conversational analysis will look at the spontaneous **speech** for features such as turn taking.

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**Conference end date:** 2021-04-15

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**Conference title:** British Neuroscience Association Festival of Neuroscience, BNA 2021

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Gregory, Sarah Edinburgh Dementia Prevention, Centre for Clinical Brain Sciences, University of Edinburgh.

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**DOI:** <http://dx.doi.org/10.1177/23982128211035062>

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**First available:** 2021-08-20

**Language:** English

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**Publication date:** Jan 2021 - Dec 2021

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**Publisher:** SAGE Publications Ltd

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**Subject:** Embase;**biological marker**;adult;algorithm (major);Alzheimer disease (major);analysis of variance;cerebrospinal fluid;conference abstract;controlled study;demography;exploratory research;female;human;language;**machine learning**;male;outcome variable;prevention;qualitative

analysis;questionnaire;randomized controlled trial;sexual education;speech analysis (major);speech rate;target variable;test retest reliability

**Updates:** 2021-08-20

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Document 180

## **Machine Learning Approaches in Parkinson's Disease**

**Author:** Landolfi, Annamaria 1 ; Ricciardi, Carlo 2 ; Donisi, Leandro 2 ; Cesarelli, Giuseppe 3 ; Troisi, Jacopo 1 ; Vitale, Carmine 4 ; Barone, Paolo 1 ; Amboni, Marianna 1

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**Publication info:** Current medicinal chemistry 28.32: 6548-6568. (2021)

### **Abstract (summary): BACKGROUND**

Parkinson's disease is the second most frequent neurodegenerative disorder. Its diagnosis is challenging and mainly relies on clinical aspects. At present, no biomarker is available to obtain a diagnosis of certainty in vivo.

### **OBJECTIVE**

The present review aims at describing machine learning algorithms as they have been variably applied to different aspects of Parkinson's disease diagnosis and characterization.

### **METHODS**

A systematic search was conducted on PubMed in December 2019, resulting in 230 publications obtained with the following search query: "Machine Learning" "AND" "Parkinson Disease".

### **RESULTS**

The obtained publications were divided into 6 categories, based on different application fields: "Gait Analysis - Motor Evaluation", "Upper Limb Motor and Tremor Evaluation", "Handwriting and typing evaluation", "Speech and Phonation evaluation", "Neuroimaging and Nuclear Medicine evaluation", "Metabolomics application", after excluding the papers of general topic. As a result, a total of 166



articles were analyzed after elimination of papers written in languages other than English or not directly related to the selected topics.

## CONCLUSION

**Machine learning** algorithms are computer-based statistical approaches that can be trained and are able to find common patterns from big amounts of data. The **machine learning** approaches can help clinicians in classifying patients according to several variables at the same time.

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**Copyright:** Copyright© Bentham Science Publishers; For any queries, please email at [epub@benthamscience.net](mailto:epub@benthamscience.net).

**Correspondence author:** Landolfi, Annamaria Department of Medicine, Surgery and Dentistry, "Scuola Medica Salernitana" Neuroscience section, University of Salerno, Baronissi (SA), Italy.

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**Document type:** Journal Article, Review

**DOI:** <http://dx.doi.org/10.2174/0929867328999210111211420>

**First available:** 2021-01-12

**Identifier (keyword):** **Machine learning**, Parkinson disease, gait analysis, handwriting analysis., metabolomics, neuroimaging, **speech** analysis

**Language:** English

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**MeSH:** Algorithms;Humans;**Machine Learning**;Neuroimaging;Parkinson Disease (major) -- diagnosis

**Notes:** Indexing method: Automated;; Publication model: Print;; Cited medium:Internet

**Publication date:** 2021

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**Publisher location:** UNITED ARAB EMIRATES

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## **Utilization of Machine Learning-Based Computer Vision and Voice Analysis to Derive Digital Biomarkers of Cognitive Functioning in Trauma Survivors**

**Author:** Schultebrucks, Katharina 1 ; Yadav, Vijay 2 ; Galatzer-Levy, Isaac R. 3

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**Publication info:** Digital Biomarkers 5.1: 16-23. S. Karger AG. (Jan 2021)

**Abstract (summary):** Background: Alterations in multiple domains of cognition have been observed in individuals who have experienced a traumatic stressor. These domains may provide important insights in identifying underlying neurobiological dysfunction driving an individual's clinical response to trauma. However, such assessments are burdensome, costly, and time-consuming. To overcome barriers, efforts have emerged to measure multiple domains of cognitive functioning through the application of machine learning (ML) models to passive data sources. Methods: We utilized automated computer vision and voice analysis methods to extract facial, movement, and speech characteristics from semi-structured clinical interviews in 81 trauma survivors who additionally completed a cognitive assessment battery. A ML-based regression framework was used to identify variance in visual and auditory measures that relate to multiple cognitive domains. Results: Models derived from visual and auditory measures collectively accounted for a large variance in multiple domains of cognitive functioning, including motor coordination ( $R^2 = 0.52$ ), processing speed ( $R^2 = 0.42$ ), emotional bias ( $R^2 = 0.52$ ), sustained attention ( $R^2 = 0.51$ ), controlled attention ( $R^2 = 0.44$ ), cognitive flexibility ( $R^2 = 0.43$ ), cognitive inhibition ( $R^2 = 0.64$ ), and executive functioning ( $R^2 = 0.63$ ), consistent with the high test-retest reliability of traditional cognitive assessments. Face, voice, speech content, and movement have all significantly contributed to explaining the variance in predicting functioning in all cognitive domains. Conclusions: The results demonstrate the feasibility of automated measurement of reliable proxies of cognitive functioning through low-burden passive patient evaluations. This makes it easier to monitor cognitive functions and to intervene earlier and at a lower threshold without requiring a time-consuming neurocognitive assessment by, for instance, a licensed psychologist with specialized training in neuropsychology.

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**DOI:** <http://dx.doi.org/10.1159/000512394>

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**First available:** 2021-01-12

**Grant:** K01MH1024153259/1-1. Deutsche Forschungsgemeinschaft.

K. Schultebrucks was supported by the German Research Foundation (SCHU 3259/1-1). The study was also supported by K01MH102415 (I.R. Galatzer-Levy).

**Identifier (keyword):** Cognitive functioning, Computer vision, Deep learning, Digital biomarkers, Emergency department, Voice analysis

**Language:** English

**Language of abstract:** English

**Number of references:** 40

**Publication date:** Jan 2021

**Publication type:** Journal

**Publisher:** S. Karger AG

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**Subject:** Embase;biological marker (major);adult;Article;attention;cognition (major);cognitive flexibility;computer vision (major);digital technology (major);emotional bias;executive function;feasibility study;feature extraction;female;head injury;human;inhibition (psychology);injury (major);machine learning (major);major clinical study;male;motor coordination;motor performance;movement (physiology);priority journal;processing speed;semi structured interview;speech;survivor (major);test retest reliability;voice;voice analysis (major)

**Updates:** 2021-01-122021-05-142021-08-032021-09-30

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Document 182

## **Speech Technology for Healthcare: Opportunities, Challenges, and State of the Art**

**Author:** Latif, Siddique 1 ; Qadir, Junaid 2 ; Qayyum, Adnan 2 ; Usama, Muhammad 2 ; Younis, Shahzad 3

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**Publication info:** IEEE Reviews in Biomedical Engineering 14 : 342-356. Institute of Electrical and Electronics Engineers Inc. (2021)

**Abstract (summary):** Speech technology is not appropriately explored even though modern advances in speech technology - especially those driven by deep learning (DL) technology - offer unprecedented opportunities for transforming the healthcare industry. In this paper, we have focused on the enormous potential of speech technology for revolutionising the healthcare domain. More specifically, we review the state-of-the-art approaches in automatic speech recognition (ASR), speech synthesis or text to speech (TTS), and health detection and monitoring using speech signals. We also present a comprehensive overview of various challenges hindering the growth of speech-based services in healthcare. To make speech-based healthcare solutions more prevalent, we discuss open issues and suggest some possible research directions aimed at fully leveraging the advantages of other technologies for making speech-based healthcare solutions more effective.

**Accession number:** 632263852

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**Correspondence author:** Latif, Siddique University of Southern Queensland (USQ), Springfield, QLD, 4350, Australia.

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**Identifier (keyword):** automatic speech recognition (ASR), Deep learning, healthcare, remote monitoring, speechbiomarkers, speech synthesis

**Language:** English

**Language of abstract:** English

**Number of references:** 217

**Publication date:** 2021

**Publication type:** Journal

**Publisher:** Institute of Electrical and Electronics Engineers Inc.

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**Subject:** Embase;MEDLINE;article;automatic speech recognition (major);human;human experiment;synthesis

**Updates:** 2020-07-102020-08-102020-09-252021-02-02

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Document 183

## Identification of Mild Cognitive Impairment among Chinese Based on Multiple Spoken Tasks

**Author:** Wang, Tianqi 1 ; Hong, Yin 2 ; Wang, Quanyi 3 ; Su, Rongfeng 3 ; Ng, Manwa Lawrence 4 ; Xu, Jun 5 ; Wang, Lan 3 ; Yan, Nan 3

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**Publication info:** Journal of Alzheimer's Disease 82.1: 185-204. IOS Press BV. (2021)

**Abstract (summary):** Background: Previous studies explored the use of noninvasive biomarkers of speech and language for the detection of mild cognitive impairment (MCI). Yet, most of them employed single task which might not have adequately captured all aspects of their cognitive functions. Objective: The present study aimed to achieve the state-of-the-art accuracy in detecting

individuals with MCI using multiple spoken tasks and uncover task-specific contributions with a tentative interpretation of features. Methods: Fifty patients clinically diagnosed with MCI and 60 healthy controls completed three spoken tasks (picture description, semantic fluency, and sentence repetition), from which multidimensional features were extracted to train **machine learning** classifiers. With a late-fusion configuration, predictions from multiple tasks were combined and correlated with the participants' cognitive ability assessed using the Montreal Cognitive Assessment (MoCA). Statistical analyses on pre-defined features were carried out to explore their association with the diagnosis. Results: The late-fusion configuration could effectively boost the final classification result (**SVM**: F1 = 0.95; RF: F1 = 0.96; LR: F1 = 0.93), outperforming each individual task classifier. Besides, the probability estimates of MCI were strongly correlated with the MoCA scores (**SVM**: -0.74; RF: -0.71; LR: -0.72). Conclusion: Each single task tapped more dominantly to distinct cognitive processes and have specific contributions to the prediction of MCI. Specifically, picture description task characterized communications at the discourse level, while semantic fluency task was more specific to the controlled lexical retrieval processes. With greater demands on working memory load, sentence repetition task uncovered memory deficits through modified **speech** patterns in the reproduced sentences.

**Accession number:** 635433050

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**Identifier (keyword):** Language, machine learning, mild cognitive impairment, screening, speech

**Language:** English

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**Subject:** Embase;MEDLINE;adult;Article;clinical article;cohort analysis;controlled study;feature extraction;female;human;language test (major);machine learning;male;middle aged;mild cognitive impairment (major);Montreal cognitive assessment;multiple spoken task + (major);picture description +;semantic fluency +;sentence repetition +;speech and language;support vector machine

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Document 184

## **Multi-layer picture of neurodegenerative diseases: Lessons from the use of big data through artificial intelligence**

**Author:** Termine, Andrea 1 ; Fabrizio, Carlo 2 ; Strafella, Claudia 3 ; Caputo, Valerio 3 ; Petrosini, Laura 2 ; Caltagirone, Carlo 4 ; Giardina, Emiliano 5 ; Cascella, Raffaella 6

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**Publication info:** Journal of Personalized Medicine 11.4 MDPI AG. (2021)

**Abstract (summary):** In the big data era, artificial intelligence techniques have been applied to tackle traditional issues in the study of neurodegenerative diseases. Despite the progress made in understanding the complex (epi)genetics signatures underlying neurodegenerative disorders, performing early diagnosis and developing drug repurposing strategies remain serious challenges for such conditions. In this context, the integration of multi-omics, neuroimaging, and electronic health records data can be exploited using deep learning methods to provide the most accurate representation of patients possible. Deep learning allows researchers to find multi-modal biomarkers to develop more effective and personalized treatments, early diagnosis tools, as well as useful information for drug discovering and repurposing in neurodegenerative pathologies. In this review, we will describe how relevant studies have been able to demonstrate the potential of deep learning to enhance the knowledge of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases through the integration of all sources of biomedical data.

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**Identifier (keyword):** Artificial intelligence, Big data, Deep learning, Neurodegenerative diseases, Precision medicine

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**Subject:** Embase;biological marker;algorithm;Alzheimer disease;artificial intelligence (major);artificial neural network;autoencoder;big data (major);bradykinesia;cancer research;cognitive defect;convolutional neural network;deep learning (major);degenerative disease (major);drug repositioning;early diagnosis;electronic health record;human;image segmentation;machine learning (major);neuroimaging;nuclear magnetic resonance imaging;Parkinson disease;personalized medicine (major);phenotype;recurrent neural network;restricted Boltzmann machine;Review;speech discrimination;telerehabilitation

**Updates:** 2021-05-212021-06-25

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Document 185

## **The next generation of speech biomarkers for the early detection of Alzheimer's disease**

**Author:** Fristed, Emil 1 ; Skirrow, Caroline 2 ; Weston, Jack 1 ; Kourtis, Lampros 3 ; Bjorklund, Nicole 4 ; Malzbender, Kristina 5 ; Purushothama, Shobha 4 ; Fillit, Howard 4

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**Publication info:** Journal of Prevention of Alzheimer's Disease 8.SUPPL 1: S7-S8. Springer. (2021)

**Abstract (summary):** 1Episodic memory tests, such as story recall tasks, show some of the earliest changes associated with Alzheimer's disease. The Automatic Story Recall Task (ASRT) consists of 36 parallel stories (18 long stories and 18 short), balanced for key linguistic and discourse metrics, and developed for self-supervised administration. The ASRT is designed to elicit naturalistic connected speech while constraining the domain of discourse, providing a natural setting for

automated **speech** assessment. We present initial results from the AMYPRED study (NCT04828122) in which a subset of participants (N=95; 32 with Mild Cognitive Impairment (MCI), and 63 cognitively normal (CN)) were assessed remotely over seven days using their personal smart devices. Stories were administered in triplets, with recall recorded immediately after presentation, and after a delay. Responses were automatically uploaded, auto-transcribed by an automatic **speech** recognition system, and auto-scored using an automated text similarity metric. Engagement with the assessment battery was high (mean 73% MCI vs 80% CN completing at least one story each day), and did not differ between groups. Lower text similarity score indicating poorer task performance was observed in participants with MCI ( $p < 0.001$ ). Correlations of task performance between individual parallel ASRT stories were moderate, as were correlations with the Wechsler Logical Memory Test (a test of verbal episodic memory administered in clinic and manually scored), indicating acceptable parallel forms reliability and concurrent validity, respectively. Despite using a generic text similarity metric to score responses, the results show that remote self-supervised administration and auto-scoring yields sensitive cognitive data in key populations, supporting the use case for longitudinal disease monitoring. New metrics targeting other changes measurable in **speech** data (acoustic, semantic, linguistic) in early-stage Alzheimer's disease could further leverage the information content of ASRTs, developing a new class of powerful, fully automated **speech biomarkers**.

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**Correspondence author:** Fristed, Emil Novoic, London, United Kingdom.

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**Subject:** Embase;biological marker (major);adult;Alzheimer disease (major);automatic speech recognition (major);concurrent validity;conference abstract;controlled study;episodic memory;female;genetic transcription;human;major clinical study;male;memory test;mild cognitive impairment;recall;reliability;task performance

**Updates:** 2021-12-06

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Document 186

### **Prospect-ad-population-based screening over speech for clinical trials in ad**

**Author:** König, Alexandra 1 ; Linz, Nicklas 2 ; Ritchie, Craig 3 ; Teipel, Stefan 4 ; Dubois, Bruno 5 ; Bombois, Stephanie 5 ; Teichmann, Marc 5 ; Palmqvist, Sebastian 6 ; Hansson, Oskar 6

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**Publication info:** Journal of Prevention of Alzheimer's Disease 8.SUPPL 1: S149-S150. Springer. (2021)

**Abstract (summary):** Background: Language and speech impairments are an early feature of neurodegenerative dementias. Consequently, digital biomarkers of language and speech performance may be promising tools for early diagnosis. The current new era of Alzheimer's disease (AD) clinical trials suggests a shift to very early identification of people at risk. Hence, digital markers of language and speech may serve the screening of at-risk populations that are at a prodromal stage of AD, eventually in combination with advanced machine learning longitudinal modelling. Here, we conceived a pre-screening battery consisting of speech-based neurocognitive tests, enabling automated first-line pre-screening to be performed remotely using a telephone. Objectives: PROSPECT-AD aims to build and validate speech-based machine learning models for the detection of the relevant phenotype through access to gold-standard phenotyped cohorts. Further, the predictive potential (sensitivity/specificity) for differential/prognostic diagnosis based on information extracted from the participant's speech in cognitive vocal and narrative speech tasks and its usefulness for remote pre-screening and monitoring will be examined. Methods: PROSPECT-AD collaborates with already ongoing cohorts such as EPAD (UK), DELCODE (Germany), INSIGHT-

preAD II (France) or BIOFINDER (Sweden) by adding the collection of **speech** data to existing protocols or as follow-up assessments over the telephone. Participants at preclinical stages are mainly recruited from existing parent cohorts across Europe to form a 'probability-spectrum' population covering the entire continuum of anticipated probability for Alzheimer's dementia development. This characterization of cognitive, **biomarker** and risk factor (genetic and environmental) status of each research participants over time combined with audio recordings of **speech** samples will provide the necessary well-phenotyped population for developing predictive longitudinal models for Alzheimer's disease covering the entire disease course and concurrently create a pool of highly characterized individuals for the validation analysis. 300 participants aged 50 or older will be included per cohort, with a clinical dementia rating scale (CDR) score of 0 or 0.5. The study protocol is planned to run over 18 months. The **speech** protocol includes the following tests which will be administered remotely: Word List, Story Retelling [Learning &Memory]; Digit Span, Phonemic Verbal Fluency, Semantic Verbal Fluency [Executive Functions], Spontaneous free **speech** [Psychological and/or behavioral symptoms]. The spoken features extracted from the recordings will be compared to data from the neuropsychological evaluations, genetic profiles, **biomarkers**, neuroimaging, family history. Based on the analysis of **vocal** performances, models will be trained to predict participant's risk to convert to AD dementia; employing advanced **machine learning** and different computational techniques to identify the most significant **speech** markers that could represent an early indicator for a pre-screening scenario. Results: The overall study protocol is being developed and will be presented at the conference in addition to previous research findings and its resulting new hypotheses. Conclusion: The outcome of PROSPECT-AD may have a major impact on the improvement of drug development research methodology by providing a validated telemedical solution for neurocognitive pre-screening and monitoring of participants of early AD clinical trials.

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**Correspondence author:** König, Alexandra Institut National De Recherche En Informatique Et En Automatique (inria), Valbonne, France.

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**Subject:** Embase;biological marker;adult;Alzheimer disease;audio recording;Clinical Dementia Rating;cohort analysis;conference abstract;controlled study;disease simulation;executive function;family history;female;follow up;France;genetic marker;genetic profile;Germany;gold standard;human;language;machine learning;major clinical study;male;memory;narrative;neuroimaging;phenotype;preclinical study;probability;risk factor;sensitivity and specificity;speech analysis (major);speech test;Sweden;telephone

**Updates:** 2021-12-06

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Document 187

## **Evaluation of a remote speech-based ai system for detection of amyloid-confirmed prodromal alzheimer's disease**

**Author:** Fristed, Emil 1 ; Skirrow, Caroline 1 ; Meszaros, Marton 1 ; Raphael, Lenain 1 ; Meepegama, Udeepa 1 ; Weston, Jack 1

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**Publication info:** Journal of Prevention of Alzheimer's Disease 8.SUPPL 1: S152. Springer. (2021)

**Abstract (summary):** Background: Disease modifying treatments are often trialled in individuals with Mild Cognitive Impairment (MCI) or Mild Alzheimer's disease (AD), and confirmed Amyloid beta (A $\beta$ ) positivity, and it is in these individuals that treatment response and risk profiles are established. MCI is typically identified through clinical interview and cognitive testing, while A $\beta$  positivity usually is established using higher cost, more invasive measures, which are ill-suited for broader screening in clinical care. Screening methods that are accessible, well tolerated, cost-effective, and simple to administer are urgently needed to improve screening for trials and treatment suitability. Subtle cognitive changes early in the AD continuum are seen in episodic and semantic memory, typically measured during verbal cognitive assessments. However the simple response indices used for scoring the verbal responses have uniformly small effect sizes for detecting A $\beta$  positivity. In recent

years AI models have surpassed humans in understanding natural language, and such models could be leveraged to extract sensitive biomarkers from spoken responses. Further, speech-testing can be rapidly implemented at scale via mobile devices. To date, no studies have combined deep speech phenotyping with an early-stage biomarker-confirmed AD population. Objectives: To develop speech-based AI algorithms to detect amyloid-confirmed prodromal Alzheimer's disease. Methods: We present initial results from the AMYPRED study (NCT04828122). Subjects were approached if they had undergone a prior A $\beta$  PET scan or CSF test (confirmed A $\beta$ -within 30 months, or A $\beta$ + within 60 months), and were cognitively unimpaired (CU; Mini mental state exam (MMSE) 26-30) or were diagnosed with MCI or Mild AD (MMSE 23-30). Participants underwent a clinical assessment via telemedicine, followed by optional remote assessments daily using their personal digital devices for 7-8 days. Assessments included the Automatic Story Recall Test (ASRT), using 18 'short' and 18 'long' parallel story variants, administered in triplets (three stories administered for immediate and delayed recall). Short story ASRTs at immediate recall were selected for onward analysis. A random triplet was picked uniformly for all participants, provided they had fully completed the three stories. Responses were transcribed using an out-of-the-box Automatic Speech Recognition (ASR) technology. Responses were analysed with ParaBLEU, a paraphrase representation learning model and evaluation metric. Static representations were obtained from ParaBLEU by inputting pairs of story target and response, and fed into a logistic regression model trained with the sklearn package in Python. Classifiers were trained using tournament leave-pair-out cross-validation analyses, where logistic regression models were trained to predict pairs of labels (MCI/Mild AD vs. CU; or A $\beta$ + vs. A $\beta$ -). Participant level probabilities were ensembled across the stories to create a ranking for each participant for Receiver Operating Curve (ROC) analysis. 95% confidence intervals for Area Under the Curve (AUC) were computed using DeLong's method. The AI system was compared to a demographic baseline (age, gender and years in education). Real-world implementation was simulated using an age 50+ sample in eight 5-year buckets with proportional representation of each age group representative of the US population, and prevalence estimates of MCI vs. CU, and A $\beta$ + vs. A $\beta$ - from prior meta-analysis. The AI system's confusion matrix within the sample was determined, using a conservative ROC cutoff value of 0.7. Prescreening simulation followed established methods. Results: One hundred and six participants (mean age=69.6, range 54-80, 54 Female/52 Male; 60 CU and 46 MCI/Mild AD (20 A $\beta$ + and 26 A $\beta$ -) completed at least one full set of remote short ASRTs. Groups did not differ on demographic variables, except in the MCI subanalysis, where a significantly higher proportion of men were in the amyloid positive group (75% A $\beta$ + vs. 42% A $\beta$ -). The AI system used an average of 2.7 minutes of automatically transcribed speech as its only input. MCI classification using the AI system had an AUC of 0.85+/-0.07. The demographic baseline (AUC = 0.50+/-0.12) was not statistically better than random. For amyloid classification within the MCI group the AI system had an AUC of 0.74+/-0.14. The demographic baseline had an AUC of 0.64+/-0.16, again not reaching statistical significance. For population wide screening for MCI in the simulated population sample the AI system had a Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of 43.2% and 95.4% at age 50+, and 54.7% and 92.8% at age 65+ (US Medicare population). For A $\beta$  pre-screening in the simulated population sample the AI system had a PPV and NPV of 61.8% and 68.0% at age 50+, and 71.2% and 58.2% at age 65+. Such prescreening would reduce the cost of a molecular screening programme at age 50+ and 65+ by 33.8% and 27.9%.

Conclusion: **Speech**-based testing offers scalable screening to identify suitable patients for clinical trials and approved treatments.

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**Subject:** Embase; amyloid beta protein; **biological marker**; endogenous compound; aged; algorithm (major); Alzheimer disease (major); area under the curve; **automatic speech recognition** (major); cerebrospinal fluid; **classifier**; clinical assessment; conference abstract; controlled study; **cross validation**; demography; diagnosis; diagnostic test accuracy study; education; effect size; **feature learning (machine learning)**; female; gender; genetic transcription; groups by age; human; interview; language; major clinical study; male; medicare; mild cognitive impairment; Mini Mental State Examination; phenotype; positron emission tomography; predictive value; prevalence; probability; protein function; recall; semantic memory; simulation; statistical significance; telemedicine; treatment response; validation process

**Substance:** Substance Substance: amyloid beta protein; CAS: 109770-29-8;

## Amyloid prediction in early-stage alzheimer's

**Author:** Fristed, Emil 1 ; Meszaros, Marton 1 ; Skirro, Caroline 1 ; Weston, Jack 1

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**Publication info:** Journal of Prevention of Alzheimer's Disease 8.SUPPL 1: S155-S156. Springer. (2021)

**Abstract (summary):** Background: Recent research has identified subtle cognitive changes during the preclinical stages of Alzheimer's disease (AD), in domains including episodic memory, potentially due to amyloid accumulation in the hippocampus, and in semantic memory, potentially due to accumulation of tau in the entorhinal and perirhinal cortex. At the prodromal stage, a similar but more pronounced impairment is observed. Other retrospective studies have identified changes in linguistic patterns decades before disease onset. These cognitive changes can be reflected in how someone speaks, for example in more vague retellings (episodic memory), less semantic diversity (semantic memory), or more improbable sentences (linguistic patterns). Today, **speech** can easily be collected remotely via mobile devices, and audio-and text-based **machine learning** models can be used to extract sensitive **biomarkers**. To date, there are no studies combining deep **speech** phenotyping with an early-stage **biomarker**-confirmed Alzheimer's disease population. Objectives: To describe the study design for the AMYPRED and AMYPRED-US studies, two sister studies to evaluate the ability of **speech**-based algorithms to detect amyloid-confirmed prodromal and preclinical Alzheimer's disease. Methods: AMYPRED and AMYPRED-US are observational, cross-sectional, case-control sister studies in the UK (multi-site) and US (single-site). The studies have been designed to allow for out-of-sample validation of the tested algorithms across geographies. AMYPRED and AMYPRED-US will enroll approximately 140 and 80 participants respectively, across four arms: Mild Cognitive Impairment (MCI) amyloid positive (Arm 1), MCI amyloid negative (Arm 2), Cognitively Normal (CN) amyloid positive (Arm 3), and CN amyloid negative (Arm 4). Inclusion required confirmation of amyloid status, either through PET or CSF sampling; with test results at most 30 months old for negatives, and 60 months for positives. Enrolled participants are aged 50-85, with MMSE scores of 23-30 for the MCI, and 26-30 for CN cohorts. Additional inclusion criteria includes English as a first language, availability of a caregiver, and an eligible smartphone device for the remote self-assessments. Key exclusion criteria include current or recent history of general anxiety disorder, major depressive disorder, unstable psychiatric illnesses, stroke or transient ischaemic attack. Participants treated with medications for symptoms related to AD are required to be on stable doses for a minimum of 8 weeks prior to participation. Visits are performed remotely through video-conference in AMYPRED and in-person in AMYPRED-US. Eligibility is evaluated at a combined screening/baseline visit, where demographic, medication and medical history information is recorded, and the Mini Mental State



Examination (MMSE) is administered. Eligible participants complete the rest of the screening/baseline visit, where neuropsychological testing, including the Preclinical Alzheimer's Clinical Composite with semantic processing (PACC5), CDR and a subjective memory decline questionnaire are administered, together with a set of audio-verbal assessments, designed to elicit open-ended, connected **speech**. Audio-verbal assessments are recorded via Novoic's mobile application using the participant's own smartphone and, in AMYPRED-US, high-definition recording equipment. In both studies, the screening/baseline visit is followed by a week of remote, self-administered testing. Here fully automated audio-verbal assessments are self-administered daily through Novoic's mobile application, and the elicited **speech** automatically recorded. Participants of all four cohorts complete the same assessments, with minor differences in the assessment schedule between AMYPRED and AMYPRED-US. Audio-verbal tasks most notably include a novel story recall task, the Automated Story Recall Task (ASRT), designed for repeated remote administration, where both the administration and analysis can be fully automated. Other tasks included multiple variations of describing pictures, describing how to carry out everyday tasks, reading a scripted passage, and semantic and phonemic category fluency tests-administered both in the visit and as remote self-assessments. Results: The primary objective of both studies is to evaluate whether **speech**-based algorithms can detect amyloid-specific cognitive impairment in early stage Alzheimer's disease, as measured by the Area Under the Curve (AUC) of the receiver operating characteristic curve of the binary classifier distinguishing amyloid positive (Arm 1 and 3) from amyloid negative (Arm 2 and 4) arms. Secondary objectives are to evaluate these algorithms as measured by binary classifier performance (AUC, sensitivity, specificity, Cohen's kappa) for detecting (1) amyloid in prodromal (Arm 1 vs 2) and preclinical AD (Arm 3 vs 4) separately; and (2) cognitive impairment (Arm 1+2 vs Arm 3+4). Additionally, agreement between the PACC5 composite and the corresponding regression model predicting PACC5 from **speech** in all arms pooled (Wilcoxon signed-rank test, coefficient of individual agreement). Participants that enroll in either AMYPRED and AMYPRED-US are offered to enroll into two extension studies: FUTURE(-US) and PAST(-US). FUTURE extension studies are three year longitudinal studies with yearly visits for neuropsychological testing and ongoing remote self-assessment. PAST extension studies are retrospective, collecting past spoken and written material. Conclusion: AMYPRED and AMYPRED-US will evaluate the ability of **speech**-based algorithms to detect amyloid-confirmed prodromal and preclinical Alzheimer's disease.

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**Subject:** Embase;biological marker;adult;aged;algorithm (major);Alzheimer disease (major);amnesia;anxiety disorder;area under the curve;caregiver;cerebrospinal fluid;child;classifier;cohort analysis;conference abstract;controlled study;demography;eligibility;episodic memory;female;human;language;longitudinal study;major clinical study;major depression;medical history;middle aged;mild cognitive impairment;Mini Mental State Examination;mobile application;neuropsychological test;phenotype;preclinical study;prediction (major);preschool child;questionnaire;recall;receiver operating characteristic;retrospective study;self evaluation;semantic memory;sensitivity and specificity;smartphone;speech;transient ischemic attack;videoconferencing;Wilcoxon signed ranks test

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Document 189

## **Neuropsychological test validation of speech markers of cognitive impairment in the Framingham Cognitive Aging Cohort**

**Author:** Zhang, Larry 1 ; Ngo, Anthony 2 ; Thomas, Jason A 3 ; Burkhardt, Hannah A 3 ; Parsey, Carolyn M 4 ; Au, Rhoda 5 ; Ghomi, Reza Hosseini 4

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**Publication info:** Exploration of medicine 2 : 232-252. (2021)

### **Abstract (summary):** AIM

Although clinicians primarily diagnose dementia based on a combination of metrics such as medical history and formal neuropsychological tests, recent work using linguistic analysis of narrative **speech** to identify dementia has shown promising results. We aim to build upon research by Thomas JA &Burkardt HA et al. (J Alzheimers Dis. 2020;76:905-22) and Alhanai et al. (arXiv:1710.07551v1. 2020) on the Framingham Heart Study (FHS) Cognitive Aging Cohort by 1) demonstrating the predictive capability of linguistic analysis in differentiating cognitively normal from cognitively impaired participants and 2) comparing the performance of the original linguistic features with the performance of expanded features.

## METHODS

Data were derived from a subset of the FHS Cognitive Aging Cohort. We analyzed a sub-selection of 98 participants, which provided 127 unique audio files and clinical observations (n = 127, female = 47%, cognitively impaired = 43%). We built on previous work which extracted original linguistic features from transcribed audio files by extracting expanded features. We used both feature sets to train logistic regression classifiers to distinguish cognitively normal from cognitively impaired participants and compared the predictive power of the original and expanded linguistic feature sets, and participants' Mini-Mental State Examination (MMSE) scores.

## RESULTS

Based on the area under the receiver-operator characteristic curve (AUC) of the models, both the original (AUC = 0.882) and expanded (AUC = 0.883) feature sets outperformed MMSE (AUC = 0.870) in classifying cognitively impaired and cognitively normal participants. Although the original and expanded feature sets had similar AUC, the expanded feature set showed better positive and negative predictive value [expanded: positive predictive value (PPV) = 0.738, negative predictive value (NPV) = 0.889; original: PPV = 0.701, NPV = 0.869].

## CONCLUSIONS

Linguistic analysis has been shown to be a potentially powerful tool for clinical use in classifying cognitive impairment. This study expands the work of several others, but further studies into the plausibility of **speech** analysis in clinical use are vital to ensure the validity of **speech** analysis for clinical classification of cognitive impairment.

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**Correspondence author:** Zhang, Larry Department of Intelligent Systems Engineering, Indiana University Bloomington, Bloomington, Indiana 47408, United States. , Department of Informatics, Indiana University Bloomington, Bloomington, Indiana 47408, United States.

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RF1 AG062109. NIA NIH HHS. United States.

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Document 190

## **Development of a novel digital speech composite measure for frontotemporal dementia**

**Author:** Robin, Jessica 1 ; Xu, Mengdan 1 ; Kaufman, Liam 1 ; Simpson, William 1 ; Ward, Michael 2 ; Paul, Robert 2

1 Winterlight Labs, Toronto, Canada 2 Alector, Inc, South San Francisco, United States

**Publication info:** Journal of Prevention of Alzheimer's Disease 8.SUPPL 1: S36. Springer. (2021)

**Abstract (summary):** Background: Changes to speech and language are common symptoms across different subtypes of FTD. These changes affect the ability to communicate, impacting everyday functions important to both patients and their caregivers. Assessing these changes can help to track disease progression and detect response to treatment. Current tools to assess speech and language abilities, however, often involve specialized neuropsychological testing, which can be lengthy, costly and burdensome to patients and their caregivers. Developing tools to objectively measure speech abilities remotely could allow for more frequent assessments, with lower patient burden and higher functional relevance to everyday life. Objectives: In this observational study, patients with FTD and their caregivers conducted remote digital speech assessments using the Winterlight app over a period of 12-months. Our objectives were to determine which aspects of speech showed significant change over time and to develop a novel composite measure for assessing speech and language patterns in FTD. Methods: 36 participants (16 female, 20 male) were enrolled in the study (mean age at enrollment = 61.3 years, standard deviation = 8.7) and 27 (75%) participants completed the 12-month assessment. Participants completed the Winterlight speech assessment remotely with the assistance of a caregiver at Months 1 (baseline), 2, 3, 6, 9 and 12. The speech assessment includes different tasks to elicit speech ranging from unstructured, open-ended tasks like picture description, to more standard clinical language assessments such as phonemic and semantic fluency tests. In each task, the participant saw and heard a set of instructions prompting them to produce a verbal response which was recorded, with responses typically ranging from a few seconds to a few minutes in duration. Speech samples were analyzed using Winterlight's natural language processing platform, generating >500 variables describing acoustic and linguistic characteristics of the speech sample. We used linear mixed models to select which speech variables demonstrated significant change over time, controlling for demographic and task-related variables. A composite measure was developed from the selected variables using principal components analysis (PCA). Results: The picture description task, which was the most naturalistic, open-ended task, generated the highest number of variables with significant change over the 12-month study. Nine speech variables were selected, based on their significant effects of time, controlling for effects of age, sex and stimulus, good test-

retest reliability and low redundancy with one another. The nine selected variables reflected different aspects of **speech** and language including the ratio of words to pauses, the types of words used (e.g. the frequency of nouns, the amount of prepositions), and the information content and complexity of sentences. We developed a novel composite score based on these variables, weighting them according to the results of a principal component analysis. When compared to a sample of healthy control participants, the FTD group had lower scores at baseline on the novel composite score. The resulting composite score had a significant effect of change over time ( $\beta = -0.055$ ,  $p < 0.001$ ) and high test-retest reliability (ICC = 0.76,  $p < 0.001$ ). This novel composite score was correlated with standard scores on the **speech** tasks (e.g. number of words correctly produced for phonemic and semantic fluency, number of correctly named items on the object naming test). Conclusion: This study demonstrated that **digital speech** assessments, which can be completed remotely in less than 15 minutes, have the potential to characterize **speech** and language abilities in FTD. We identified aspects of **speech** that demonstrate significant decline over the course of a year, potentially tracking disease progression. The novel composite measure developed in this study could be used to characterize **speech** patterns in FTD in future studies and detect change over time and response to treatment. Further validation is required by comparing this measure to **biomarkers** or clinical standards and replicating its ability to track disease-related changes in independent samples. **Digital** tools to assess patients remotely can reduce the burden of clinical research and help create novel measures sensitive to disease and relevant to everyday function.

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**Conference end date:** 2021-11-12

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**Conference title:** 14th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** Robin, Jessica Winterlight Labs, Toronto, Canada.

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**Subject:** Embase;biological marker;adult;caregiver;clinical article;clinical assessment;clinical research;conference abstract;controlled study;demography;female;frontotemporal dementia (major);human;human tissue;language ability;male;middle aged;natural language processing;observational study;outcome assessment;principal component analysis;speech analysis (major);speech test;test retest reliability;treatment response

**Updates:** 2021-12-06

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Document 191

### **Associative dysregulation and impaired expressivity in schizophrenia: Latent structures of clinical and automated speech analysis features**

**Author:** Hänsel, Katrin 1 ; Cho, Sunghye 1 ; Berretta, Sarah 1 ; Mehta, Aarush 1 ; Nikzad, Amir 1 ; Dhar, Aamina 1 ; Guo, Jessica 1 ; Cong, Yan 1 ; Pradhan, Sameer 1 ; Fiumara, James 1 ; Liberman, Mark 1 ; Tang, Sunny 1

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**Publication info:** Neuropsychopharmacology 46 : 339-340. Springer Nature. (2021)

**Abstract (summary):** Background: Recent computational advances have enabled objective, automated measurements of speech biomarkers which have accurately predicted clinical phenotypes such as schizophrenia spectrum disorder (SSD) diagnosis and conversion to psychotic disorder from clinical high risk. However, if we are to use features from acoustic analysis and natural language processing to understand brain dysfunction, it is important to understand the underlying structure at the appropriate level of granularity. Here, we extracted latent factors representing associative dysregulation and impaired expressivity in speech, and sought to explore their relationships to clinical status and features from automated speech analysis. Methods: Cohort 1 included 83 prospectively evaluated participants (34 SSD, 11 other psychiatric disorders, 38 healthy control). Cohort 2 included 47 speech samples derived from publicly available psychiatric interviews on YouTube (28 psychotic disorders, 19 other psychiatric disorders). Both cohorts were rated on the Scale for the Assessment of Thought Language and Communication (TLC) and two items from the Scale for the Assessment of Negative Symptoms (SANS; decreased vocal inflection and increased latency). Cohort 1 was additionally rated on the full SANS for negative symptoms, the Brief Psychotic Rating Scale (BPRS) for overall psychosis symptoms, and role and interpersonal functioning items from the Quality of Life

Scale (QLS). Cohort 2 **speech** underwent transcription and processing for acoustic (e.g. pauses, pitch), lexical (e.g. parts of **speech**), coherence (e.g. cosine distance of sentence embeddings, and graph features where edges connect consecutive words, represented as nodes (e.g. density, degree). Exploratory factor analysis (eFA, promax rotation) was used to identify latent factors for clinical ratings of **speech** disturbance across both cohorts. We excluded items with poor sampling adequacy, based on low frequency of non-zero ratings and the Kayser-Meyer-Olkin test. In Cohort 1, factor scores were evaluated against participant characteristics and clinical ratings using multiple linear and logistic regressions. In Cohort 2, principal component analysis (PCA, promax rotation) and correlational analyses were used to examine relationships between the clinical factors and features from automated **speech** analysis. All analyses were completed using R. Results: Two latent factors were found for the clinical ratings of **speech** disturbance across Cohort 1 and Cohort 2, explaining 41% and 12% of variance, respectively: F1) "Associative Dysregulation" - derailment, loss of goal, circumstantiality, tangentiality, poverty of content of **speech**, incoherence, illogicality, pressured **speech**, perseveration, and distractibility; F2) "Impaired Expressivity" - poverty of **speech**, decreased **vocal** inflections, and increased response latency. Factor scores showed expected relationships with clinical variables in Cohort 1. SSD diagnosis significantly predicted higher scores in both factors (F1,  $B = 0.87$ ,  $p < 0.001$ ; F2,  $B = 0.97$ ,  $p < 0.001$ ); this relationship remained significant for F1 but became trend-level for F2 when covarying for demographic variables. Accounting for diagnosis group, F1 remained a significant predictor of overall psychosis symptoms ( $B = 0.23$ ,  $p = 0.02$ ), while F2 did not ( $B = 0.15$ ,  $p = 0.14$ ). Both were significant predictors of negative symptoms (F1,  $B = 0.21$ ,  $p = 0.01$ ; F2,  $B = 0.30$ ,  $p < 0.001$ ), and role functioning (F1,  $B = -0.29$ ,  $p = 0.002$ ; F2,  $B = -0.32$ ,  $p = 0.001$ ). Only F2 predicted interpersonal functioning ( $B = -0.27$ ,  $p = 0.001$ ). Several notable patterns emerged among clinical factors and **speech** features in Cohort 2. F1-Associative Dysregulation was negatively correlated with coherence as measured by cosine distance between adjacent sentence embeddings using Word2-Vec ( $r = -0.53$ ), use of pronouns and verbs ( $r = -0.61$ ,  $r = -0.50$ ), while positively correlated with speaking partial words ( $r = 0.45$ ) and negative valence ( $r = 0.41$ ). F2-Impaired Expressivity was negatively correlated with total word count ( $r = -0.61$ ) and the graph metric for number of nodes on the largest strongly connected component ( $r = -0.63$ ), while positively correlated with graph density ( $r = 0.76$ ) and use of interjections ( $r = 0.49$ ). Conclusions: **Speech** and language dysfunction in SSD can be described by latent factors representing F1) Associative Dysfunction, principally characterized by derailment, loss of goal, and circumstantiality, and F2) Impaired Expressivity, characterized by poverty of **speech**, decreased **vocal** inflections, and increased response latency. Both factors are elevated in SSD, even while covarying for demographic variables, and both predict dimensional clinical and functional status, even when accounting for diagnosis. F1 is more related to overall psychosis symptoms, and can be characterized by **speech** features reflecting decreased coherence, among others. F2 is more related to functioning, and is reflected by graph metrics for restricted connectivity among words.

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**Correspondence author:** Tang, Sunny Feinstein Institutes for Medical Research, Glen Oaks, NY, United States.

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**Subject:** Embase;biological marker (major);adult;cohort analysis;conference abstract;controlled study;demography;diagnosis;distractibility;embedding;exploratory factor analysis;female;functional status;genetic transcription;human;interview;latent schizophrenia (major);logorrhea;machine learning (major);major clinical study;male;natural language processing (major);negative syndrome;perseveration;pitch;poverty;principal component analysis;promax rotation;prospective study;quality of life;rating scale;reaction time;social media;speech analysis (major)

**Updates:** 2021-12-20

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Document 192

## Automated profiling of spontaneous **speech** in primary progressive aphasia and behavioral-variant frontotemporal dementia: An approach based on usage-frequency

**Author:** Zimmerer, Vitor C. 1 ; Hardy, Chris J.D. 2 ; Eastman, James 3 ; Dutta, Sonali 4 ; Varnet, Leo 5 ; Bond, Rebecca L. 2 ; Russell, Lucy 2 ; Rohrer, Jonathan D. 2 ; Warren, Jason D. 2 ; Varley, Rosemary A. 1

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**Publication info:** Cortex 133 : 103-119. Masson SpA. (Dec 2020)

**Abstract (summary):** Language production provides important markers of neurological health. One feature of impairments of language and cognition, such as those that occur in stroke aphasia or Alzheimer's disease, is an overuse of high frequency, "familiar" expressions. We used computerized analysis to profile narrative **speech** samples from speakers with variants of frontotemporal dementia (FTD), including subtypes of primary progressive aphasia (PPA). Analysis was performed on language samples from 29 speakers with semantic variant PPA (svPPA), 25 speakers with logopenic variant PPA (lvPPA), 34 speakers with non-fluent variant PPA (nfvPPA), 14 speakers with behavioral variant FTD (bvFTD) and 20 older normal controls (NCs). We used frequency and collocation strength measures to determine use of familiar words and word combinations. We also computed word counts, content word ratio and a combination ratio, a measure of the degree to which the individual produces connected language. All dementia subtypes differed significantly from NCs. The most discriminating variables were word count, combination ratio, and content word ratio, each of which distinguished at least one dementia group from NCs. All participants with PPA, but not participants with bvFTD, produced significantly more frequent forms at the level of content words, word combinations, or both. Each dementia group differed from the others on at least one variable, and language production variables correlated with established behavioral measures of disease progression. A **machine learning** classifier, using narrative **speech** variables, achieved 90% accuracy when classifying samples as NC or dementia, and 59.4% accuracy when matching samples to their diagnostic group. Automated quantification of spontaneous **speech** in both language-led and non-language led dementias, is feasible. It allows extraction of syndromic profiles that complement those derived from standardized tests, warranting further evaluation as candidate **biomarkers**. Inclusion of frequency-based language variables benefits profiling and classification.

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**Correspondence author:** Zimmerer, Vitor C. , Chandler House, 2 Wakefield Street, London, WC1N 1PF, United Kingdom.

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**Subject:** Embase;MEDLINE;biological marker;adult;aged;Article;clinical article;cognition;depth perception;disease exacerbation;episodic memory;executive function;facial recognition;female;frontal variant frontotemporal dementia (major);human;language;machine learning;male;Mini Mental State

Examination; primary progressive aphasia (major); speech (major); task performance; verbal memory test; working memory

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Document 193

## **Voice perturbations under the stress overload in young individuals: phenotyping and suboptimal health as predictors for cascading pathologies**

**Author:** Kunin, A. 1 ; Sargheini, N. 2 ; Birkenbihl, C. 3 ; Moiseeva, N. 1 ; Fröhlich, Holger 3 ; Golubnitschaja, Olga 4

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**Publication info:** EPMA Journal 11.4: 517-527. Springer Science and Business Media Deutschland GmbH. (Dec 2020)

**Abstract (summary):** Verbal communication is one of the most sophisticated human motor skills reflecting both—the mental and physical health of an individual. Voice parameters and quality changes are usually secondary towards functional and/or structural laryngological alterations under specific systemic processes, syndrome and pathologies. These include but are not restricted to dry mouth and Sicca syndromes, body dehydration, hormonal alterations linked to pubertal, menopausal, and andropausal status, respiratory disorders, gastrointestinal reflux, autoimmune diseases, endocrinologic disorders, underweight versus overweight and obesity, and diabetes mellitus. On the other hand, it is well-established that stress overload is a significant risk factor of cascading pathologies, including but not restricted to neurodegenerative and psychiatric disorders, diabetes mellitus, cardiovascular disease, stroke, and cancers. Our current study revealed voice perturbations under the stress overload as a potentially useful biomarker to identify individuals in suboptimal health conditions who might be strongly predisposed to associated pathologies. Contextually, extended surveys applied in the population might be useful to identify, for example, persons at high risk for respiratory complications under pandemic conditions such as COVID-19. Symptoms of dry mouth syndrome, disturbed microcirculation, altered sense regulation, shifted circadian rhythm, and low BMI were positively associated with voice perturbations under the stress overload. Their functional interrelationships and relevance for cascading associated pathologies are presented in the article. Automated analysis of voice recordings via artificial intelligence (AI) has a potential to derive digital

**biomarkers**. Further, predictive **machine learning** models should be developed that allows for detecting a suboptimal health condition based on **voice** recordings, ideally in an automated manner using derived digital **biomarkers**. Follow-up stratification and monitoring of individuals in suboptimal health conditions are recommended using disease-specific cell-free nucleic acids (ccfDNA, ctDNA, mtDNA, miRNA) combined with metabolic patterns detected in body fluids. Application of the cost-effective targeted prevention within the phase of reversible health damage is recommended based on the individualised patient profiling.

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Document 194

### **Towards the automatic detection of social biomarkers in autism spectrum disorder: introducing the simulated interaction task (SIT)**

**Author:** Drimalla, Hanna 1 ; Scheffer, Tobias 2 ; Landwehr, Niels 3 ; Baskow, Irina 4 ; Roepke, Stefan 5 ; Behnia, Behnoush 5 ; Dziobek, Isabel 6

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**Publication info:** npj Digital Medicine 3.1 Nature Research. (Dec 1, 2020)

**Abstract (summary):** Social interaction deficits are evident in many psychiatric conditions and specifically in autism spectrum disorder (ASD), but hard to assess objectively. We present a digital tool to automatically quantify **biomarkers** of social interaction deficits: the simulated interaction task (SIT), which entails a standardized 7-min simulated dialog via video and the automated analysis of facial expressions, gaze behavior, and **voice** characteristics. In a study with 37 adults with ASD without intellectual disability and 43 healthy controls, we show the potential of the tool as a diagnostic instrument and for better description of ASD-associated social phenotypes. Using **machine-learning** tools, we detected individuals with ASD with an accuracy of 73%, sensitivity of 67%, and specificity of 79%, based on their facial expressions and **vocal** characteristics alone. Especially reduced social smiling and facial mimicry as well as a higher **voice** fundamental frequency and harmony-to-noise-ratio were characteristic for individuals with ASD. The time-effective and cost-effective computer-based analysis outperformed a majority vote and performed equal to clinical expert ratings.

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Document 195

## Evaluation of Speech-Based Digital Biomarkers: Review and Recommendations

**Author:** Robin, Jessica 1 ; Harrison, John E 2 ; Kaufman, Liam D 1 ; Rudzicz, Frank 3 ; Simpson, William 4 ; Yancheva, Maria 1

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**Publication info:** Digital biomarkers 4.3: 99-108. (Oct 19, 2020)

**Abstract (summary):** Speech represents a promising novel biomarker by providing a window into brain health, as shown by its disruption in various neurological and psychiatric diseases. As with many novel digital biomarkers, however, rigorous evaluation is currently lacking and is required for these measures to be used effectively and safely. This paper outlines and provides examples from the literature of evaluation steps for speech-based digital biomarkers, based on the recent V3 framework (Goldsack et al., 2020). The V3 framework describes 3 components of evaluation for digital biomarkers: verification, analytical validation, and clinical validation. Verification includes assessing the quality of speech recordings and comparing the effects of hardware and recording conditions on the integrity of the recordings. Analytical validation includes checking the accuracy and reliability of data processing and computed measures, including understanding test-retest reliability, demographic variability, and comparing measures to reference standards. Clinical validity involves verifying the correspondence of a measure to clinical outcomes which can include diagnosis, disease progression, or response to treatment. For each of these sections, we provide recommendations for



the types of evaluation necessary for **speech-based biomarkers** and review published examples. The examples in this paper focus on **speech-based biomarkers**, but they can be used as a template for **digital biomarker** development more generally.

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**Correspondence author:** Robin, Jessica Winterlight Labs, Toronto, Ontario, Canada.

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**Notes:** J.R., L.D.K., W.S., and M.Y. are employees of Winterlight Labs. J.E.H. reports receipt of personal fees in the past 3 years from AlzeCure, Aptinyx, Astra Zeneca, Athira Therapeutics, Axon Neuroscience, Axovant, Biogen Idec, BlackThornRx, Boehringer Ingelheim, Cerecin, Cognition Therapeutics, Compass Pathways, CRF Health, Curasen, EIP Pharma, Eisai, FSV7, G4X Discovery, GfHEU, Heptares, Lundbeck, Lysosome Therapeutics, MyCognition, Neurocentria, Neurocog, Neurodyn Inc, Neurotrack, Novartis, Nutricia, Probiodrug, Regeneron, Rodin Therapeutics, Samumed, Sanofi, Servier, Signant, Syndesi Therapeutics, Takeda, Vivoryon Therapeutics, vTv Therapeutics, and Winterlight Labs. Additionally, he holds stock options in Neurotrack Inc. and is a joint holder of patents with My Cognition Ltd. F.R. is an employee of Surgical Safety Technologies.;; Publication model: Electronic-eCollection;; Cited medium:Internet

**Publication date:** Oct 19, 2020

**Publication type:** Journal

**Publisher location:** SWITZERLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2020-11-302020-12-01

## Detection of Mild Cognitive Impairment Through Natural Language and Touchscreen Typing Processing

**Author:** Ntracha, Anastasia 1 ; Iakovakis, Dimitrios 1 ; Hadjidimitriou, Stelios 1 ; Charisis, Vasileios S 1 ; Tsolaki, Magda 2 ; Hadjileontiadis, Leontios J 3

1 Department of Electrical and Computer Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece, Greece 2 Third Department of Neurology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece, Greece 3 Department of Electrical and Computer Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece, Department of Electrical and Computer Engineering, Khalifa University of Science and Technology, Abu Dhabi, United Arab Emirates, United Arab Emirates

**Publication info:** Frontiers in digital health 2 : 567158. (Oct 8, 2020)

**Abstract (summary):** Mild cognitive impairment (MCI), an identified prodromal stage of Alzheimer's Disease (AD), often evades detection in the early stages of the condition, when existing diagnostic methods are employed in the clinical setting. From an alternative perspective, smartphone interaction behavioral data, unobtrusively acquired in a non-clinical setting, can assist the screening and monitoring of MCI and its symptoms' progression. In this vein, the diagnostic ability of digital **biomarkers**, drawn from Fine Motor Impairment (FMI)- and Spontaneous Written **Speech** (SWS)-related data analysis, are examined here. In particular, keystroke dynamics derived from touchscreen typing activities, using **Convolutional Neural Networks**, along with linguistic features of SWS through Natural Language Processing (NLP), were used to distinguish amongst MCI patients and healthy controls (HC). Analytically, three indices of FMI (rigidity, bradykinesia and alternate finger tapping) and nine NLP features, related with lexical richness, grammatical, syntactical complexity, and word deficits, formed the feature space. The proposed approach was tested on two demographically matched groups of 11 MCI patients and 12 HC, having undergone the same neuropsychological tests, producing 4,930 typing sessions and 78 short texts, within 6 months, for analysis. A cascaded-classifier scheme was realized under three different feature combinations and validated via a Leave-One-Subject-Out cross-validation scheme. The acquired results have shown: (a) keystroke features with a k-NN classifier achieved an Area Under Curve (AUC) of 0.78 [95% confidence interval (CI):0.68-0.88; specificity/sensitivity (SP/SE): 0.64/0.92], (b) NLP features with a Logistic regression classifier achieved an AUC of 0.76 (95% CI: 0.65-0.85; SP/SE: 0.80/0.71), and (c) an ensemble model with the fusion of keystroke and NLP features resulted in AUC of 0.75 (95% CI:0.63-0.86; SP/SE 0.90/0.60). The current findings indicate the potentiality of new digital **biomarkers** to capture early stages of cognitive decline, providing a highly specific remote screening tool in-the-wild.

**Accession number:** 34713039

**Copyright:** Copyright © 2020 Ntracha, Iakovakis, Hadjidimitriou, Charisis, Tsolaki and Hadjileontiadis.

**Correspondence author:** Ntracha, Anastasia Department of Electrical and Computer Engineering, Aristotle University of Thessaloniki, Thessaloniki, Greece.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2021-10-29

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**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.3389/fdgth.2020.567158>

**First available:** 2021-10-29

**Identifier (keyword):** Alzheimer's disease, **deep learning**, fine motor impairment, keystroke dynamics, **machine learning**, natural language processing, remote screening, smartphone

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Electronic-eCollection;; Cited medium:Internet

**Publication date:** Oct 8, 2020

**Publication type:** Journal

**Publisher location:** SWITZERLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2021-10-292021-10-30

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Document 197

### **Digital phenotyping in bipolar disorder: Which integration with clinical endophenotypes and biomarkers?**

**Author:** Orsolini, Laura 1 ; Fiorani, Michele 1 ; Volpe, Umberto 1

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**Publication info:** International Journal of Molecular Sciences 21.20: 1-21. MDPI AG. (Oct 2, 2020)

**Abstract (summary):** Bipolar disorder (BD) is a complex neurobiological disorder characterized by a pathologic mood swing. **Digital** phenotyping, defined as the 'moment-by-moment quantification of the individual-level human phenotype in its own environment', represents a new approach aimed at measuring the human behavior and may theoretically enhance clinicians' capability in early identification, diagnosis, and management of any mental health conditions, including BD. Moreover, a **digital** phenotyping approach may easily introduce and allow clinicians to perform a more personalized and patient-tailored diagnostic and therapeutic approach, in line with the framework of precision psychiatry. The aim of the present paper is to investigate the role of **digital** phenotyping in BD. Despite scarce literature published so far, extremely heterogeneous methodological strategies, and limitations, **digital** phenotyping may represent a grounding research and clinical field in BD, by owning the potentialities to quickly identify, diagnose, longitudinally monitor, and evaluating clinical response and remission to psychotropic drugs. Finally, **digital** phenotyping might potentially constitute a possible predictive marker for mood disorders.

**Accession number:** 2005223084

**Author e-mail address:** laura.orsolini01@gmail.com, michele.fiorani88@gmail.com, u.volpe@staff.univpm.it

**Copyright:** Copyright 2020 Elsevier B.V., All rights reserved.

**Correspondence author:** Orsolini, Laura Unit of Clinical Psychiatry, Department of Neurosciences/DIMSC, School of Medicine, Polytechnic University of Marche, Ancona, 60126, Italy.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-11-25

**Document status:** Revised

**Document type:** Review

**DOI:** <http://dx.doi.org/10.3390/ijms21207684>

**Embase document status:** Embase; In-Process (MEDLINE in Embase)

**First available:** 2020-10-20

**Identifier (keyword):** Bipolar disorder, **Digitalbiomarkers**, **Digital** phenotyping, **Digital** psychiatry, **Digital** tool, Phenotyping

**Language:** English

**Language of abstract:** English

**Number of references:** 56

**Publication date:** Oct 2, 2020

**Publication type:** Journal

**Publisher:** MDPI AG

**Publisher location:** Switzerland

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;biological marker -- endogenous compound (major);lithium -- drug therapy -- bipolar disorder;psychotropic agent;mobile health application;smartphone;algorithm;bipolar disorder -- drug therapy -- lithium (major);digital phenotyping + (major);endophenotype (major);human;major depression;mood disorder;phenotype (major);Review;speech

**Substance:** Substance Substance: lithium; CAS: 7439-93-2;

**Updates:** 2020-10-202020-10-292020-11-25

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Document 198

## VOICE-BASED SCREENING AND MONITORING OF CHRONIC RESPIRATORY CONDITIONS

**Author:** Ashraf, Obaid; Rabold, Erica; Schlichtkrull, Katrina; Singh, Anil; Venneti, Satya; Daanish Ali Khan, Mir Mohammed; Kulshreshtha, Rajat; Pradeep Naval, Prakhar

**Publication info:** Chest, suppl. Supplement 158.4: A1687. Elsevier Inc. (Oct 2020)

**Abstract (summary):** SESSION TITLE: Phenotyping and Management of COPD SESSION TYPE: Original Investigations PRESENTED ON: October 18-21, 2020 PURPOSE: Spirometry is the most important diagnostic test to diagnose and manage many different lung diseases. Voice is an important biomarker of many medical conditions; in particular, diseases of the respiratory system which leave signatures in breath and speech. We hypothesize that voice and breath sounds in human speech are strongly correlated to lung function, and using voice as a biomarker enables non-invasive and accurate detection of lung function. METHODS: We present the interim results of an ongoing study correlating voice and breath samples to lung function. This is a prospective cohort study collecting cross sectional data from participants during regularly-scheduled PFT visits where they provide pre- and post PFT voice and breath sound samples, which correspond to pre and post bronchodilator samples. We collect demographics, medical information and pre- and post- PFT FEV1 and FVC results from all patients. We analyze voice and breath samples and develop a regression algorithm to predict FEV1 and FVC from audio features, and a binary classification algorithm to predict obstruction. We recruited a total of 133 participants aged 18 to 85 years into this study during regularly scheduled PFT visits at a large suburban general hospital in Western Pennsylvania. We recorded voice and breath audio samples on a commodity smart tablet. We developed a proprietary software app to record audio samples and analyzed recorded data off-line on the secure Telling.ai cloud. RESULTS: Our FEV1 model has the following results, averaged across all folds: R squared = 0.75, Mean squared error = 0.17, Mean absolute error = 0.32 L, Binarized Accuracy = 71.5%. Our FVC model has the following results, averaged across all folds: R squared = 0.79, Mean squared error = 0.19, Mean absolute error = 0.35 L, Binarized Accuracy = 71.4%. Our obstruction classifier has a F1 score of 0.75. CONCLUSIONS: We demonstrate that automated voice and breath analysis delivers good diagnostic accuracy in the prediction of FVC (0.79 R<sup>2</sup>) and FEV1 (0.75 R<sup>2</sup>) and classification of obstructed vs non obstructed participants (78% accuracy). This technology requires

no additional custom built hardware, is cost effective, non invasive and practical for ubiquitous and frequent use. **Voice** and breath data is an ideal medium to detect and monitor lung functioning, especially respiration impairment at scale. This data can be collected passively (e.g., as a byproduct of regular human interaction) using widespread, existing infrastructure (e.g., mobile phones). The technique offers the promise of widespread, affordable medical screening and real-time monitoring of respiratory disease. **CLINICAL IMPLICATIONS:** The solution is ideally suited for personalized, frequent monitoring and analysis of an individual's lung function to enable the development of clinical decision support systems and advance personalized medicine for chronic and acute respiratory care. **DISCLOSURES:** Employee relationship with Telling.ai Please note: \$20001 - \$100000 Added 06/01/2020 by Mir Mohammed Daanish Ali Khan, source=Web Response, value=Salary Employee relationship with Telling.ai Please note: \$20001 - \$100000 Added 06/01/2020 by Rajat Kulshreshtha, source=Web Response, value=Salary Employee relationship with Telling.ai Please note: >\$100000 Added 06/01/2020 by Prakhar Pradeep Naval, source=Web Response, value=Salary Chief Technical Officer relationship with Telling.ai Please note: >\$100000 Added 05/31/2020 by Satya Venneti, source=Web Response, value=Salary

**Accession number:** 2008026088

**Conference end date:** 2020-10-21

**Conference location:** Virtual, Online

**Conference start date:** 2020-10-18

**Conference title:** CHEST 2020 Annual Meeting

**Copyright:** Copyright 2020 Elsevier B.V., All rights reserved.

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**Date created:** 2020-10-16

**Document status:** Revised

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1016/j.chest.2020.08.1509>

**Embase document status:** Embase

**First available:** 2020-10-19

**Language:** English

**Language of abstract:** English

**Publication date:** Oct 2020

**Publication type:** Journal

**Publisher:** Elsevier Inc.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;bronchodilating agent;abnormal respiratory sound;adult;aged;binary classification (major);breath analysis;classifier;clinical decision support system;cohort analysis;conference abstract;controlled study;demography;diagnostic accuracy;diagnostic test accuracy study;drug therapy;employee;female;forced expiratory volume;forced vital capacity;general hospital;human;human tissue;lung function;major clinical study;male;medical information;mobile phone;obstruction;Pennsylvania;personalized medicine;prediction;prospective study;respiratory care;salary;software;speech;tablet computer (major);voice (major)

**Updates:** 2020-10-192020-11-03

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Document 199

## **Analysis of Smartphone Recordings in Time, Frequency, and Cepstral Domains to Classify Parkinson's Disease**

**Author:** Tougui, Ilias 1 ; Jilbab, Abdelilah 1 ; Mhamdi, Jamal El 1

1 Department of Biomedical Engineering, Mohammed V University in Rabat, Morocco, Electronic Systems Sensors and Nanobiotechnologies (E2SN), ENSET, Mohammed V University in Rabat, Morocco, Morocco

**Publication info:** Healthcare informatics research 26.4: 274-283. (Oct 2020)

### **Abstract (summary): OBJECTIVES**

Parkinson's disease (PD) is the second most common neurodegenerative disorder; it affects more than 10 million people worldwide. Detecting PD usually requires a professional assessment by an expert, and investigation of the voice as a biomarker of the disease could be effective in speeding up the diagnostic process.

### **METHODS**

We present our methodology in which we distinguish PD patients from healthy controls (HC) using a large sample of 18,210 smartphone recordings. Those recordings were processed by an audio processing technique to create a final dataset of 80,594 instances and 138 features from the time, frequency, and cepstral domains. This dataset was preprocessed and normalized to create baseline machinelearning models using four classifiers, namely, linear support vector machine, K-nearest neighbor, random forest, and extreme gradient boosting (XGBoost). We divided our dataset into training and held-out test sets. Then we used stratified 5-fold cross-validation and four performance measures: accuracy, sensitivity, specificity, and F1-score to assess the performance of the models. We applied two feature selection methods, analysis of variance (ANOVA) and least absolute

shrinkage and selection operator (LASSO), to reduce the dimensionality of the dataset by selecting the best subset of features that maximizes the performance of the classifiers.

## RESULTS

LASSO outperformed ANOVA with almost the same number of features. With 33 features, XGBoost achieved a maximum accuracy of 95.31% on training data, and 95.78% by predicting unseen data.

## CONCLUSIONS

Developing a smartphone-based system that implements machine-learning techniques is an effective way to diagnose PD using the voice as a biomarker.

**Accession number:** 33190461

**Correspondence author:** Tougui, Ilias Department of Biomedical Engineering, Mohammed V University in Rabat, Morocco. , Electronic Systems Sensors and Nanobiotechnologies (E2SN), ENSET, Mohammed V University in Rabat, Morocco.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2020-11-16

**Date revised:** 2020-11-20

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.4258/hir.2020.26.4.274>

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**Identifier (keyword):** Classification, Machine Learning, Parkinson Disease, Telemedicine, Voice Disorders

**Language:** English

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**Notes:** Publication model: Print-Electronic;; Cited medium:Print

**Publication date:** Oct 2020

**Publication type:** Journal

**Publisher location:** KOREA (SOUTH)

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Document 200

## Alexa, do I have COVID-19?

**Author:** Anthes, Emily

**Publication info:** Nature 586.7827: 22-25. (Oct 2020)

**Accession number:** 32999487

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2020-10-06

**Date created:** 2020-10-01

**Date revised:** 2021-07-24

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1038/d41586-020-02732-4>

**First available:** 2020-10-01

**Identifier (keyword):** Medical research, Neurodegeneration, SARS-CoV-2

**Language:** English

**Medline document status:** MEDLINE

**MeSH:** Autism Spectrum Disorder -- diagnosis; **Biomarkers** (major); COVID-19; Coronavirus Infections - complications; Coronavirus Infections -- diagnosis (major); Coronavirus Infections -- physiopathology; Dementia -- diagnosis; Dementia -- physiopathology; Depression -- diagnosis; Dyspnea -- complications; Dyspnea -- diagnosis; False Positive Reactions; Humans; **Machine Learning** (major); Mass Screening -- methods (major); Mobile Applications (major); Pandemics; Parkinson Disease -- diagnosis; Parkinson Disease -- physiopathology; Pneumonia, Viral -- complications; Pneumonia, Viral -- diagnosis (major); Pneumonia, Viral -- physiopathology; Privacy -- legislation & jurisprudence; Pulmonary Disease, Chronic Obstructive -- diagnosis; **Speech Disorders** -- complications (major); **Speech Disorders** -- diagnosis (major); Speech Recognition Software; Triage -- methods; **Voice** (major)

**Notes:** Publication model: Print;; Cited medium: Internet

**Publication date:** Oct 2020

**Publication type:** Journal

**Publisher location:** ENGLAND

**Source attribution:** Medline, © Publisher specific

**Substance:** Substance Substance: Biomarkers; CAS: 0;

Document 201

## Identification of Parkinson's disease via smartphones

**Author:** Goñi, M. 1 ; Patil, K. 1 ; Eickhoff, S. 1 ; Dukart, J. 1

1 Forschungszentrum Jülich, Institute of Neuroscience and Medicine, Jülich, Germany, Heinrich-Heine-Universität Düsseldorf, Institute of Systems Neuroscience, Düsseldorf, Germany

**Publication info:** Parkinsonism and Related Disorders, suppl. Supplement 1 79 : e44. Elsevier Ltd. (Oct 2020)

**Abstract (summary):** Objective: Standard evaluation of Parkinson's disease (PD) is performed in clinical environment, is time-consuming, expensive and often subjective. Digital **biomarkers**, i.e. smartphone based assessments, hold the promise for accurate and objective daily-life activities of PD symptoms addressing the above limitations. Here we apply a **machine learning** approach to a large publicly available dataset (mPower) of smartphone-based assessments in PD patients and controls to assess their usability of differentiation of PD and control subjects. Methods: We use the data from the mPower study (647 PD and 1087 controls) to evaluate the accuracy of the following 5 smart-phone based tasks for differentiation of PD patients and healthy controls: walking, balance, **voice**, tapping and memory tasks. We extracted about 700 commonly reported features reported for these tasks in previous PD studies. These features are based on the accelerometer readings during the walking and balance tasks, fundamental frequency series of **voice** signals, inter-tap distance and inter-tap time signals from tapping task and performance of memory test. Using 10-fold cross-validation repeated 1000 times, we compare the classification performance of 5 **machine learning** methods including LASSO, Random Forest (RF), Relevance Vector Machine (RVM), **Support Vector Machine (SVM)** (with Recursive Feature Elimination (**SVM-RFE**) or a genetic algorithm (**SVM-GA**) for feature selection). Results: The highest balanced accuracy (78.29%) was achieved using RVM on tapping data. Only low accuracies were achieved for other tasks (best accuracy reported): RF on balance data (64.43%), RVM on **voice** data (63.44%), RVM on memory data (62.67%) and RF on walking (59.06%) data. The most discriminating features with greatest accuracy for the tapping task were the number of taps and the frequency of tapping outside the buttons. Conclusion: These findings demonstrate the ability of smartphone-based evaluations to identify PD symptoms but also highlight the need for further methodological or procedural improvements for such measures.

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**Conference country:** Czech Republic

**Conference end date:** 2020-06-10

**Conference location:** Prague

**Conference start date:** 2020-06-07

**Conference title:** IAPRD XXV World Congress on Parkinson's Disease and Related Disorders, 2020

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-03-20

**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1016/j.parkreldis.2020.06.177>

**Embase document status:** Embase

**First available:** 2022-03-21

**Grant:** GA. FP7 Coordination of Non-Community Research Programmes.

**Methods:** We use the data from the mPower study (647 PD and 1087 controls) to evaluate the accuracy of the following 5 smart-phone based tasks for differentiation of PD patients and healthy controls: walking, balance, voice, tapping and memory tasks. We extracted about 700 commonly reported features reported for these tasks in previous PD studies. These features are based on the accelerometer readings during the walking and balance tasks, fundamental frequency series of voice signals, inter-tap distance and inter-tap time signals from tapping task and performance of memory test. Using 10-fold cross-validation repeated 1000 times, we compare the classification performance of 5 machine learning methods including LASSO, Random Forest (RF), Relevance Vector Machine (RVM), Support Vector Machine (SVM) (with Recursive Feature Elimination (SVM-RFE) or a genetic algorithm (SVM-GA) for feature selection).

**Language:** English

**Language of abstract:** English

**Publication date:** Oct 2020

**Publication type:** Journal

**Publisher:** Elsevier Ltd

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;accelerometer;adult;conference abstract;controlled study;cross validation;feature selection;female;genetic algorithm (major);human;least absolute shrinkage and selection operator;machine learning (major);major clinical study;male;memory;memory test;Parkinson disease (major);random forest;recursive feature elimination;relevance vector machine;smartphone (major);support vector machine;usability;validation process;voice;walking

**Updates:** 2022-03-21

## **Depression Severity Assessment for Adolescents at High Risk of Mental Disorders**

**Author:** Muszynski, Michal 1 ; Zelazny, Jamie 2 ; Girard, Jeffrey M 1 ; Morency, Louis-Philippe 1

1 Carnegie Mellon University, Pittsburgh, PA, USA, USA 2 University of Pittsburgh, Pittsburgh, PA, USA, USA

**Publication info:** Proceedings of the ... ACM International Conference on Multimodal Interaction. ICMI (Conference) 2020 : 70-78. (Oct 2020)

**Abstract (summary):** Recent progress in **artificial intelligence** has led to the development of automatic behavioral **marker** recognition, such as facial and **vocal** expressions. Those automatic tools have enormous potential to support mental health assessment, clinical decision making, and treatment planning. In this paper, we investigate nonverbal behavioral **markers** of depression severity assessed during semi-structured medical interviews of adolescent patients. The main goal of our research is two-fold: studying a unique population of adolescents at high risk of mental disorders and differentiating mild depression from moderate or severe depression. We aim to explore computationally inferred facial and **vocal** behavioral responses elicited by three segments of the semi-structured medical interviews: Distress Assessment Questions, Ubiquitous Questions, and Concept Questions. Our experimental methodology reflects best practise used for analyzing small sample size and unbalanced datasets of unique patients. Our results show a very interesting trend with strongly discriminative behavioral **markers** from both acoustic and visual modalities. These promising results are likely due to the unique classification task (mild depression vs. moderate and severe depression) and three types of probing questions.

**Accession number:** 33782675

**Correspondence author:** Muszynski, Michal Carnegie Mellon University, Pittsburgh, PA, USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date created:** 2021-03-30

**Date revised:** 2021-05-11

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1145/3382507.3418859>

**First available:** 2021-03-30

**Grant:** R01 MH096951. NIMH NIH HHS. United States.

**Identifier (keyword):** Adolescent Depression, Depression Diagnosis, Health Informatics, Mental Disorders, Non-verbal Behavioral **Markers**

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Print;; Cited medium:Print

**Publication date:** Oct 2020

**Publication type:** Journal

**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

**Updates:** 2021-03-302021-04-012021-04-022021-05-11

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Document 203

## **COVID-19 **Artificial Intelligence** Diagnosis Using Only Cough Recordings**

**Author:** Laguarta, Jordi 1 ; Hueto, Ferran 2 ; Subirana, Brian 2

1 MIT AutoID Laboratory Cambridge MA 02139 USA 2 MIT AutoID Laboratory Cambridge MA 02139 USA, Harvard University Cambridge MA 02138 USA

**Publication info:** IEEE open journal of engineering in medicine and biology 1 : 275-281. (Sep 29, 2020)

**Abstract (summary):** Goal: We hypothesized that COVID-19 subjects, especially including asymptomatics, could be accurately discriminated only from a forced-cough cell phone recording using **Artificial Intelligence**. To train our MIT Open **Voice** model we built a data collection pipeline of COVID-19 cough recordings through our website (opensigma.mit.edu) between April and May 2020 and created the largest audio COVID-19 cough balanced dataset reported to date with 5,320 subjects. Methods: We developed an **AI speech** processing framework that leverages acoustic **biomarker** feature extractors to pre-screen for COVID-19 from cough recordings, and provide a personalized patient saliency map to longitudinally monitor patients in real-time, non-invasively, and at essentially zero variable cost. Cough recordings are transformed with Mel Frequency Cepstral Coefficient and inputted into a **Convolutional Neural Network (CNN)** based architecture made up of one Poisson **biomarker** layer and 3 pre-trained ResNet50's in parallel, outputting a binary pre-screening diagnostic. Our **CNN**-based models have been trained on 4256 subjects and tested on the

remaining 1064 subjects of our dataset. **Transfer learning** was used to learn **biomarker** features on larger datasets, previously successfully tested in our Lab on Alzheimer's, which significantly improves the COVID-19 discrimination accuracy of our architecture. Results: When validated with subjects diagnosed using an official test, the model achieves COVID-19 sensitivity of 98.5% with a specificity of 94.2% (AUC: 0.97). For asymptomatic subjects it achieves sensitivity of 100% with a specificity of 83.2%. Conclusions: **AI** techniques can produce a free, non-invasive, real-time, any-time, instantly distributable, large-scale COVID-19 asymptomatic screening tool to augment current approaches in containing the spread of COVID-19. Practical use cases could be for daily screening of students, workers, and public as schools, jobs, and transport reopen, or for pool testing to quickly alert of outbreaks in groups. General **speech biomarkers** may exist that cover several disease categories, as we demonstrated using the same ones for COVID-19 and Alzheimer's.

**Accession number:** 34812418

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**Correspondence author:** Laguarta, Jordi MIT AutoID Laboratory Cambridge MA 02139 USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Identifier (keyword):** **AI** diagnostics, COVID-19 screening, **convolutional neural networks**, **deep learning**, **speech** recognition

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

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**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

**Updates:** 2021-11-23 2021-11-24 2022-02-24

## Using **speech** recognition technology to investigate the association between timing-related **speech** features and depression severity

**Author:** Yamamoto, Mao 1 ; Takamiya, Akihiro 1 ; Sawada, Kyosuke 1 ; Yoshimura, Michitaka 1 ; Kitazawa, Momoko 1 ; Liang, Kuo-Ching 1 ; Fujita, Takanori 1 ; Mimura, Masaru 1 ; Kishimoto, Taishiro 1

1 Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan, Japan

**Publication info:** PloS one 15.9: e0238726. (Sep 11, 2020)

### **Abstract (summary):** BACKGROUND

There are no reliable and validated objective **biomarkers** for the assessment of depression severity. We aimed to investigate the association between depression severity and timing-related **speech** features using **speech** recognition technology.

## METHOD

Patients with major depressive disorder (MDD), those with bipolar disorder (BP), and healthy controls (HC) were asked to engage in a non-structured interview with research psychologists. Using automated **speech** recognition technology, we measured three timing-related **speech** features: **speech** rate, pause time, and response time. The severity of depression was assessed using the Hamilton Depression Rating Scale 17-item version (HAMD-17). We conducted the current study to answer the following questions: 1) Are there differences in **speech** features among MDD, BP, and HC? 2) Do **speech** features correlate with depression severity? 3) Do changes in **speech** features correlate with within-subject changes in depression severity?

## RESULTS

We collected 1058 data sets from 241 individuals for the study (97 MDD, 68 BP, and 76 HC). There were significant differences in **speech** features among groups; depressed patients showed slower **speech** rate, longer pause time, and longer response time than HC. All timing-related **speech** features showed significant associations with HAMD-17 total scores. Longitudinal changes in **speech** rate correlated with changes in HAMD-17 total scores.

## CONCLUSIONS

Depressed individuals showed longer response time, longer pause time, and slower **speech** rate than healthy individuals, all of which were suggestive of psychomotor retardation. Our study suggests that **speech** features could be used as objective **biomarkers** for the assessment of depression severity.

**Accession number:** 32915846

**Correspondence author:** Yamamoto, Mao Department of Neuropsychiatry, Keio University School of Medicine, Tokyo, Japan.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2020-11-02

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**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** **Artificial Intelligence**;Bipolar Disorder -- physiopathology (major);Case-Control Studies;Depressive Disorder, Major -- physiopathology (major);Female;Humans;Male;Middle Aged;**Speech** (major);Time Factors

**Notes:** The authors have declared that no competing interests exist.;; Publication model: ElectronicCollection;; Cited medium:Internet

**Publication date:** Sep 11, 2020

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**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

**Updates:** 2020-09-122020-09-142020-10-012020-10-222020-11-03

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Document 205

**Questioning the status of aberrant **speech** patterns as psychiatric symptoms**



**Author:** Tan, Eric J. 1 ; Rossell, Susan L. 1

1 Centre for Mental Health, Swinburne University of Technology, Australia erictan@swin.edu.au

**Publication info:** British Journal of Psychiatry 217.3: 469-470. Cambridge University Press. (Sep 1, 2020)

**Abstract (summary):** **Speech** disturbances manifest in various psychiatric conditions and demonstrate temporal variability in relation to acute and stable symptom periods. They can be externally assessed, which facilitates their potential use as an objective **marker** of illness stage. Continued research will have positive implications for diagnostics and long-term management in clinical settings.

**Accession number:** 632820558

**Author e-mail address:** erictan@swin.edu.au

**Copyright:** Copyright 2020 Elsevier B.V., All rights reserved.

**Correspondence author:** Tan, Eric J. Centre for Mental Health, Swinburne University of Technology, Australia.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-09-22

**Document status:** Revised

**Document type:** Review

**DOI:** <http://dx.doi.org/10.1192/bjp.2020.60>

**Embase document status:** Embase; In-Data-Review (MEDLINE in Embase)

**First available:** 2020-09-15

**Identifier (keyword):** formal thought disorder, Nosology, psychotic disorders, schizophrenia, **speech**

**Language:** English

**Language of abstract:** English

**Number of references:** 5

**Publication date:** Sep 1, 2020

**Publication type:** Journal

**Publisher:** Cambridge University Press

**Publisher location:** United Kingdom

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;abdominal pain;bipolar disorder;delirium;delusion;dementia;diagnostic value;disease severity;disorientation;formal thought disorder +;hallucination;human;machine learning;mental disease (major);negative syndrome;psychosis;quality of life;rating scale;Review;schizophrenia;speech disorder (major);symptom;thought disorder;traumatic brain injury

**Updates:** 2020-09-152020-09-22

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Document 206

## **The project for objective measures using computational psychiatry technology (PROMPT): Rationale, design, and methodology**

**Author:** Kishimoto, Taishiro 1 ; Takamiya, Akihiro 1 ; Liang, Kuo-ching 1 ; Funaki, Kei 1 ; Fujita, Takanori 2 ; Kitazawa, Momoko 1 ; Yoshimura, Michitaka 1 ; Tazawa, Yuki 1 ; Horigome, Toshiro 1 ; Eguchi, Yoko 1 ; Kikuchi, Toshiaki 1 ; Tomita, Masayuki 3 ; Bun, Shogyoku 4 ; Murakami, Junichi 5 ; Sumali, Brian 6 ; Warnita, Tifani 7 ; Kishi, Aiko 6 ; Yotsui, Mizuki 8 ; Toyoshiba, Hiroyoshi 9 ; Mitsukura, Yasue 6 ; Shinoda, Koichi 7 ; Sakakibara, Yasubumi 8 ; Mimura, Masaru 1

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**Publication info:** Contemporary Clinical Trials Communications 19 Elsevier Inc. (Sep 2020)

**Abstract (summary):** Introduction: Depressive and neurocognitive disorders are debilitating conditions that account for the leading causes of years lived with disability worldwide. However, there are no biomarkers that are objective or easy-to-obtain in daily clinical practice, which leads to difficulties in assessing treatment response and developing new drugs. New technology allows quantification of features that clinicians perceive as reflective of disorder severity, such as facial expressions, phonic/speech information, body motion, daily activity, and sleep. Methods: Major depressive disorder, bipolar disorder, and major and minor neurocognitive disorders as well as healthy controls are recruited for the study. A psychiatrist/psychologist conducts conversational 10-min interviews with participants ≤10 times within up to five years of follow-up. Interviews are recorded using RGB and infrared cameras, and an array microphone. As an option, participants are asked to

wear wrist-band type devices during the observational period. Various software is used to process the raw video, voice, infrared, and wearable device data. A machine learning approach is used to predict the presence of symptoms, severity, and the improvement/deterioration of symptoms. Discussion: The overall goal of this proposed study, the Project for Objective Measures Using Computational Psychiatry Technology (PROMPT), is to develop objective, noninvasive, and easy-to-use biomarkers for assessing the severity of depressive and neurocognitive disorders in the hopes of guiding decision-making in clinical settings as well as reducing the risk of clinical trial failure. Challenges may include the large variability of samples, which makes it difficult to extract the features that commonly reflect disorder severity. Trial Registration: UMIN000021396, University Hospital Medical Information Network (UMIN).

**Accession number:** 2007582638

**Author e-mail address:** taishiro-k@mti.biglobe.ne.jp

**Copyright:** Copyright 2020 Elsevier B.V., All rights reserved.

**Correspondence author:** Kishimoto, Taishiro Associate Professor of Psychiatry, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo, 160-8582, Japan.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-09-04

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1016/j.conctc.2020.100649>

**Embase document status:** Embase

**First available:** 2020-08-28

**Grant:** JP18he1102004. , AMED. Japan Agency for Medical Research and Development.

This research is supported by the Japan Agency for Medical Research and Development (AMED) under Grant Number JP18he1102004. The Grant was awarded on Oct. 29, 2015 and ends on Mar. 31, 2019. The funding source did not participate in the design of this study and will not have any hand in the study's execution, analyses, or submission of results.

**Identifier (keyword):** Depression, Machine learning, Natural language processing, Neurocognitive disorder, Screening

**Language:** English

**Language of abstract:** English

**Number of references:** 52

**Publication date:** Sep 2020

**Publication type:** Journal

**Publisher:** Elsevier Inc

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;adult;Article;Beck Depression Inventory;bipolar disorder (major);clinical assessment tool;clinical decision making;clinical study (major);controlled study;Diagnostic and Statistical Manual of Mental Disorders;disease severity;disorders of higher cerebral function (major);Hamilton Depression Rating Scale;hospital patient;human;machine learning (major);major depression (major);methodology;Mini Mental State Examination;Montgomery Asberg Depression Rating Scale;observational study;outpatient;priority journal;prospective study;psychologic assessment;semi structured interview;study design

**Updates:** 2020-08-282020-09-04

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Document 207

## Repeatability of Commonly Used **Speech** and Language Features for Clinical Applications

**Author:** Stegmann, Gabriela M. 1 ; Hahn, Shira 1 ; Liss, Julie 1 ; Shefner, Jeremy 2 ; Rutkove, Seward B. 3 ; Kawabata, Kan 4 ; Bhandari, Samarth 4 ; Shelton, Kerisa 2 ; Duncan, Cayla Jessica 2 ; Berisha, Visar 1

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**Publication info:** Digital Biomarkers 4.3: 109-122. S. Karger AG. (Sep 2020)

**Abstract (summary):** Introduction: Changes in **speech** have the potential to provide important information on the diagnosis and progression of various neurological diseases. Many researchers have relied on open-source **speech** features to develop algorithms for measuring **speech** changes in clinical populations as they are convenient and easy to use. However, the repeatability of open-source features in the context of neurological diseases has not been studied. Methods: We used a longitudinal sample of healthy controls, individuals with amyotrophic lateral sclerosis, and individuals with suspected frontotemporal dementia, and we evaluated the repeatability of acoustic and language features separately on these 3 data sets. Results: Repeatability was evaluated using intraclass correlation (ICC) and the within-subjects coefficient of variation (WSCV). In 3 sets of tasks, the median ICC were between 0.02 and 0.55, and the median WSCV were between 29 and 79%. Conclusion: Our results demonstrate that the repeatability of **speech** features extracted using open-

source tool kits is low. Researchers should exercise caution when developing digital health models with open-source **speech** features. We provide a detailed summary of feature-by-feature repeatability results (ICC, WSCV, SE of measurement, limits of agreement for WSCV, and minimal detectable change) in the online supplementary material so that researchers may incorporate repeatability information into the models they develop.

**Accession number:** 633642746

**Author e-mail address:** gabriela.stegmann@auralanalytics.com

**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

**Correspondence author:** Stegmann, Gabriela M. Aural Analytics, 1355 N Scottsdale Rd. Unit 110, Scottsdale, AZ, 85257, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2021-05-11

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1159/000511671>

**Embase document status:** Embase

**First available:** 2020-12-14

**Grant:** This work was supported by NIH SBIR (1R43DC017625-01), NSF SBIR (1853247), and NIH R01 (5R01DC006859-13), as well as by an ALS Finding a Cure Grant.

**Identifier (keyword):** Automatic **speech** analysis, Digital **biomarkers**, Mobile technology, Repeatability, **Speech**

**Language:** English

**Language of abstract:** English

**Number of references:** 33

**Publication date:** Sep 2020

**Publication type:** Journal

**Publisher:** S. Karger AG

**Publisher location:** Switzerland

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;**biological marker** (major);adult;algorithm;Alzheimer disease;amyotrophic lateral sclerosis;Article;clinical feature;clinical research;cognition;controlled study;correlation coefficient;degenerative disease (major);disease exacerbation;frontotemporal

dementia;human;longitudinal study;machine learning;major clinical study;measurement repeatability (major);middle aged;Montreal cognitive assessment;motor control;phonation;priority journal;scanning electron microscopy;speech and language (major);speech disorder (major);speech test

**Updates:** 2020-12-142021-01-072021-05-112021-09-30

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Document 208

## **The voice as a bio-marker of Covid-19: Preliminary results of the CO-VOICE-19 study**

**Author:** Pietrantonio, F. 1 ; Delli Castelli, M. 1 ; Barbieri, M.M. 1 ; D'Agostino, M. 2 ; Aluigi, S. 2 ; Albano, M. 2 ; Cicchini, L. 2 ; Piccione, A. 2 ; Tavasci, M. 3 ; Costantini, G. 4 ; Saggio, G. 4

1 UOC Medicina Interna Ospedale Dei Castelli, ASL Roma 6, Ariccia (RM), Italy 2 UOC Cardiologia Ospedale Dei Castelli, ASL Roma 6, Ariccia (RM), Italy 3 Voicewise, Università di Tor Vergata, Roma, Italy 4 Dipartimento di Ingegneria Elettronica, Università di Tor Vergata, Roma, Italy

**Publication info:** Italian Journal of Medicine 14.SUPPL 2: 114-115. Page Press Publications. (Sep 2020)

**Abstract (summary):** Background: Covid-19 has an impact on lung function and, consequently, on voice emission. By registering an adequate number of patients with Covid-19, we can 'train' artificial intelligence algorithms in order to highlight the disease status of any person whose voice is registered. Impact on voice increases with disease progression, allowing staging. Materials and Methods: Prospective pilot study to evaluate the condition of Covid-19 affection of critically ill patients hospitalized and monitored by evaluating their speech capacity through measurement and recording of the voice. Primary End Point: remotely locate people infected with Covid-19. Secondary end-points: establish the presence of any geographic areas with 'outbreaks', by 'crossing' the geo-location data, staging the disease. Results: 85 patients evaluated and 18 (10F and 8M) recruited, average age 62, subjected to intubation 3/18. WHO stage 2: 50%; comorbidity >3: 61%; only 2 with P/F < 200. Conclusions: Recruited patients have features of lower functional impairment than other patients, however a high incidence of previous intubation. Preliminary audio signal analysis of the patient's voice recordings are underway and will be treated with Artificial Intelligence algorithms in order to select voice parameters that can identify the presence of the disease. By training appropriate machine learning and data classification systems it will be possible to determine whether the recorded voice belongs to a healthy subject or affected by Covid-19 and use these skills to screen suspect patients by telephone triage.

**Accession number:** 633718727

**Conference country:** United States

**Conference end date:** 2020-09-29

**Conference location:** Virtual

**Conference start date:** 2020-09-26

**Conference title:** 25 Congresso Nazionale della Societa Scientifica FADOI

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**Correspondence author:** Pietrantonio, F. UOC Medicina Interna Ospedale Dei Castelli, ASL Roma 6, Ariccia (RM), Italy.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-12-24

**Document status:** New

**Document type:** Conference Abstract

**Embase document status:** Embase

**First available:** 2020-12-24

**Language:** English

**Language of abstract:** English

**Publication date:** Sep 2020

**Publication type:** Journal

**Publisher:** Page Press Publications

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase; **biological marker** (major); adult; algorithm (major); comorbidity; conference abstract; coronavirus disease 2019 (major); critically ill patient; data classification; emergency health service; female; human; incidence; intubation; learning; major clinical study; male; middle aged; pilot study; prospective study; skill; telephone; **voice parameter** (major)

**Updates:** 2020-12-24

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Document 209

### **Measurement of **speech** as a **biomarker** of neurodegenerative disease using acoustic profiles and **machine learning****

**Author:** Schultz, B. 1 ; Joukhader, Z. 1 ; Nattala, U. 1 ; Noffs, G. 1 ; Chan, J. 1 ; Rojas-Azaocar, S. 1 ; Reece, H. 1 ; Magee, M. 1 ; Delatycki, M. 1 ; Corben, L. 1 ; Walt, A. 1 ; Vogel, A. 1

1 University of Melbourne

**Publication info:** Movement Disorders 35.SUPPL 1: S141. John Wiley and Sons Inc. (Sep 2020)

**Abstract (summary):** Objective: To examine the utility of **speech** biometrics for describing and delineating neurodegenerative diseases using acoustic measures and **machine learning** procedures. Background: Progressive neurological disorders often result in changes to **speech** production. These changes can act as markers of disease onset or progression and treatment response. Acoustic analysis is an objective way to measure **speech**. Most work in this space has compared healthy controls with one disease, and not considered distinctions between multiple pathologies. Methods: We applied **machine learning** algorithms (**support vector machines**) to identify **speech** features to discriminate between different neurodegenerative diseases including multiple sclerosis (N=144) and Friederich's ataxia (N=80), as well as healthy controls (N=174). Participants performed a diadochokinetic task where they repeated the alternating syllables /PA/, /TA/, and /KA/. Signal processing techniques were used to extract a wide range of spectral and temporal prosodic features from the **speech** recordings. Summary statistics of these acoustic features were subjected to **machine learning**. Results: Data suggest that multiple-parameter acoustic sets distinguish neurodegenerative diseases including **speech** rate, pause and **speech** rate variability, spectral energy, spectral entropy, spectral crest, f0 duration, and spectral spread. **Machine learning** techniques produced high discrimination accuracy (M = ~84%) by simultaneously considering combinations of these acoustic features. Friederich's ataxia (~82%) and multiple sclerosis (~91%) were both identified with high accuracy and sensitivity. Conclusions: **Speech** biometrics can differentiate between neurodegenerative diseases and healthy **speech** with high accuracy, supporting the assumption of specific **speech** profiles in neurological disorders. We emphasize the importance examining multiple acoustic features when assessing key indicators of neurological disease.

**Accession number:** 633833981

**Conference end date:** 2020-09-16

**Conference location:** Virtual

**Conference start date:** 2020-09-12

**Conference title:** MDS International Congress

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**Correspondence author:** Schultz, B. University of Melbourne.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2021-01-07

**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1002/mds.28268>

**Embase document status:** Embase



**First available:** 2021-01-07

**Language:** English

**Language of abstract:** English

**Publication date:** Sep 2020

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker (major);acoustic analysis;adult;ataxia;biometry;conference abstract;controlled study;degenerative disease (major);entropy;female;human;major clinical study;male;multiple sclerosis;signal processing;speech rate (major);support vector machine (major)

**Updates:** 2021-01-07

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Document 210

## **DrOncoRight: A natural language-oriented analytics platform for cancer omics data**

**Author:** Li, Jun 1 ; Chen, Hu 1 ; Wang, Yumeng 1 ; Chen, Mei-Ju 1 ; Liang, Han 1

1 UT MD Anderson Cancer Center, Houston, TX, United States

**Publication info:** Cancer Research 80.16 SUPPL American Association for Cancer Research Inc. (Aug 2020)

**Abstract (summary):** Over the past decade, high-throughput molecular profiling technologies have revolutionized cancer research. Petabytes of omics data (e.g., genomic, transcriptomic, proteomic, epigenomic, and metabolic data) have been generated from thousands of patients, animal models, and cell line samples, especially through some large consortium projects such as The Cancer Genome Atlas (TCGA) and International Cancer Genome Consortium (ICGC). These rich, high-throughput cancer omics data have provided an unprecedented opportunity to characterize cancer-related molecular mechanisms and identify biomarkers and therapeutic targets systematically. However, this tidal wave of molecular data also presents a major challenge for cancer researchers in analyzing the data and obtaining meaningful biological and clinical insights effectively. This is particularly true for a large proportion of researchers who have no or limited bioinformatics and statistical expertise. Many efforts have been made to overcome this challenge. First, many programming languages with specially designed modules or libraries to allow easy analysis and visualization of omics data have been developed. However, these tools still require users to acquire some programming skills, such as Python, R, and Perl, which is not feasible for most experimental researchers. Second, many web-based and stand-alone bioinformatics databases and

applications have been developed to allow users to explore and analyze cancer omics data through a user-friendly, interactive interface. But these bioinformatics tools usually focus on one specific type of molecular data, provide only predefined analysis, and do not allow the customization of analytic and visualization tasks. Moreover, users still have to spend considerable time identifying appropriate tools, learning distinct user interfaces/procedures, in addition to keeping track of the status and updates for these quickly evolving tools. As a result, there is still a substantial barrier that prevents a large body of cancer researchers from performing cancer omics data analyses in an intuitive, efficient, reproducible way. To address this challenge, our team has developed DrOncoRight (<https://drbioright.org>), an open-access, natural language-oriented, artificial intelligence (AI)-driven analytics platform for analyzing and visualizing cancer omics data. A major attractive feature of this platform is that it allows users to ask biological questions through natural language (text or voice). It automatically understands users' intentions, identifies related cancer genomic datasets, performs diverse analyses, and returns the results in a timely, visually attractive manner. Further, based on user feedback, the platform improves itself through active learning. Taken together, equipped with cutting-edge AI, informatics, and analytic technologies, DrOncoRight represents a revolutionary approach to next generation cancer science which greatly increases the efficiency and reproducibility of data analysis in cancer research.

**Accession number:** 633636742

**Conference country:** United States

**Conference end date:** 2020-06-24

**Conference location:** Philadelphia, PA

**Conference start date:** 2020-06-22

**Conference title:** American Association for Cancer Research Annual Meeting, AACR 2020

**Copyright:** Copyright 2020 Elsevier B.V., All rights reserved.

**Correspondence author:** Li, Jun UT MD Anderson Cancer Center, Houston, TX, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-12-14

**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1158/1538-7445.AM2020-3383>

**Embase document status:** Embase

**First available:** 2020-12-15

**Language:** English

**Language of abstract:** English

**Publication date:** Aug 2020

**Publication type:** Journal

**Publisher:** American Association for Cancer Research Inc.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;adult;animal cell;animal experiment;animal model;artificial intelligence;bioinformatics;cancer model (major);cancer research;computer interface;computer language (major);conference abstract;controlled study;data analysis;epigenetics;female;human;learning;library;male;molecular fingerprinting;nonhuman;reproducibility;skill;voice

**Updates:** 2020-12-15

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Document 211

### **Automated voice biomarkers for depression symptoms using an online cross-sectional data collection initiative**

**Author:** Zhang, Larry 1 ; Duvvuri, Radhika 2 ; Chandra, Kiranmayi K. L. 3 ; Nguyen, Theresa 4 ; Ghomi, Reza H. 5

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**Publication info:** Depression and Anxiety 37.7: 657-669. Blackwell Publishing Inc. (Jul 1, 2020)

**Abstract (summary):** Importance: Depression is an illness affecting a large percentage of the world's population throughout the lifetime. To date, there is no available biomarker for depression detection and tracking of symptoms relies on patient self-report. Objective: To explore and validate features extracted from recorded voice samples of depressed subjects as digital biomarkers for suicidality, psychomotor disturbance, and depression severity. Design: We conducted a cross-sectional study over the course of 12 months using a frequently visited web form version of the PHQ9 hosted by Mental Health America (MHA) to ask subjects for anonymous voice samples via a separate web form hosted by NeuroLex Laboratories. Subjects were asked to provide demographics, answers to the PHQ9, and two voice samples. Setting: Online only. Participants: Users of the MHA website. Main Outcomes and Measures: Performance of statistical models using extracted voice features to predict psychomotor disturbance, suicidality, and depression severity as indicated by the PHQ9. Results: Voice features extracted from recorded audio of depressed subjects were able to predict PHQ9 question 9 and total scores with an area under the curve of 0.821 and a mean absolute error of

4.7, respectively. Psychomotor Disturbance prediction was less powerful with an area under the curve of 0.61. Conclusion and Relevance: Automated **voice** analysis using short recordings of patient **speech** may be used to augment depression screen and symptom management.

**Accession number:** 2004856833

**Author e-mail address:** rhosseinighomi@gmail.com

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**Correspondence author:** Ghomi, Reza H. Neurology, University of Washington, Seattle, WA, United States.

Ghomi, Reza H. NeuroLex Laboratories, Newnan, GA, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-07-08

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**DOI:** <http://dx.doi.org/10.1002/da.23020>

**Embase document status:** Embase; Publisher (MEDLINE in Embase)

**First available:** 2020-05-25

**Grant:** Funding for this study was provided by NeuroLex Laboratories, Inc. Funding supported study staff time only and there were no honoraria provided to participants. Our study partner, Mental Health America, provided a depression survey and demographic data in addition to directing users to the voice survey.

**Identifier (keyword):** **biological markers**, depression, mood disorders, suicide, web-based

**Language:** English

**Language of abstract:** English

**Number of references:** 29

**Publication date:** Jul 1, 2020

**Publication type:** Journal

**Publisher:** Blackwell Publishing Inc.

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;**biological marker** (major);adolescent;adult;aged;Article;**automatic speech recognition** (major);child;cross-sectional study;demography;depression (major);disease severity;female;human;major clinical study;male;online system (major);Patient Health Questionnaire

9;pilot study;prediction;priority journal;psychomotor disorder;suicidal behavior;voice analysis  
(major);web browser

**Updates:** 2020-05-252020-07-062020-07-08

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Document 212

## **Spoken words as biomarkers: using machine learning to gain insight into communication as a predictor of anxiety**

**Author:** Demiris, George 1 ; Corey Magan, Kristin L 1 ; Parker Oliver, Debra 2 ; Washington, Karla T 2 ; Chadwick, Chad 3 ; Voigt, Jeffrey D 3 ; Brotherton, Sam 3 ; Naylor, Mary D 1

1 School of Nursing, University of Pennsylvania, Philadelphia, Pennsylvania, USA, USA 2 Family Medicine, School of Medicine, University of Missouri, Columbia, Missouri, USA, USA 3 Live Circle Inc, Ridgewood, New Jersey, USA, USA

**Publication info:** Journal of the American Medical Informatics Association : JAMIA 27.6: 929-933. (Jun 1, 2020)

### **Abstract (summary): OBJECTIVE**

The goal of this study was to explore whether features of recorded and transcribed audio communication data extracted by machine learning algorithms can be used to train a classifier for anxiety.

## **MATERIALS AND METHODS**

We used a secondary data set generated by a clinical trial examining problem-solving therapy for hospice caregivers consisting of 140 transcripts of multiple, sequential conversations between an interviewer and a family caregiver along with standardized assessments of anxiety prior to each session; 98 of these transcripts (70%) served as the training set, holding the remaining 30% of the data for evaluation.

## **RESULTS**

A classifier for anxiety was developed relying on language-based features. An 86% precision, 78% recall, 81% accuracy, and 84% specificity were achieved with the use of the trained classifiers. High anxiety inflections were found among recently bereaved caregivers and were usually connected to issues related to transitioning out of the caregiving role. This analysis highlighted the impact of lowering anxiety by increasing reciprocity between interviewers and caregivers.

## **CONCLUSION**

Verbal communication can provide a platform for **machine learning** tools to highlight and predict behavioral health indicators and trends.

**Accession number:** 32374378

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**Correspondence author:** Demiris, George School of Nursing, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2021-03-12

**Date created:** 2020-05-07

**Date revised:** 2021-05-07

**Document status:** Revised

**Document type:** Journal Article, Research Support, N.I.H., Extramural

**DOI:** <http://dx.doi.org/10.1093/jamia/ocaa049>

**First available:** 2020-05-06

**Grant:** R01 NR012213. NINR NIH HHS. United States.

**Identifier (keyword):** anxiety, caregivers, communication, behavioral research, **machine learning**

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Algorithms;Anxiety -- diagnosis (major);Caregivers (major);Communication (major);Family;Female;Humans;Interviews as Topic;Language;**Machine Learning** (major);Male;Middle Aged;Proof of Concept Study;**Speech**

**Notes:** Publication model: Print;; Cited medium:Internet

**Publication date:** Jun 1, 2020

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**Publisher location:** ENGLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2020-05-062020-06-052020-06-082020-06-302020-11-072020-11-102021-02-082021-03-132021-05-07

**Smartphone as a monitoring tool for bipolar disorder: a systematic review including data analysis, machine learning algorithms and predictive modelling**

**Author:** Antosik-Wójcińska, Anna Z. 1 ; Dominiak, Monika 2 ; Chojnacka, Magdalena 1 ; Kaczmarek-Majer, Katarzyna 3 ; Opara, Karol R. 3 ; Radziszewska, Weronika 3 ; Olwert, Anna 3 ; Święcicki, Łukasz 1

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**Publication info:** International Journal of Medical Informatics 138 Elsevier Ireland Ltd. (Jun 2020)

**Abstract (summary):** Background: Bipolar disorder (BD) is a chronic illness with a high recurrence rate. Smartphones can be a useful tool for detecting prodromal symptoms of episode recurrence (through real-time monitoring) and providing options for early intervention between outpatient visits. Aims: The aim of this systematic review is to overview and discuss the studies on the smartphone-based systems that monitor or detect the phase change in BD. We also discuss the challenges concerning predictive modelling. Methods: Published studies were identified through searching the electronic databases. Predictive attributes reflecting illness activity were evaluated including data from patients' self-assessment ratings and objectively measured data collected via smartphone. Articles were reviewed according to PRISMA guidelines. Results: Objective data automatically collected using smartphones (voice data from phone calls and smartphone-usage data reflecting social and physical activities) are valid markers of a mood state. The articles surveyed reported accuracies in the range of 67% to 97% in predicting mood status. Various machine learning approaches have been analyzed, however, there is no clear evidence about the superiority of any of the approach. Conclusions: The management of BD could be significantly improved by monitoring of illness activity via smartphone.

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**Identifier (keyword):** bipolar disorder, machine learning, manic and depressive episode, objective data collected via smartphone, smartphone-based monitoring, systematic review, voice analysis

**Language:** English

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**Number of references:** 75

**Publication date:** Jun 2020

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**Subject:** Embase;MEDLINE;smartphone;accuracy;bipolar disorder (major);data analysis;Hamilton Depression Rating Scale;human;interpersonal communication;machine learning (major);mobile application (major);physical activity;practice guideline;priority journal;Review;self evaluation;self monitoring;systematic review;Young Mania Rating Scale

**Updates:** 2020-04-202020-04-282020-04-29

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Document 214

## **Anomalies in language as a biomarker for schizophrenia**

**Author:** De Boer, Janna N. 1 ; Brederoo, Sanne G. 2 ; Voppel, Alban E. 2 ; Sommer, Iris E.C. 2

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Department of Psychiatry, Groningen, Netherlands

**Publication info:** Current Opinion in Psychiatry 33.3: 212-218. Lippincott Williams and Wilkins. (May 1, 2020)

**Abstract (summary):** Purpose of review After more than a century of neuroscience research, reproducible, clinically relevant **biomarkers** for schizophrenia have not yet been established. This article reviews current advances in evaluating the use of language as a diagnostic or prognostic tool in schizophrenia. Recent findings The development of computational linguistic tools to quantify language disturbances is rapidly gaining ground in the field of schizophrenia research. Current applications are the use of semantic space models and acoustic analyses focused on **phonetic** markers. These features are used in **machine learning** models to distinguish patients with schizophrenia from healthy controls or to predict conversion to psychosis in high-risk groups, reaching accuracy scores (generally ranging from 80 to 90%) that exceed clinical raters. Other potential applications for a language **biomarker** in schizophrenia are monitoring of side effects, differential diagnostics and relapse prevention. Summary Language disturbances are a key feature of schizophrenia. Although in its early stages, the emerging field of research focused on computational linguistics suggests an important role for language analyses in the diagnosis and prognosis of schizophrenia. Spoken language as a **biomarker** for schizophrenia has important advantages because it can be objectively and reproducibly quantified. Furthermore, language analyses are low-cost, time efficient and noninvasive in nature.

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**Copyright:** Copyright 2020 Elsevier B.V., All rights reserved.

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**Identifier (keyword):** Language, Psychosis, Schizophrenia, Semantic Space, **Speech**

**Language:** English

**Language of abstract:** English

**Number of references:** 87

**Publication date:** May 1, 2020

**Publication type:** Journal

**Publisher:** Lippincott Williams and Wilkins

**Publisher location:** United Kingdom

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**Subject:** Embase;MEDLINE;biological marker -- endogenous compound (major);clinical evaluation;content analysis;human;language;language disability (major);language test;lingua franca;meta analysis (topic);nonverbal communication;phonetics;prognosis;Review;schizophrenia -- diagnosis (major);speech;written language

**Updates:** 2020-08-112020-08-19

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Document 215

## **Improving the Assessment of Mild Cognitive Impairment in Advanced Age With a Novel Multi-Feature Automated Speech and Language Analysis of Verbal Fluency**

**Author:** Chen, Liu 1 ; Asgari, Meysam 1 ; Gale, Robert 1 ; Wild, Katherine 2 ; Dodge, Hiroko 3 ; Kaye, Jeffrey 2

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**Publication info:** *Frontiers in psychology* 11 : 535. (Apr 9, 2020)

**Abstract (summary):** Introduction: Clinically relevant information can go uncaptured in the conventional scoring of a verbal fluency test. We hypothesize that characterizing the temporal aspects of the response through a set of time related measures will be useful in distinguishing those with MCI from cognitively intact controls. Methods: Audio recordings of an animal fluency test administered to 70 demographically matched older adults (mean age 90.4 years), 28 with mild cognitive impairment (MCI) and 42 cognitively intact (CI) were professionally transcribed and fed into an automatic speech recognition (ASR) system to estimate the start time of each recalled word in the response. Next, we semantically cluster participant generated animal names and through a novel set of time-based measures, we characterize the semantic search strategy of subjects in retrieving words from animal

name clusters. This set of time-based features along with standard count-based features (e.g., number of correctly retrieved animal names) were then used in a **machine learning** algorithm trained for distinguishing those with MCI from CI controls. Results: The combination of both count-based and time-based features, automatically derived from the test response, achieved 77% on AUC-ROC of the **support vector machine (SVM)** classifier, outperforming the model trained only on the raw test score (AUC, 65%), and well above the chance model (AUC, 50%). Conclusion: This approach supports the value of introducing time-based measures to the assessment of verbal fluency in the context of this generative task differentiating subjects with MCI from those with intact cognition.

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**Copyright:** Copyright © 2020 Chen, Asgari, Gale, Wild, Dodge and Kaye.

**Correspondence author:** Chen, Liu Center for Spoken Language Understanding, Oregon Health & Science University (OHSU), Portland, OR, United States.

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R01 AG033581. NIA NIH HHS. United States.

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**Identifier (keyword):** animal fluency, **biomarkers**, computerized assessment, mild cognitive impairment (MCI), neuropsychological tests, short term memory

**Language:** English

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**Notes:** Publication model: Electronic-eCollection;; Cited medium:Print

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Document 216

## **Quantitative Assessment of **Speech** in Cerebellar Ataxia Using Magnitude and Phase Based Cepstrum**

**Author:** Kashyap, Bipasha 1 ; Pathirana, Pubudu N. 1 ; Horne, Malcolm 2 ; Power, Laura 3 ; Szmulewicz, David 4

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**Publication info:** Annals of Biomedical Engineering 48.4: 1322-1336. Springer. (Apr 1, 2020)

**Abstract (summary):** The clinical assessment of **speech** abnormalities in Cerebellar Ataxia (CA) is time-consuming and inconsistent. We have developed an automated objective system to quantify CA severity and thereby facilitate remote monitoring and optimisation of therapeutic interventions. A quantitative acoustic assessment could prove to be a viable **biomarker** for this purpose. Our study explores the use of phase-based cepstral features extracted from the modified group delay function as a complement to the features obtained from the magnitude cepstrum. We selected a combination of 15 acoustic measurements using RELIEF feature selection algorithm during the feature optimisation process. These features were used to segregate ataxic speakers from normal speakers (controls) and objectively assess them based on their severity. The effectiveness of our study has been experimentally evaluated through a clinical study involving 42 patients diagnosed with CA and 23 age-matched controls. A radial basis function kernel based **support vector machine (SVM)** classifier achieved a classification accuracy of 84.6% in CA–Control discrimination [area under the ROC curve (AUC) of 0.97] and 74% in the modified 3-level CA severity estimation (AUC of 0.90) deduced from the clinical ratings. The strong classification ability of selected features and the **SVM** model supports this scheme's suitability for monitoring CA related **speech** motor abnormalities.

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**Identifier (keyword):** Cepstrum, Feature selection, Mel-frequency cepstral coefficients (MFCCs), Modified group delay (MGD), Phase, Random Forests (RF), **Support vector machines (SVM)**

**Language:** English

**Language of abstract:** English

**Number of references:** 44

**Publication date:** Apr 1, 2020

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**Subject:** Embase;MEDLINE;**biological marker** -- endogenous compound;acoustic analysis;adult;aged;Article;cepstrum + (major);cerebellar ataxia (major);clinical article;clinical assessment (major);clinical study;cohort analysis;controlled study;disease severity;disease severity assessment;**feature selection algorithm**;female;human;**kernel method**;male;priority journal;**radial basis**

function;random forest;remote sensing;signal processing (major);speech analysis (major);speech disorder;support vector machine

**Updates:** 2020-01-272020-04-022020-04-13

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Document 217

## **Validation of freely-available pitch detection algorithms across various noise levels in assessing speech captured by smartphone in Parkinson's disease**

**Author:** Illner, Vojtech 1 ; Sovka, Pavel 1 ; Ruzs, Jan 1

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**Publication info:** Biomedical Signal Processing and Control 58 Elsevier Ltd. (Apr 2020)

**Abstract (summary):** Measuring the fundamental frequency of the vocal folds  $F_0$  is recognized as an important parameter in the assessment of speech impairments in Parkinson's disease (PD). Although a number of  $F_0$  trackers currently exist, their performance in smartphone-based evaluation and robustness against background noise have never been tested. Monologues from 30 newly-diagnosed, untreated PD patients and 30 matched healthy control participants were collected. Additive non-stationary urban and household noise at different SNR levels was added to the recordings, which were subsequently assessed by 10 freely-available and widely-used pitch-tracking algorithms. According to the comparison of all investigated pitch detectors, sawtooth inspired pitch estimator (SWIPE) was the most robust and accurate method in estimating mean  $F_0$  and its standard deviation. However, at a low 6 dB SNR level, a combination of more algorithms may be needed to achieve the desired precision. Monopitch, calculated as  $F_0$  standard deviation and estimated by SWIPE, proved to be robust in distinguishing between the PD and healthy control groups ( $p < 0.001$ ). We anticipate that monopitch may serve as a quick and inexpensive biomarker of disease progression based on longitudinal data collected via smartphone, without any logistical or time constraints for patients and physicians.

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**Copyright:** Copyright 2021 Elsevier B.V., All rights reserved.

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**Identifier (keyword):** Dysarthria, Fundamental frequency, Parkinson's disease, Pitch, Smartphones, Speech, Voice

**Language:** English

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**Publication date:** Apr 2020

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**Subject:** Embase;biological marker;smartphone (major);adult;aged;Article;clinical article;comparative study;controlled study;detection algorithm (major);disease duration;female;household;human;male;measurement accuracy;middle aged;noise (major);Parkinson disease (major);pitch discrimination (major);priority journal;signal noise ratio;speech and language assessment (major);Unified Parkinson Disease Rating Scale;urban area

**Updates:** 2020-01-102020-01-152021-10-22

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Document 218

**Investigating voice as a biomarker: Deep phenotyping methods for early detection of Parkinson's disease**

**Author:** Tracy, John M. 1 ; Özkanca, Yasin 2 ; Atkins, David C. 3 ; Hosseini Ghomi, Reza 4

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**Publication info:** Journal of Biomedical Informatics 104 Academic Press Inc. (Apr 2020)

**Abstract (summary):** Voice technology has grown tremendously in recent years and using voice as a biomarker has also been gaining evidence. We demonstrate the potential of voice in serving as a deep phenotype for Parkinson's Disease (PD), the second most common neurodegenerative disorder worldwide, by presenting methodology for voice signal processing for clinical analysis. Detection of PD symptoms typically requires an exam by a movement disorder specialist and can be hard to access and inconsistent in findings. A vocal digital biomarker could supplement the cumbersome existing manual exam by detecting and quantifying symptoms to guide treatment. Specifically, vocal biomarkers of PD are a potentially effective method of assessing symptoms and severity in daily life, which is the focus of the current research. We analyzed a database of PD patient and non-PD subjects containing voice recordings that were used to extract paralinguistic features, which served as inputs to machine learning models to predict PD severity. The results are presented here and the limitations are discussed given the nature of the recordings. We note that our methodology only advances biomarker research and is not cleared for clinical use. Specifically, we demonstrate that conventional machine learning models applied to voice signals can be used to differentiate participants with PD who exhibit little to no symptoms from healthy controls. This work highlights the potential of voice to be used for early detection of PD and indicates that voice may serve as a deep phenotype for PD, enabling precision medicine by improving the speed, accuracy, accessibility, and cost of PD management.

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**Identifier (keyword):** Audio features, Deep phenotype, Feature selection, Parkinson's disease, Voicebiomarkers, Voice technology

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**Subject:** Embase;MEDLINE;biological marker (major);adult;Article;clinical outcome;controlled study;disease severity;female;human;life;machine learning;major clinical study;male;middle aged;paralanguage;Parkinson disease -- diagnosis (major);phenotype (major);priority journal;quality of life;quantitative analysis;voice (major)

**Updates:** 2020-01-142020-04-102020-04-22

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Document 219

## **Classifying schizophrenia using phonological, semantic and syntactic features of language; a combinatory machine learning approach**

**Author:** Voppel, Alban 1 ; De Boer, Janna 2 ; Slegers, Fleur 3 ; Schnack, Hugo 2 ; Sommer, Iris 1

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**Publication info:** Schizophrenia Bulletin, suppl. Supplement 1 46 : S87. Oxford University Press. (Apr 2020)

**Abstract (summary):** Background: The diagnosis of schizophrenia is currently based on anamnesis and psychiatric examination only. Language **biomarkers** may be useful to provide a quantitative and reproducible risk estimate for this spectrum of disorders. While people with schizophrenia spectrum disorders may show one or more language abnormalities, such as incoherence, affective flattening, failure of reference as well as changes in sentence length and complexity, the clinical picture can vary largely between individuals and language abnormalities will reflect this heterogeneity. Computational linguistics can be used to quantify these features of language. Because of the heterogeneous character of the various symptoms present in schizophrenia spectrum subjects, we expect some subjects to show semantic incoherence, while others may have more affective symptoms such as monotonous **speech**. Here, we combine phonological, semantic and syntactic features of semi-spontaneous language with **machine learning** algorithms for classification in order to develop a **biomarker** sensitive to the broad spectrum of schizophrenia. Methods: Semi-spontaneous natural language samples were collected from 50 subjects with schizophrenia spectrum disorders and 50 age, gender and parental education matched controls, using recorded neutral-topic, open-ended interviews. The audio samples were speaker coded; audio belonging to the subject was extracted and transcribed. Phonological features were extracted using OpenSMILE; semantic features were calculated using a word2vec model using a moving windows of coherence approach, and finally syntactic aspects were calculated using the T-scan tool. Feature reduction was applied to each of the domains. To distinguish groups, results from **machine learning** classifiers trained using leave-oneout cross-validation on each of these aspects were combined, incorporating a voting mechanism. Results: The **machine-learning** classifier approach obtained 75-78% accuracy for the semantic, syntactic and phonological domains individually. As most distinguishing features of their respective domain, we found reduced timbre and intonation for the phonological domain, increased variance of coherence for the semantic domain and decreased complexity of **speech** in the syntactic domain. The combined approach, using a voting algorithm across the domains, achieved an accuracy of 83% and a precision score of 89%. No significant differences in age, gender or parental education between healthy controls and subjects with schizophrenia spectrum disorders was found. Discussion: In this study we demonstrated that computational features derived from different linguistic domains capture aspects of symptomatic language of schizophrenia spectrum disorder subjects. The combination of these features was useful to improve classification for this heterogeneous disorder, as we showed high accuracy and precision from the language parameters in distinguishing schizophrenia patients from healthy controls. These values are better than those obtained with imaging or blood analyses, while language is a more easily obtained and cheaper measure than those derived from other methods. Validation in an independent sample is required, and further features of differentiation should be extracted for their respective domains. Our positive results in using language abnormalities to automatically detect schizophrenia show that computational linguistics is a promising method in the search for reliable markers in psychiatry.

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**Conference country:** Italy

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**Conference location:** Florence

**Conference start date:** 2020-04-04

**Conference title:** 2020 Congress of the Schizophrenia International Research Society, SIRS 2020

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**Correspondence author:** Voppel, Alban UMC Groningen.

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**Subject:** Embase;biological marker;adult;algorithm (major);blood analysis;classifier (major);clinical article;conference abstract;controlled study;cross validation;education;emotional disorder;female;gender;genetic transcription;human;interview;linguistics (major);male;psychiatry;schizophrenia spectrum disorder (major);speech;validation process

**Updates:** 2020-09-15

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Document 220

### **Acoustic speech markers for schizophrenia**

**Author:** De Boer, Janna 1 ; Voppel, Alban 2 ; Wijnen, Frank 3 ; Sommer, Iris 2

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**Publication info:** Schizophrenia Bulletin, suppl. Supplement 1 46 : S253-S254. Oxford University Press. (Apr 2020)

**Abstract (summary):** Background: Clinicians routinely use impressions of **speech** as an element of mental status examination, including 'pressured' **speech** in mania and 'monotone' or 'soft' **speech** in depression or psychosis. In psychosis in particular, descriptions of **speech** are used to monitor (negative) symptom severity. Recent advances in computational linguistics have paved the way towards automated **speech** analyses as a **biomarker** for psychosis. In the present study, we assessed the diagnostic value of acoustic **speech** features in schizophrenia. We hypothesized that a classifier would be highly accurate (~ 80%) in classifying patients and healthy controls. Methods: Natural **speech** samples were obtained from 86 patients with schizophrenia and 77 age and gender matched healthy controls through a semi-structured interview, using a set of neutral open-ended questions. Symptom severity was rated by consensus rating of two trained researchers, blinded to **phonetic** analysis, with the Positive And Negative Syndrome Scale (PANSS). Acoustic features were extracted with OpenSMILE, employing the Geneva Acoustic Minimalistic Parameter Set (GeMAPS), which comprises standardized analyses of pitch (F0), formants (F1, F2 and F3, i.e. acoustic resonance frequencies that indicate the position and movement of the articulatory muscles during **speech** production), **speech** quality, length of voiced and unvoiced regions. **Speech** features were fed into a linear kernel **support vector machine (SVM)** with leave-one-out cross-validation to assess their value for psychosis diagnosis. Results: Demographic analyses revealed no differences between patients with schizophrenia and healthy controls in age or parental education. An automated **machine-learning speech** classifier reached an accuracy of 82.8% in classifying patients with schizophrenia and controls on **speech** features alone. Important features in the model were variation in loudness, spectral slope (i.e. the gradual decay in energy in high frequency **speech** sounds) and the amount of voiced regions (i.e. segments of the interview where the participant was speaking). PANSS positive, negative and general scores were significantly correlated with pitch, formant frequencies and length of voiced and unvoiced regions. Discussion: This study demonstrates that an algorithm using quantified features of **speech** can objectively differentiate patients with schizophrenia from controls with high accuracy. Further validation in an independent sample is required. Employing standardized parameter sets ensures easy replication and comparison of analyses and can be used for cross linguistic studies. Although at an early stage, the field of clinical computational linguistics introduces a powerful tool for diagnosis and prognosis of psychosis and neuropsychiatric disorders in general. We consider this new diagnostic tool to be of high potential given its ease of acquirement, low costs and patient burden. For example, this tool could easily be implemented as a smartphone app to be used in treatment settings.

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**Conference country:** Italy

**Conference end date:** 2020-04-08

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**Conference title:** 2020 Congress of the Schizophrenia International Research Society, SIRS 2020

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**Correspondence author:** De Boer, Janna UMC Utrecht.

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**Subject:** Embase;adult;conference abstract;consensus;controlled study;demography;diagnosis;diagnostic value;education;female;gender;human;leave one out cross validation;linguistics;loudness;machine learning;major clinical study;male;muscle;negative syndrome (major);pitch;Positive and Negative Syndrome Scale;positive syndrome;prognosis;semi structured interview;smartphone;speech analysis (major);support vector machine (major)

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Document 221

### **Quantitative assessment of mania and psychosis during hospitalization using automated analysis of face, voice, and language**

**Author:** Kilciksiz, Can 1 ; Brown, Katrina 2 ; Vail, Alexandria 3 ; Baltrusaitis, Tadas 3 ; Pennant, Luciana 2 ; Liebson, Elizabeth 4 ; Ongur, Dost 4 ; Morency, Louis-Philippe 3 ; Baker, Justin 4

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**Publication info:** Schizophrenia Bulletin, suppl. Supplement 1 46 : S177. Oxford University Press. (Apr 2020)

**Abstract (summary):** Background: A major challenge for reliable and effective mental health care is the lack of objective **markers** of illness. Computational approaches to measuring naturalistic behavior in clinical settings could therefore provide an objective backstop for mental health assessment and disease monitoring. This study aimed to train **machine-learning** (ML) classifiers to estimate conventional clinical measures of severe mental illness using quantitative metrics derived from computational analysis of facial and **vocal** behaviors. Methods: Individuals hospitalized for any active psychotic condition were recruited to participate in up to ten recorded study visits, comprised of three segments. Each visit was captured using two synchronized HD webcams and cardioid microphones, to obtain high quality audiovisual (AV) data from both patient and interviewer. We performed automated facial action coding, **vocal** analysis, and **speech** transcription using publicly available software (e.g., openFace, openSmile, TranscribeMe). Results: A total of 34 participants, participated in 66 sessions between 2015 and 2018, resulting in over 40 hours of AV recordings. In our visual and **vocal** analysis, we found that several features derived from face, **voice**, and use of language (i.e. eyebrow furrowing, eye widening, smile variability, characteristics of vowels) were both robustly measured using our approach, and allowed us to accurately estimate multiple symptom domains (i.e. mania, depression, psychosis) with ( $R = >0.7$ ,  $p = <0.05$ ). In our linguistic analysis, we found that abundance of power words (i.e. superiority, important) and lack of contextual language (i.e. yesterday, nearby) are highly indicative of positive psychotic symptoms with ( $R = +0.417$ ,  $p = 0.002$ ) and ( $R = -0.302$ ,  $p = 0.028$ ) respectively. Discussion: Automated analysis of face, **voice**, and **speech** provides a number of robust behavioral **markers** sensitive enough to detect changes in psychopathology within individuals over time. Therefore, naturalistic, quantitative assessments can yield objective **markers** of mood and cognition that can be used to optimize both access and quality of treatments for a wide range of psychiatric conditions.

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**Conference country:** Italy

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**Conference title:** 2020 Congress of the Schizophrenia International Research Society, SIRS 2020

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**Correspondence author:** Kilciksiz, Can BIDMC/Harvard Medical School.

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**Subject:** Embase;adult;audiovisual recording;classifier;clinical article;conference abstract;controlled study;eyebrow;facial expression;female;genetic transcription;hospitalization (major);human;male;mania (major);microphone;mood;psychosis (major);quantitative analysis (major);software;speech;voice (major);vowel (major)

**Updates:** 2020-09-15

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Document 222

## Applying speech technologies to assess verbal memory in patients with serious mental illness

**Author:** Holmlund, Terje B 1 ; Chandler, Chelsea 2 ; Foltz, Peter W 3 ; Cohen, Alex S 4 ; Cheng, Jian 5 ; Bernstein, Jared C 5 ; Rosenfeld, Elizabeth P 5 ; Elvevåg, Brita 6

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**Publication info:** NPJ digital medicine 3 : 33. (Mar 11, 2020)

**Abstract (summary):** Verbal memory deficits are some of the most profound neurocognitive deficits associated with schizophrenia and serious mental illness in general. As yet, their measurement in clinical settings is limited to traditional tests that allow for limited administrations and require substantial resources to deploy and score. Therefore, we developed a digital ambulatory verbal memory test with automated scoring, and repeated self-administration via smart devices. One hundred and four adults participated, comprising 25 patients with serious mental illness and 79 healthy volunteers. The study design was successful with high quality speech recordings produced to 92% of prompts (Patients: 86%, Healthy: 96%). The story recalls were both transcribed and scored by humans, and scores generated using natural language processing on transcriptions were comparable

to human ratings ( $R = 0.83$ , within the range of human-to-human correlations of  $R = 0.73-0.89$ ). A fully automated approach that scored transcripts generated by automatic **speech** recognition produced comparable and accurate scores ( $R = 0.82$ ), with very high correlation to scores derived from human transcripts ( $R = 0.99$ ). This study demonstrates the viability of leveraging **speech** technologies to facilitate the frequent assessment of verbal memory for clinical monitoring purposes in psychiatry.

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**Copyright:** © The Author(s) 2020.

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**Identifier (keyword):** **Biomarkers**, Diagnosis, Human behaviour, Language

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Document 223

**Automated assessment of psychiatric disorders using **speech**: A systematic review**

**Author:** Low, Daniel M. 1 ; Bentley, Kate H. 2 ; Ghosh, Satrajit S. 3



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**Publication info:** Laryngoscope Investigative Otolaryngology 5.1: 96-116. John Wiley and Sons Inc. (Feb 1, 2020)

**Abstract (summary):** Objective: There are many barriers to accessing mental health assessments including cost and stigma. Even when individuals receive professional care, assessments are intermittent and may be limited partly due to the episodic nature of psychiatric symptoms. Therefore, machine-learning technology using speech samples obtained in the clinic or remotely could one day be a biomarker to improve diagnosis and treatment. To date, reviews have only focused on using acoustic features from speech to detect depression and schizophrenia. Here, we present the first systematic review of studies using speech for automated assessments across a broader range of psychiatric disorders. Methods: We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. We included studies from the last 10 years using speech to identify the presence or severity of disorders within the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). For each study, we describe sample size, clinical evaluation method, speech-eliciting tasks, machine learning methodology, performance, and other relevant findings. Results: 1395 studies were screened of which 127 studies met the inclusion criteria. The majority of studies were on depression, schizophrenia, and bipolar disorder, and the remaining on post-traumatic stress disorder, anxiety disorders, and eating disorders. 63% of studies built machine learning predictive models, and the remaining 37% performed null-hypothesis testing only. We provide an online database with our search results and synthesize how acoustic features appear in each disorder. Conclusion: Speech processing technology could aid mental health assessments, but there are many obstacles to overcome, especially the need for comprehensive transdiagnostic and longitudinal studies. Given the diverse types of data sets, feature extraction, computational methodologies, and evaluation criteria, we provide guidelines for both acquiring data and building machine learning models with a focus on testing hypotheses, open science, reproducibility, and generalizability. Level of Evidence: 3a.

**Accession number:** 2004175436

**Author e-mail address:** dlow@mit.edu, satra@mit.edu

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**Correspondence author:** Low, Daniel M. Program in Speech and Hearing Bioscience and Technology, Harvard Medical School, Boston, MA, United States.

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**Identifier (keyword):** machine learning, mental health, psychiatry, speech, voice

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**Publisher:** John Wiley and Sons Inc

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**Subject:** Embase;microphone;anxiety;comorbidity;DSM-5;head and neck surgery;human;machine learning;measurement accuracy;measurement precision;mental disease (major);mental health;meta analysis;Patient Health Questionnaire 9;personality disorder;personalized medicine;posttraumatic stress disorder;power analysis;practice guideline;psychiatry;receiver operating characteristic;Review;schizophrenia;self control;speech discrimination;systematic review;systematic review (topic);task performance

**Updates:** 2020-02-062020-03-032020-03-052021-09-02

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Document 224

**Voice patterns in schizophrenia: A systematic review and Bayesian meta-analysis**

**Author:** Parola, Alberto 1 ; Simonsen, Arndis 2 ; Bliksted, Vibeke 2 ; Fusaroli, Riccardo 3

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**Publication info:** Schizophrenia Research 216 : 24-40. Elsevier B.V. (Feb 2020)

**Abstract (summary):** Voice atypicalities have been a characteristic feature of schizophrenia since its first definitions. They are often associated with core negative symptoms such as flat affect and alogia, and with the social impairments seen in the disorder. This suggests that voice atypicalities may represent a marker of clinical features and social functioning in schizophrenia. We systematically reviewed and meta-analyzed the evidence for distinctive acoustic patterns in schizophrenia, as well as their relation to clinical features. We identified 46 articles, including 55 studies with a total of 1254 patients with schizophrenia and 699 healthy controls. Summary effect sizes (Hedges'g and Pearson's r) estimates were calculated using multilevel Bayesian modeling. We identified weak atypicalities in pitch variability (g = -0.55) related to flat affect, and stronger atypicalities in proportion of spoken time, speech rate, and pauses (g's between -0.75 and -1.89) related to alogia and flat affect. However, the effects were mostly modest (with the important exception of pause duration) compared to perceptual and clinical judgments, and characterized by large heterogeneity between studies. Moderator analyses revealed that tasks with a more demanding cognitive and social component showed larger effects both in contrasting patients and controls and in assessing symptomatology. In conclusion, studies of acoustic patterns are a promising but, yet unsystematic avenue for establishing markers of schizophrenia. We outline recommendations towards more cumulative, open, and theory-driven research.

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**Identifier (keyword):** Acoustic analysis, Biomarker, Machine learning, Negative symptoms, Social communication, Speech signal

**Language:** English

**Language of abstract:** English

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**Subject:** Embase;MEDLINE;biological marker (major);Bayes theorem;clinical feature;decision making;evidence based medicine;human;measurement accuracy;perception;priority journal;Review;schizophrenia (major);social status;symptomatology;systematic review;voice parameter (major)

**Updates:** 2019-12-212019-12-282020-05-182020-05-26

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Document 225

## **Clinical state tracking in serious mental illness through computational analysis of speech**

**Author:** Arevian, Armen C 1 ; Bone, Daniel 2 ; Malandrakis, Nikolaos 2 ; Martinez, Victor R 2 ; Wells, Kenneth B 3 ; Miklowitz, David J 1 ; Narayanan, Shrikanth 2

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United States of America 3 Jane and Terry Semel Institute for Neuroscience and Human Behavior, University of California Los Angeles, Los Angeles, CA, United States of America, RAND Corporation, Santa Monica, CA, United States of America, United States of America

**Publication info:** PloS one 15.1: e0225695. (Jan 15, 2020)

**Abstract (summary):** Individuals with serious mental illness experience changes in their clinical states over time that are difficult to assess and that result in increased disease burden and care utilization. It is not known if features derived from **speech** can serve as a transdiagnostic **marker** of these clinical states. This study evaluates the feasibility of collecting **speech** samples from people with serious mental illness and explores the potential utility for tracking changes in clinical state over time. Patients (n = 47) were recruited from a community-based mental health clinic with diagnoses of bipolar disorder, major depressive disorder, schizophrenia or schizoaffective disorder. Patients used an interactive **voice** response system for at least 4 months to provide **speech** samples. Clinic providers (n = 13) reviewed responses and provided global assessment ratings. We computed features of **speech** and used **machine learning** to create models of outcome measures trained using either population data or an individual's own data over time. The system was feasible to use, recording 1101 phone calls and 117 hours of **speech**. Most (92%) of the patients agreed that it was easy to use. The individually-trained models demonstrated the highest correlation with provider ratings ( $\rho = 0.78$ ,  $p < 0.001$ ). Population-level models demonstrated statistically significant correlations with provider global assessment ratings ( $\rho = 0.44$ ,  $p < 0.001$ ), future provider ratings ( $\rho = 0.33$ ,  $p < 0.05$ ), BASIS-24 summary score, depression sub score, and self-harm sub score ( $\rho = 0.25, 0.25$ , and  $0.28$  respectively;  $p < 0.05$ ), and the SF-12 mental health sub score ( $\rho = 0.25$ ,  $p < 0.05$ ), but not with other BASIS-24 or SF-12 sub scores. This study brings together longitudinal collection of objective behavioral **markers** along with a transdiagnostic, personalized approach for tracking of mental health clinical state in a community-based clinical setting.

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**Correspondence author:** Arevian, Armen C Jane and Terry Semel Institute for Neuroscience and Human Behavior, University of California Los Angeles, Los Angeles, CA, United States of America.

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**MeSH:** Computational Biology -- methods (major);Female;Humans;Male;Mental Disorders -- epidemiology (major);Middle Aged;Pilot Projects;Residence Characteristics;Speech (major);Support Vector Machine

**Notes:** AA has a financial interest in Insight Health Systems, Inc., Arevian Technologies Inc. AA has a family relationship to Memorial Psychiatric Health Services, a company that provides psychiatric services for the R.O.A.D.S. Foundation clinic where participants were recruited. SN is Chief Scientist at Behavioral Signal Technologies and Lyssn.io. There are no patents, products in development or marketed products to declare. The above interests do not alter our adherence to PLOS ONE policies on sharing data and materials. The specific roles of the authors are articulated in the 'author contributions' section.;; Publication model: Electronic-eCollection.;; Cited medium:Internet

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Document 226

## **Parkinson disease prediction using intrinsic mode function based features from speech signal**

**Author:** Karan, Biswajit 1 ; Sahu, Sitanshu Sekhar 1 ; Mahto, Kartik 1

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**Publication info:** Biocybernetics and Biomedical Engineering 40.1: 249-264. Elsevier Sp. z o.o. (Jan 2020 - Mar 2020)

**Abstract (summary):** Parkinson's disease (PD) is a progressive neurological disorder prevalent in old age. Past studies have shown that **speech** can be used as an early **marker** for identification of PD. It affects a number of **speech** components such as **phonation**, **speech** intensity, articulation, and respiration, which alters the **speech** intelligibility. **Speech** feature extraction and classification always have been challenging tasks due to the existence of non-stationary and discontinuity in the **speech** signal. In this study, empirical mode decomposition (EMD) based features are demonstrated to capture the **speech** characteristics. A new feature, intrinsic mode function cepstral coefficient (IMFCC) is proposed to efficiently represent the characteristics of Parkinson **speech**. The performances of proposed features are assessed with two different datasets: dataset-1 and dataset-2 each having 20 normal and 25 Parkinson affected peoples. From the results, it is demonstrated that the proposed intrinsic mode function cepstral coefficient feature provides superior classification accuracy in both datasets. There is a significant increase of 10–20% in accuracy compared to the standard acoustic and Mel-frequency cepstral coefficient (MFCC) features.

**Accession number:** 2004351093

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**Correspondence author:** Sahu, Sitanshu Sekhar Department of Electronics and Communication Engineering, Birla Institute of Technology, Mesra, Ranchi, India.

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**Identifier (keyword):** Empirical mode decomposition, IMFCC, Intrinsic mode function, MFCC, Parkinson disease, **Support vector machine**

**Language:** English

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**Subject:** Embase;adult;aged;Article;clinical article;controlled study;empirical mode decomposition;**feature extraction**;female;human;intrinsic mode function (major);male;Parkinson disease (major);priority journal;**speech discrimination** (major);**vocal cord**

**Updates:** 2019-12-272020-01-06

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Document 227

## **Automated analysis of natural **speech** in amyotrophic lateral sclerosis**

**Author:** Nevler, Naomi 1 ; Ash, Sharon 1 ; McMillan, Corey 1 ; Elman, Lauren 1 ; McCluskey, Leo 1 ; Irwin, David 1 ; Cho, Sunghye 2 ; Liberman, Mark 2 ; Grossman, Murray 1

1 Neurology 2 Linguistic Data Consortium, University of Pennsylvania

**Publication info:** Neurology, suppl. Supplement 94.15 Lippincott Williams and Wilkins. (2020)

**Abstract (summary):** Objective: To study acoustic **speech** signals in ALS and identify specific acoustic-prosodic **markers** of motor and cognitive impairments. Background: In amyotrophic lateral sclerosis (ALS), motor and cognitive deficits may disrupt **speech**. We implement **automated speech recognition** methods to characterize acoustic-prosodic properties of **speech** in patients with ALS spectrum disorders. Design/Methods: We recruited 44 patients with motor ALS, 23 with ALS-frontotemporal degeneration (ALS-FTD) as well as normal and FTD (non-ALS) controls. **Speech** samples of picture descriptions were automatically segmented with a **speech** activity detector. Continuous **speech** segments were pitch-tracked and duration measures for **speech** and silent pause segments were extracted. We calculated acoustic measures, including fundamental frequency (f0) range, mean **speech** and total **speech** durations, and pause rate. We compared groups and related performance on acoustic measures to clinical tests of cognitive and motor functions and cortical atrophy in MRI-T1 scans of ALS. Results: f0 range was impaired and related to bulbar disease (beta=-0.59, p=0.012) in ALS. f0 range was associated with MRI atrophy in primary motor cortex and left



peri-Sylvian regions. Shortened **speech** segments (beta=0.01, p=0.02) and total **speech** duration (beta=0.38, p=0.006) were related to cognitive impairment. Total **speech** time was associated with atrophy in the frontal opercula and IFG bilaterally, the left anterior insula and the superior temporal gyri (STG). Only timed measures of **speech**, including pause rate and shortened **speech** segments, were related to respiratory restriction and associated with atrophy in the right frontal operculum and left STG. Conclusions: **Speech** samples in ALS spectrum disorders can provide highly objective and reproducible **markers** of disease derived purely from the acoustic signal. Such acoustic **markers** relate to prosodic elements of natural language such as fluency and intonation and reflect specific motor and cognitive impairments in ALS.

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**Conference country:** Canada

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**Correspondence author:** Nevler, Naomi Neurology.

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**Language:** English

**Language of abstract:** English

**Publication date:** 2020

**Publication type:** Journal

**Publisher:** Lippincott Williams and Wilkins

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**Subject:** Embase;adult;amyotrophic lateral sclerosis (major);anterior insula;brain cortex atrophy;clinical article;cognitive defect;conference abstract;controlled study;female;frontal operculum;genetic susceptibility;human;language;male;motor performance;nuclear magnetic resonance imaging;**pitch**;primary motor cortex;**speech analysis** (major);superior temporal gyrus

## **Automatic assessment of cognitive tests for differentiating mild cognitive impairment: A proof of concept study of the digit span task**

**Author:** Asgari, Meysam 1 ; Gale, Robert 1 ; Wild, Katherine 2 ; Dodgeb, Hiroko 3 ; Kaye, Jeffrey 2

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**Publication info:** Current Alzheimer Research 17.7: 658-666. Bentham Science Publishers. (2020)

**Abstract (summary):** Background: Current conventional cognitive assessments are limited in their efficiency and sensitivity, often relying on a single score such as the total correct items. Typically, multiple features of response go uncaptured. Objectives: We aim to explore a new set of automatically derived features from the Digit Span (DS) task that address some of the drawbacks in the conventional scoring and are also useful for distinguishing subjects with Mild Cognitive Impairment (MCI) from those with intact cognition. Methods: Audio-recordings of the DS tests administered to 85 subjects (22 MCI and 63 healthy controls, mean age 90.2 years) were transcribed using an Automatic **Speech** Recognition (ASR) system. Next, five correctness measures were generated from Levenshtein distance analysis of responses: number correct, incorrect, deleted, inserted, and substituted words compared to the test item. These per-item features were aggregated across all test items for both Forward Digit Span (FDS) and Backward Digit Span (BDS) tasks using summary statistical functions, constructing a global feature vector representing the detailed assessment of each subject's response. A **support vector machine** classifier distinguished MCI from cognitively intact participants. Results: Conventional DS scores did not differentiate MCI participants from controls. The automated multi-feature DS-derived metric achieved 73% on AUC-ROC of the **SVM** classifier, independent of additional clinical features (77% when combined with demographic features of subjects); well above chance, 50%. Conclusion: Our analysis verifies the effectiveness of

introduced measures, solely derived from the DS task, in the context of differentiating subjects with MCI from those with intact cognition.

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**Correspondence author:** Asgari, Meysam Center for Spoken Language Understanding, Oregon Health & Science University (OHSU), Portland, OR, OR-97239, United States.

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**Identifier (keyword):** Biomarkers, Computerized assessment, Digit span, Mild cognitive impairment (MCI), Neuropsychological tests, Short term memory

**Language:** English

**Language of abstract:** English

**Number of references:** 23

**Publication date:** 2020

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**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;biological marker (major);aged;Article;audio recording;automatic speech recognition;automation (major);backward digit span + (major);clinical feature;cognitive function test (major);comparative study;controlled study;demography;disease classification;female;forward digit span + (major);human;learning;major clinical study;male;mental task (major);mild cognitive impairment (major);priority journal;proof of concept (major);scoring system;statistical analysis;support vector machine;very elderly;word processing

**Updates:** 2020-10-182020-10-212020-11-24

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Document 229

## **Assessing the Utility of Language and Voice Biomarkers to Predict Cognitive Impairment in the Framingham Heart Study Cognitive Aging Cohort Data**

**Author:** Thomas, Jason A 1 ; Burkhardt, Hannah A 1 ; Chaudhry, Safina 1 ; Ngo, Anthony D 1 ; Sharma, Saransh 1 ; Zhang, Larry 1 ; Au, Rhoda 2 ; Hosseini Ghomi, Reza 1

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**Publication info:** Journal of Alzheimer's disease : JAD 76.3: 905-922. (2020)

### **Abstract (summary): BACKGROUND**

There is a need for fast, accessible, low-cost, and accurate diagnostic methods for early detection of cognitive decline. Dementia diagnoses are usually made years after symptom onset, missing a window of opportunity for early intervention.

### **OBJECTIVE**

To evaluate the use of recorded voice features as proxies for cognitive function by using neuropsychological test measures and existing dementia diagnoses.

### **METHODS**

This study analyzed 170 audio recordings, transcripts, and paired neuropsychological test results from 135 participants selected from the Framingham Heart Study (FHS), which includes 97 recordings of cognitively normal participants and 73 recordings of cognitively impaired participants. Acoustic and linguistic features of the voice samples were correlated with cognitive performance measures to verify their association.

### **RESULTS**

Language and **voice** features, when combined with demographic variables, performed with an AUC of 0.942 (95% CI 0.929-0.983) in predicting cognitive status. Features with good predictive power included the acoustic features mean spectral slope in the 500-1500Hz band, variation in the F2 bandwidth, and variation in the Mel-Frequency Cepstral Coefficient (MFCC) 1; the demographic features employment, education, and age; and the text features of number of words, number of compound words, number of unique nouns, and number of proper names.

## CONCLUSION

Several linguistic and acoustic **biomarkers** show correlations and predictive power with regard to neuropsychological testing results and cognitive impairment diagnoses, including dementia. This initial study paves the way for a follow-up comprehensive study incorporating the entire FHS cohort.

**Accession number:** 32568190

**Correspondence author:** Thomas, Jason A University of Washington, Seattle, WA, USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2021-06-03

**Date created:** 2020-06-23

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**Document type:** Journal Article, Research Support, N.I.H., Extramural, Research Support, U.S. Gov't, Non-P.H.S.

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**Grant:** T15 LM007442. NLM NIH HHS. United States.

N01 HC025195. NHLBI NIH HHS. United States.

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**Identifier (keyword):** Alzheimer's disease, **artificial intelligence**, **biomarkers**, cognitive dysfunction, data collection, dementia, early diagnosis, language, neuropsychological tests, **voice**

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Aged;Aged, 80 and over;Alzheimer Disease -- complications;Alzheimer Disease -- diagnosis;Alzheimer Disease -- physiopathology;**Biomarkers** -- analysis (major);Cognitive Aging -- physiology (major);Cognitive Dysfunction -- diagnosis (major);Cognitive Dysfunction --

physiopathology;Disease Progression;Female;Humans;Language (major);Male;Neuropsychological Tests;Predictive Value of Tests;Voice -- physiology (major)

**Notes:** Publication model: Print;; Cited medium:Internet

**Publication date:** 2020

**Publication type:** Journal

**Publisher location:** NETHERLANDS

**Source attribution:** Medline, © Publisher specific

**Substance:** Substance Substance: Biomarkers; CAS: 0;

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Document 230

### Identification of digital voice biomarkers for cognitive health

**Author:** Lin, Honghuang 1 ; Karjadi, Cody 2 ; Ang, Ting F A 3 ; Prajakta, Joshi 2 ; McManus, Chelsea 2 ; Alhanai, Tuka W 4 ; Glass, James 5 ; Au, Rhoda 6

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**Publication info:** Exploration of medicine 1 : 406-417. (2020)

**Abstract (summary):** AIM

Human **voice** contains rich information. Few longitudinal studies have been conducted to investigate the potential of **voice** to monitor cognitive health. The objective of this study is to identify **voice biomarkers** that are predictive of future dementia.

## METHODS

Participants were recruited from the Framingham Heart Study. The **vocal** responses to neuropsychological tests were recorded, which were then diarized to identify participant **voice** segments. Acoustic features were extracted with the OpenSMILE toolkit (v2.1). The association of each acoustic feature with incident dementia was assessed by Cox proportional hazards models.

## RESULTS

Our study included 6, 528 **voice** recordings from 4, 849 participants (mean age  $63 \pm 15$  years old, 54.6% women). The majority of participants (71.2%) had one **voice** recording, 23.9% had two **voice** recordings, and the remaining participants (4.9%) had three or more **voice** recordings. Although all asymptomatic at the time of examination, participants who developed dementia tended to have shorter segments than those who were dementia free ( $P < 0.001$ ). Additionally, 14 acoustic features were significantly associated with dementia after adjusting for multiple testing ( $P < 0.05/48 = 1 \times 10^{-3}$ ). The most significant acoustic feature was jitterDDP\_sma\_de ( $P = 7.9 \times 10^{-7}$ ), which represents the differential frame-to-frame Jitter. A **voice** based linear classifier was also built that was capable of predicting incident dementia with area under curve of 0.812.

## CONCLUSIONS

Multiple acoustic and linguistic features are identified that are associated with incident dementia among asymptomatic participants, which could be used to build better prediction models for passive cognitive health monitoring.

**Accession number:** 33665648

**Correspondence author:** Lin, Honghuang Section of Computational Biomedicine, Department of Medicine, Boston University School of Medicine, Boston, MA 02118, USA. , The Framingham Heart Study, Boston University School of Medicine, Boston, MA 02118, USA.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Document type:** Journal Article

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R01 AG049810. NIA NIH HHS. United States.

RF1 AG062109. NIA NIH HHS. United States.

R01 AG008122. NIA NIH HHS. United States.

R56 AG062109. NIA NIH HHS. United States.

N01HC25195. NHLBI NIH HHS. United States.

UL1 TR001430. NCATS NIH HHS. United States.

RF1 AG054156. NIA NIH HHS. United States.

**Identifier (keyword):** Digitalvoice, acoustic features, dementia, epidemiology, prediction

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Print-Electronic;; Cited medium:Internet

**Publication date:** 2020

**Publication type:** Journal

**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

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Document 231

## **Digital voice biomarkers in neurological and psychiatric disorders**

**Author:** Matías-Guiu, Jordi A. 1

1 Servicio de Neurología, Hospital Universitario Clínico San Carlos, Instituto de Investigación Sanitaria San Carlos, Universidad Complutense de Madrid, Madrid, Spain  
jordimatiaguiu@hotmail.com

**Publication info:** Kranion 15.4: 141-147. Publicaciones Permanyer. (2020)



**Abstract (summary):** Digital **biomarkers** (DB) are objective and quantifiable measures of physiological and behavioural variables. They could be acquired using several devices, including tablets, apps, smartphones, or wearables, among others. **Voice** is an emergent DB because of the relevance of **speech** and language in daily living and a wide range of neurological and psychiatric disorders. We review the main **speech** and language disorders in dementia, Parkinson's disease, multiple sclerosis, depression, and schizophrenia, and the potential use of DB in these disorders. Main advantages and challenges of DB in the field are discussed. Automated **voice** analysis may potentially be applied to multiple clinical settings. Technological advances may improve the **voice** data acquisition with high frequency and remotely, which could imply more ecological assessments. There are several issues, including the adaptation of **speech** recognition systems to patients with **speech** or language disorders, ethics, and validation processes, which should be bear in mind before the clinical use of DB.

**Accession number:** 2012116165

**Alternate title:** Biomarcadores digitales de voz en enfermedades neurológicas y psiquiátricas

**Author e-mail address:** jordimatiassguiu@hotmail.com

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**Correspondence author:** Matías-Guiu, Jordi A. Servicio de Neurología, Hospital Universitario Clínico San Carlos, Instituto de Investigación Sanitaria San Carlos, Universidad Complutense de Madrid, Madrid, Spain.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2021-07-20

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**Document type:** Article

**Embase document status:** Embase

**First available:** 2021-06-09

**Identifier (keyword):** Alzheimer, **Artificial intelligence**, Depression, Digital **biomarkers**, Parkinson, Schizophrenia

**Language:** Spanish

**Language of abstract:** English

**Number of references:** 44

**Publication date:** 2020

**Publication type:** Journal

**Publisher:** Publicaciones Permanyer

**Publisher location:** Spain

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker -- endogenous compound (major);Article;automatic speech recognition;automation;dementia;depression;digital technology (major);ethics;human;information processing;language disability;multiple sclerosis;Parkinson disease;schizophrenia;speech disorder;validation process;voice analysis

**Updates:** 2021-06-092021-07-20

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Document 232

## **Objectively Monitoring Amyotrophic Lateral Sclerosis Patient Symptoms During Clinical Trials With Sensors: Observational Study**

**Author:** Garcia-Gancedo, Luis 1 ; Kelly, Madeline L. 2 ; Lavrov, Arseniy 3 ; Parr, Jim 4 ; Hart, Rob 4 ; Marsden, Rachael 5 ; Turner, Martin R. 5 ; Talbot, Kevin 5 ; Chiwera, Theresa 6 ; Shaw, Christopher E. 6 ; Al-Chalabi, Ammar 6

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**Publication info:** JMIR mHealth and uHealth 7.12: e13433. NLM (Medline). (Dec 20, 2019)

**Abstract (summary):** BACKGROUND: Objective symptom monitoring of patients with Amyotrophic Lateral Sclerosis (ALS) has the potential to provide an important source of information to evaluate the impact of the disease on aspects of real-world functional capacity and activities of daily living in the home setting, providing useful objective outcome measures for clinical trials. OBJECTIVE: This study aimed to investigate the feasibility of a novel digital platform for remote data collection of multiple symptoms-physical activity, heart rate variability (HRV), and digital speech characteristics-in 25 patients with ALS in an observational clinical trial setting to explore the impact of the devices on patients' everyday life and to record tolerability related to the devices and study procedures over 48 weeks. METHODS: In this exploratory, noncontrolled, nondrug study, patients attended a clinical site visit every 3 months to perform activity reference tasks while wearing a sensor, to conduct digital speech tests and for conventional ALS monitoring. In addition, patients wore the sensor in their daily life for approximately 3 days every month for the duration of the study. RESULTS: The amount and quality of digital speech data captured at the clinical sites were as intended, and there were no significant issues. All the home monitoring sensor data available were propagated through the system and were received as expected. However, the amount and quality of physical activity home monitoring

data were lower than anticipated. A total of 3 or more days (or partial days) of data were recorded for 65% of protocol time points, with no data collected for 24% of time points. At baseline, 24 of 25 patients provided data, reduced to 13 of 18 patients at Week 48. Lower-than-expected quality HRV data were obtained, likely because of poor contact between the sensor and the skin. In total, 6 of 25 patients had mild or moderate adverse events (AEs) in the skin and subcutaneous tissue disorders category because of skin irritation caused by the electrode patch. There were no reports of serious AEs or deaths. Most patients found the sensor comfortable, with no or minimal impact on daily activities. **CONCLUSIONS:** The platform can measure physical activity in patients with ALS in their home environment; patients used the equipment successfully, and it was generally well tolerated. The quantity of home monitoring physical activity data was lower than expected, although it was sufficient to allow investigation of novel physical activity end points. Good-quality in-clinic **speech** data were successfully captured for analysis. Future studies using objective patient monitoring approaches, combined with the most current technological advances, may be useful to elucidate novel **digital biomarkers** of disease progression.

**Accession number:** 630362922

**Copyright:** This record is sourced from MEDLINE/PubMed, a database of the U.S. National Library of Medicine

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-09-22

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.2196/13433>

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**First available:** 2020-01-02

**Grant:** Department of Health, Australian Government.

G0500289. , MRC. Medical Research Council.

MC\_PC\_17115. , MRC. Medical Research Council.

TURNER/OCT18/989-797. , MNDA. Motor Neurone Disease Association.

**Identifier (keyword):** accelerometer, amyotrophic lateral sclerosis, clinical trial, **digitalbiomarker**, **digital** phenotyping, heart rate, objective symptom monitoring, physical activity, **speech**, wearable

**Language:** English

**Language of abstract:** English

**Publication date:** Dec 20, 2019

**Publication type:** Journal

**Publisher:** NLM (Medline)

**Publisher location:** Canada

**Source attribution:** Embase, © Publisher specific

**Subject:** MEDLINE;biological marker (major);adult;adverse device effect (major);amyotrophic lateral sclerosis -- diagnosis;clinical trial;daily life activity;devices (major);disease exacerbation;electronic device;ethnology;exercise;feasibility study;female;heart rate;human;information processing;male;middle aged;phenotype;physiologic monitoring;physiology;procedures (major);speech;technology

**Updates:** 2020-01-022020-09-22

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Document 233

### **Cerebral correlates of switching during verbal fluency task and its impairment in depression: A surface-based morphometry study**

**Author:** Domain, L. 1 ; Robert, G. 1 ; Guillery, M. 1 ; Linz, N. 2 ; König, A. 3 ; Drapier, D. 4 ; Bannier, E. 5 ; Corouge, I. 5

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**Publication info:** French Journal of Psychiatry, suppl. Supplement 2 1 : S49-S50. Elsevier Masson s.r.l. (Dec 2019)

**Abstract (summary):** Background: Major depressive disorder (MDD) is a highly disabling disease of which is related to chronic course. Currently, there is no robust prognosis biomarker. Cognitive dysfunction associated with the disease has been shown to predict treatment outcome. However, its cerebral substrate is poorly known. Verbal fluency (VF), which are broadly used neuropsychological test, assess the production of words according to a required criterion within a constrained time frame. During this task, subjects produce words within subcategories or "clusters" and occasionally "switch" to other clusters. The measurement of the cluster size and number of switches are relevant cognitive markers. Deep learning-based computational analysis method have been shown to improve the reproducibility and scalability of this measurement. The main objective of the current study was to characterize the cortical thickness (CT) surface-based morphometry (SBM) correlates of the switching and clustering scores in patients with MDD using an artificial intelligence empowered speech analysis system. The secondary objective was to compare those cognitive scores with the ones of the control group. Method: The study included 26 depressed women and 25 matched in age and education level healthy females' controls. All subjects underwent VF tests and had a structural Magnetic Resonance

Imaging (MRI). The clustering and switching scores were assessed using the computational analysis method introduced by Linz et al (<https://ki-elements.de>). SBM was performed using SPM and CAT12 toolbox. Results: In the depressed group, we observed a positive correlation between the switching score in semantic VF test and the CT, in few cortical areas. The main significant correlation was found in the left lingual gyrus ( $P = 0.003$ ). The switching scores were lower in the depressed group in each VF task ( $P = 0.019$  and  $P = 0.007$ ). There was no difference between the two groups concerning the cluster size. Conclusion: Our study revealed the relationship existing between the number of switches produced by depressed subjects in a semantic VF task and the CT in prefrontal regions and in more posterior areas. These results possibly suggest that switching and clustering scores assessment in VF tasks, and its cerebral correlates, may constitute potential prognosis **biomarkers** for depression. Although much work is still required, the establishment of such **biomarkers** has substantial implications for reducing the burden of the disease.

**Accession number:** 2003668206

**Author e-mail address:** leadomain@gmail.com

**Conference country:** France

**Conference end date:** 2019-12-07

**Conference location:** NICE

**Conference start date:** 2019-12-04

**Conference title:** Congrès Français de Psychiatrie 2019

**Copyright:** Copyright 2022 Elsevier B.V., All rights reserved.

**Correspondence author:** Domain, L. University of Rennes, "Behavior and Basal Ganglia" research unit (EA4712), Rennes, France.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1016/j.fjpsy.2019.10.142>

**Embase document status:** Embase

**First available:** 2022-02-22

**Identifier (keyword):** **Biomarkers**, Cortical thickness, **Deep learning**, Major depressive disorder, Verbal fluency

**Language:** French

**Language of abstract:** French

**Publication date:** Dec 2019

**Publication type:** Journal

**Publisher:** Elsevier Masson s.r.l.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker (major);conference abstract;deep learning (major);major depression (major);thickness (major)

**Updates:** 2022-02-22

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Document 234

## **Pre- and Paralinguistic Vocal Production in ASD: Birth Through School Age**

**Author:** Yankowitz, Lisa D. 1 ; Schultz, Robert T. 2 ; Parish-Morris, Julia 3

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**Publication info:** Current Psychiatry Reports 21.12 Springer. (Dec 1, 2019)

**Abstract (summary):** Purpose of Review: We review what is known about how pre-linguistic vocal differences in autism spectrum disorder (ASD) unfold across development and consider whether vocalization features can serve as useful diagnostic indicators. Recent Findings: Differences in the frequency and acoustic quality of several vocalization types (e.g., babbles and cries) during the first year of life are associated with later ASD diagnosis. Paralinguistic features (e.g., prosody) measured during early and middle childhood can accurately classify current ASD diagnosis using cross-validated machine learning approaches. Summary: Pre-linguistic vocalization differences in infants are promising behavioral markers of later ASD diagnosis. In older children, paralinguistic features hold promise as diagnostic indicators as well as clinical targets. Future research efforts should focus on (1) bridging the gap between basic research and practical implementations of early vocalization-based risk assessment tools, and (2) demonstrating the clinical impact of targeting atypical vocalization features during social skill interventions for older children.

**Accession number:** 2003655120

**Author e-mail address:** lisayank@sas.upenn.edu

**Copyright:** Copyright 2019 Elsevier B.V., All rights reserved.

**Correspondence author:** Yankowitz, Lisa D. Department of Psychology, University of Pennsylvania, 3720 Walnut Street, Philadelphia, PA, 19104, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2019-11-28

**Document status:** New

**Document type:** Review

**DOI:** <http://dx.doi.org/10.1007/s11920-019-1113-1>

**Embase document status:** In Process; In-Data-Review (MEDLINE in Embase)

**First available:** 2019-11-29

**Identifier (keyword):** Acoustic properties, Autism, Early diagnosis, Paralinguistics, Prosody, **Speech** production

**Language:** English

**Language of abstract:** English

**Number of references:** 96

**Publication date:** Dec 1, 2019

**Publication type:** Journal

**Publisher:** Springer

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;autism (major);basic research;child;diagnosis;early diagnosis (major);human;infant;**machine learning**;paralanguage (major);review;risk assessment;social competence;**vocalization** (major)

**Updates:** 2019-11-29

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Document 235

**Digital **markers** of behavioral and physiological functioning as predictors of post-traumatic stress response**

**Author:** Levy, Isaac Galatzer 1

1 AiCure, New York, NY, United States

**Publication info:** Neuropsychopharmacology, suppl. Supplement 1 44 : 12. Springer Nature. (Dec 2019)

**Abstract (summary):** Background: Direct behavioral and physiological features such as facial expression of emotion, body and eye movement, acoustic elements and content of **speech** may represent indices of clinical functioning that more closely represent underlying central nervous system functioning when compared to existing psychiatric nosology and associated paper and pencil measures. Mental health assessment has traditionally relied on self-report or clinician assessment of psychiatric symptoms. We present a **machine learning** based model to detect clinical risk based on automated measurement and integration of face, **voice**, and **speech** features, captured during unstructured **speech** as predictors of PTSD severity trajectories (chronic, recovery, resilient) from 1 month to 12 months following admission to the emergency room following a life threatening traumatic event. Methods: We utilized computer vision, and **voice/speech**-based feature of 1) emotions and their intensity; 2) movement; 3) **speech** prosody; 4) natural language content; 5) movement in n = 90 individuals who completed a qualitative interview about their experience 1 month after admission to the emergency room (ER) following a significant accident or injury. Neural networks were utilized to build classification and forecasting models of PTSD at 1 month and across 12 months using audio and video features. Results: Audio and video features correctly classified clinical trajectories (PTSD AUC = 0.87) and predicted the chronic trajectory at the highest accuracy (Chronic PTSD AUC = 0.90). Facial features of emotion, **voice** prosody, **speech** content, and movement all contributed to the model. Conclusions: **Machine learning** based detection of behavioral and physiological **markers** in unstructured data can accurately identify clinical functioning and predict clinical course.

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**Conference country:** United States

**Conference end date:** 2019-12-11

**Conference location:** Orlando, FL

**Conference start date:** 2019-12-08

**Conference title:** 58th Annual Meeting of the American College of Neuropsychopharmacology, ACNP 2019

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**Correspondence author:** Levy, Isaac Galatzer AiCure, New York, NY, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2020-05-23

**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1038/s41386-019-0544-z>



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**First available:** 2020-05-25

**Language:** English

**Language of abstract:** English

**Publication date:** Dec 2019

**Publication type:** Journal

**Publisher:** Springer Nature

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;accident;adult;animal experiment;animal model;computer vision;conference abstract;controlled study;emergency

ward;facies;female;forecasting;human;interview;language;machine

learning;male;nonhuman;posttraumatic stress disorder (major);speech;videorecording;voice

**Updates:** 2020-05-25

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Document 236

## **A machine learning approach to predicting psychosis using semantic density and latent content analysis**

**Author:** Rezaii, Neguine 1 ; Walker, Elaine 2 ; Wolff, Phillip 2

1 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States, Department of Psychiatry, Emory School of Medicine, Atlanta, GA, United States nrezaii@mgh.harvard.edu 2 Department of Psychology, Emory University, Atlanta, GA, United States

**Publication info:** npj Schizophrenia 5.1 Nature Publishing Group. (Dec 1, 2019)

**Abstract (summary):** Subtle features in people's everyday language may harbor the signs of future mental illness. Machine learning offers an approach for the rapid and accurate extraction of these signs. Here we investigate two potential linguistic indicators of psychosis in 40 participants of the North American Prodrome Longitudinal Study. We demonstrate how the linguistic marker of semantic density can be obtained using the mathematical method of vector unpacking, a technique that decomposes the meaning of a sentence into its core ideas. We also demonstrate how the latent semantic content of an individual's speech can be extracted by contrasting it with the contents of conversations generated on social media, here 30,000 contributors to Reddit. The results revealed that conversion to psychosis is signaled by low semantic density and talk about voices and sounds. When combined, these two variables were able to predict the conversion with 93% accuracy in the training and 90% accuracy in the holdout datasets. The results point to a larger project in which

automated analyses of language are used to forecast a broad range of mental disorders well in advance of their emergence.

**Accession number:** 628097515

**Author e-mail address:** nrezaii@mgh.harvard.edu

**Copyright:** Copyright 2019 Elsevier B.V., All rights reserved.

**Correspondence author:** Rezaii, Neguine Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2019-06-25

**Document status:** Revised

**Document type:** Article

**DOI:** <http://dx.doi.org/10.1038/s41537-019-0077-9>

**Embase document status:** Embase

**First available:** 2019-06-21

**Language:** English

**Language of abstract:** English

**Number of references:** 49

**Publication date:** Dec 1, 2019

**Publication type:** Journal

**Publisher:** Nature Publishing Group

**Publisher location:** Houndmills, RG21 6XS, United Kingdom

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;accuracy;Article;clinical article;content analysis (major);embedding;follow up;hearing;human;language;latent content analysis + (major);longitudinal study;machine learning (major);priority journal;psychosis -- diagnosis (major);semantic density + (major);semantics (major);social media;sound;speech;voice

**Updates:** 2019-06-212019-06-26

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Document 237

**Alignment of objective markers of speech with listener based judgements and disease severity in Friedreich ataxia**

**Author:** Vogel, A. 1 ; Tsanas, A. 1 ; Reece, H. 1 ; Corben, L. 1 ; Tai, G. 1 ; Delatycki, M. 1

1 , Melbourne, Australia

**Publication info:** Movement Disorder, suppl. Supplement 2 34 : S120. John Wiley and Sons Inc. (Oct 2019)

**Abstract (summary):** Objective: To identify a subset of acoustic **markers of speech** that objectively describe listener perceptions, disease severity and **speech** related quality of life in Friedreich ataxia. Background: **Dysarthria** is a key aspect of Friedreich ataxia (FA). **Speech** changes as disease progresses and in response to both behavioral and pharmacological treatment. Current assessment practices rely on clinical impressions and listener based examinations of **speech** which are subjective and have poor inter/intra-rater reliability. Objective evaluation of **speech** (acoustic analysis) can yield valuable insights into how disease progresses over time, and how individuals respond to therapy. Methods: We applied a wide range of known and novel **speech** signal processing algorithms to a large database (1000+ recordings from >130 individuals with FA over a 10-year period). We used principled variable selection methods to determine a subset of the extracted **markers**, which was presented into a classifier using a standard supervised learning setup to map onto (a) listener perceptions of intelligibility and naturalness, (b) a disease severity scale (Friedreich Ataxia Rating Scale) and (c) **speech** related quality of life scale (sub-domain of the Friedreich Ataxia Impact Scale). Results: We have assessed the resulting models using 10-fold crossvalidation with 100 iterations for statistical confidence. Findings suggest there are specific objective **markers of speech** that change over time and reflect to some degree other clinical features of the disease. Conclusions: Our ability to develop objective features of **dysarthria** require large longitudinal datasets combined with a variety of clinical endpoints. Here we describe an important advance in our ability to quantify this meaningful outcome measure. Wholistic **speech** descriptors will better serve investigations seeking to capture meaningful metrics of change resulting from progression or treatment.

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**Conference country:** France

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**Conference title:** 2019 International Parkinson and Movement Disorder Society, MDS 2019

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**Correspondence author:** Vogel, A. , Melbourne, Australia.

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**Publication date:** Oct 2019

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**Subject:** Embase;acoustic analysis;adult;algorithm (major);classifier;clinical feature;conference abstract;controlled study;cross validation;decision making (major);disease severity assessment;dysarthria (major);female;Friedreich ataxia (major);human;intrarater reliability;learning;major clinical study;male;outcome assessment;perception;quality of life;quantitative analysis;rating scale;signal processing;speech intelligibility

**Updates:** 2020-04-09

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Document 238

### **Treatment monitoring using objective and frequent digital testing in the D1PAM (LY3154207) phase 1B Parkinson's disease clinical trial**

**Author:** Wang, J. 1 ; Battioui, C. 1 ; Li, Y. 1 ; Calvin, A. 1 ; Wu, L. 1 ; Romano, A. 1 ; Miller, B. 1

1 , Indianapolis, IN, United States

**Publication info:** Movement Disorder, suppl. Supplement 2 34 : S95. John Wiley and Sons Inc. (Oct 2019)

**Abstract (summary):** Objective: This study evaluates the feasibility, reliability, and validity of smartphone app-based testing in patients with Parkinson's disease (PD) in the D1PAM (D1 positive allosteric modulator) phase 1B clinical trial. Background: Currently, the lack of well-validated biomarkers to diagnose and monitor PD is a significant hurdle in the discovery of disease-modifying therapeutics. Smartphones, equipped with sensitive touchscreen and sensors, promise an unbiased approach to assess disease state and treatment response. Methods: An iPhone trial app, modeled after the public mPower study [1], was custom designed using the ResearchKit software framework incorporating tests to assess (1) sustained phonation, (2) finger tapping, (3) walking and resting, and (4) cognition in PD patients. The iPhones were locked-down with only the trial app and accompanying training materials accessible. During the two-week at-home pre-treatment, 6-week in-clinic D1PAM

intervention and 2-week at-home post-treatment, 24 participants were instructed to complete the four active tests daily at 8 am, 10 am, 2 pm and 8 pm. During the 2-week intervention, each participant received daily doses of LY3154207 or placebo [2]. Compliance was quantified as completion of required daily tests during pre-treatment, intervention, and post-treatment. Test-retest reliability was quantified as the intra-class correlation coefficient (ICC) using features derived from pre-treatment sensor data. Clinical validity was quantified as the correlation between features and MDS-UPDRS clinical severity rating. Results: Compliance: compliance was superior during D1PAM treatment averaging above 75% and about 50% during pre-treatment and posttreatment. Test-retest reliability: multiple features from tapping, walking and rest, and cognition tests had good reliability (ICC >0.75). Clinical validity: among the most reliable features, some of tapping and walking features are moderately yet significantly correlated with MDSUPDRS total and subscores (Spearman  $r > 0.4$ ). Conclusions: The results demonstrated the applicability of incorporating smartphone app-based testing in PD clinical study. These tests are amenable to regular at-home or in-clinic use and have the potential to enable **digital biomarker** development to objectively detect a subtle disease state change in response to treatment [3].

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**Conference start date:** 2019-09-22

**Conference title:** 2019 International Parkinson and Movement Disorder Society, MDS 2019

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**Correspondence author:** Wang, J. , Indianapolis, IN, United States.

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**Document type:** Conference Abstract

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**Publisher:** John Wiley and Sons Inc.

**Publisher location:** Netherlands

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**Subject:** Embase;biological marker;placebo;adult;allosterism;averaging;clinical article;cognitive function test;conference abstract;controlled study;correlation coefficient;diagnosis;feasibility study;female;finger;human;male;Parkinson disease (major);phase 1 clinical trial;phonation;quantitative analysis;sensor;smartphone;software;test retest reliability;treatment response;Unified Parkinson Disease Rating Scale;validity;walking

**Updates:** 2020-04-09

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Document 239

### **P.190** Feasibility, reliability and convergent validity for digital biomarkers captured via a smartphone application (app) to assess motor behaviors in individuals with spinal muscular atrophy (SMA) in the JEWELFISH trial

**Author:** Fischer, D. 1 ; Ewing, S. 2 ; Wolf, D. 2 ; Pointeau, G. 2 ; Zhang, Y. 2 ; Lipsmeier, F. 2 ; Qian, Y. 3 ; Eng, L. 3 ; Salazar, R. 4 ; Dunaway Young, S. 4 ; Sprengel, J. 2 ; Czech, C. 5 ; Gossens, C. 2 ; Lindemann, M. 2

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**Publication info:** Neuromuscular Disorders, suppl. Supplement 1 29 : S104. Elsevier Ltd. (Oct 2019)

**Abstract (summary):** Frequent visits to the clinic to complete assessments impose a large burden on individuals with spinal muscular atrophy (SMA) and their caregivers. New tools may complement or improve regular assessment of symptom severity and progression. Smartphones enable remote patient monitoring through widely accepted platforms and have previously demonstrated value in disorders such as Parkinson's disease. We developed a smartphone application (app) comprising nine tests for the assessment of finger, hand, arm and lung functions via tapping, tracing, squeezing, sustained-phonation and phone-turning games. Using the app, we are assessing the feasibility, reliability and convergent validity of potential digital biomarkers captured via smartphone in patients with Type 2 or 3 SMA from the JEWELFISH trial (NCT03032172)—an ongoing, multicenter, open-label study evaluating the safety, tolerability and PK/PD relationship of risdiplam (RG7916/RO7034067) in non-naïve patients with SMA (who have previously received olesoxime, AVXS-101 or therapies targeting SMN2-splicing). Risdiplam is an investigational, orally administered, centrally and peripherally distributed small molecule that modulates SMN2 pre-mRNA splicing to increase survival of motor neuron (SMN) protein levels. Patients perform daily active tests at home and data features are computed from sensor data. We are using the aggregated sensor data features over all tests to quantify convergent validity relative to clinical assessment of disease severity

(determined by motor function measurement and forced vital capacity). Smartphones may enable long-term, frequent, reliable, low-burden and disease-relevant monitoring for individuals with type 2 or 3 SMA. We will present data from JEWELFISH exploring the validity of this approach.

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**Conference country:** Denmark

**Conference end date:** 2019-10-05

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**Conference title:** 24th International Congress of the World Muscle Society

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**Correspondence author:** Ewing, S. Roche Innovation Center Basel, Basel, Switzerland.

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**Subject:** Embase;biological marker (major);endogenous compound;olesoxime;onasemnogene abeparavovec;risdiplam;survival motor neuron protein;survival motor neuron protein 2;adult;case report;clinical article;conference abstract +;convergent validity (major);disease severity assessment;drug safety;drug therapy;feasibility study (major);female;finger;forced vital capacity;gene expression;human;locomotion (major);lung function;male;motor performance;multicenter study;open study;oral drug administration;Parkinson disease;pharmacokinetics;phonation;quantitative analysis;reliability (major);RNA splicing;sensor;smartphone (major);spinal muscular atrophy (major)

**Substance:** Substance Substance: olesoxime; CAS: 22033-87-0; Substance: onasemnogene abeparvovec; CAS: 1922968-73-7; Substance: risdiplam; CAS: 1825352-65-5;

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Document 240

## **The Promise of Automation: Development and preliminary testing of a language-based machine learning algorithm in PD**

**Author:** Fujii, B. 1 ; Richter, R. 1 ; Roberts, A. 1

1 , Evanston, IL, United States

**Publication info:** Movement Disorder, suppl. Supplement 2 34 : S688. John Wiley and Sons Inc. (Oct 2019)

**Abstract (summary):** Objective: The proposed work seeks to expand current machine learning algorithms in PD using both motor and language features to discriminate affected speakers from healthy controls. Background: The use of automated analysis approaches in the clinical diagnosis of PD, and other neurodegenerative disorders, is appealing because it is fast, inexpensive, highly scalable, and requires little to no setup [1]. Machine learning approaches for discriminating PD speakers largely use motor features [2]. Extant research suggests that cognitive declines manifest as speech and language errors in spontaneous production tasks [3]. Consequently, algorithms based purely on motor features may have limited clinical utility for detecting cognitive impairment in PD. Methods: We used language production errors and pausing to classify standardized reading passages (Grandfather Passage) and phonetically balanced sentence sets produced by individuals with PD (n = 35 language samples) and healthy controls (n=35). Language samples were manually annotated (in CHAT/CLAN) for word retrieval, morphology, and sound production errors. We included select language production markers shown previously to reflect cognitive impairment in PD [4]. Manually coded language data were used to train classifiers based on K-Nearest Neighbor, ZeroR, decision tree, and multilayer perceptron approaches. Results: The K-Nearest Neighbor approach applied to a phonetically balanced set of 11 standardized sentences produced the most robust solution correctly classifying 87.5% of the sentence samples and 60.53% of the standardized reading passage samples. Conclusions: Acceptable classification of PD speakers was achieved using a language-feature based machine learning algorithm. While the work requires replication using larger samples, it is a promising first step for a machine learning algorithm sensitive to potential language markers of cognitive decline in PD. Such language-based algorithms can be important tools for remote monitoring of speech cognitive changes in PD. (Figure Presented).

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**Subject:** Embase;adult;algorithm (major);automation (major);classifier;clinical article;cognitive defect;conference abstract;controlled study;decision tree;grandfather;human;human tissue;information retrieval;k nearest neighbor;language (major);male;multilayer perceptron (major);reading;remote sensing;sound;speech

**Updates:** 2020-04-08

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Document 241

### **Machine learning as a method to detect vocal fold immobility**

**Author:** Law, Anthony; Merati, Albert L.; Meyer, Tanya K.; Whipple, Mark

**Publication info:** Otolaryngology - Head and Neck Surgery, suppl. Supplement 161.2: P91. SAGE Publications Inc. (Sep 2019)

**Abstract (summary):** Objectives: Diagnosing **vocal** fold paresis and paralysis often poses a significant clinical challenge. The endoscopic **markers** of dysfunction are often subtle, and there has been a well-described less-than-optimal interrater reliability for identifying paresis, paralysis, or even the side of dysfunction. We aim to quantify **vocal** fold motion using a **deep neural network** on previously recorded endoscopic exams in an attempt to identify objective measures of **vocal** fold motion abnormalities. Methods: We use retrospectively collected endoscopic exams of 50 patients with normal motion (20), paresis (15), or paralysis (15) of the true **vocal** fold (unilateral) to train a **deep neural network** to identify the borders of the true **vocal** folds from recorded endoscopic exams. Labeled **vocal** folds were used to calculate the angle between the medial borders of the true **vocal** fold as a function of time. The trained model is then applied to 40 independent patients with normal and abnormal **vocal** fold motion. Clustering of resultant curves were correlated with pathological groups as determined via electromyography (EMG), namely, normal, paresis, or paralysis. Results: Our model showed good classification of **vocal** fold paresis and paralysis when compared with the gold standard EMG. No correlation, however, could be determined between studied variables and the side of **vocal** cord dysfunction. Conclusions: Computer-aided analysis of **vocal** fold motion offers a reliable and accurate means of determining normal motion from paresis or from complete paralysis. Further study is necessary to aid with determining the side of dysfunction.

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**Correspondence author:** Law, Anthony

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**Subject:** Embase;adult;clinical article;conference abstract +;controlled study;deep neural network (major);electromyography;female;gold standard;human;immobility (major);male;motion;quantitative analysis;retrospective study;vocal cord disorder (major);vocal cord paralysis

**Updates:** 2019-09-23

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Document 242

## **NOVEL DIGITALIZED MARKERS FOR SCREENING AND DISEASE TRAJECTORY TRACKING IN CLINICAL TRIALS**

**Author:** König, Alexandra 1 ; Narayan, Vaibhav 2 ; Aalten, Pauline 3 ; Ramakers, Inez H.G.B. 3 ; Linz, Nicklas 4 ; Tröger, Johannes 4 ; Robert, Philippe 5

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P158. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Currently, to enroll participants into pharmaceutical trials strenuous and costly procedures are applied to test whether participants meet inclusion criteria or not; this includes travel to clinics, costly brain imaging, invasive assessments, or costly f2f assessments with experts. Moreover, screening for such inclusion criteria in clinical trials has significant fail rates and significant resources have to be spent on participant screening to enroll only a fraction of them (10%). Standard cognitive assessment typically uses a set of speech-based cognitive tests which have the potential to be conducted remotely in telecommunication settings. However, only recently speech analysis and automatic speech recognition, as well as semantic speech processing have become mature enough to automate such speech-based testing procedures. The European DeepSpA project aims to replace in-person manual pre-screening procedures by remote (semi-)automated analyses methods detecting relevant phenotype for novel Alzheimer trials automatically. Methods: To evaluate the feasibility of the phone-based solution in a real-world scenario and examine the predictive potential for prognostic diagnosis, information extracted over the phone from the participant's speech

in cognitive and narrative **speech** tasks will be analyzed for its usefulness for remote pre-screening. 120 participants at preclinical stages of cognitive impairment will be recruited from the local memory clinic. At baseline, a complete dataset (including **speech** recordings) will be collected, consisting of clinical data and biobank materials, e.g. blood samples, MRI and cerebrospinal fluid. After 6 months the participants will be called for a brief remote follow up evaluation on the phone consisting of a short interview on subjective cognitive decline, a verbal memory task, and fluency tasks in which **speech** features will be collected through a semi-automatic phone-based interface. Final data sets will be compared to each other. Results: We expect to obtain comparable results between the telecommunication administration method and the traditional application. First preliminary results as well as a working demo version will be presented at the preconference. Conclusions: Built on existing **speech** technologies, we expect this first-of-its-kind service to allow to remotely conduct neurocognitive testing thus pre-screening of potential trial participants. This will significantly reduce the overall costs associated with the screening and speed up the trials' preparatory activities.

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**Subject:** Embase;adult;Alzheimer disease;automatic speech recognition;biobank;brain;cerebrospinal fluid;conference abstract +;controlled study;feasibility study;female;follow up;human;interview;major clinical study;male;narrative;nuclear magnetic resonance imaging;phenotype;preclinical study;preliminary data;speech analysis;speech test;telecommunication;travel;treatment failure;velocity;verbal memory test

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Document 243

## **Stress measurement using speech: Recent advancements, validation issues, and ethical and privacy considerations**

**Author:** Slavich, George M. 1 ; Taylor, Sara 2 ; Picard, Rosalind W. 2

1 Cousins Center for Psychoneuroimmunology and Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, CA, United States gslavich@mednet.ucla.edu 2 Affective Computing Group, MIT Media Lab, Massachusetts Institute of Technology, Cambridge, MA, United States

**Publication info:** Stress 22.4: 408-413. Taylor and Francis Ltd. (Jul 4, 2019)

**Abstract (summary):** Life stress is a well-established risk factor for a variety of mental and physical health problems, including anxiety disorders, depression, chronic pain, heart disease, asthma, autoimmune diseases, and neurodegenerative disorders. The purpose of this article is to describe emerging approaches for assessing stress using speech, which we do by reviewing the methodological advantages of these digital health tools, and the validation, ethical, and privacy issues raised by these technologies. As we describe, it is now possible to assess stress via the speech signal using smartphones and smart speakers that employ software programs and artificial intelligence to analyze several features of speech and speech acoustics, including pitch, jitter, energy, rate, and length and number of pauses. Because these digital devices are ubiquitous, we can now assess individuals' stress levels in real time in almost any natural environment in which people speak. These technologies thus have great potential for advancing digital health initiatives that involve continuously monitoring changes in psychosocial functioning and disease risk over time. However, speech-based indices of stress have yet to be well-validated against stress biomarkers (e.g., cortisol, cytokines) that predict disease risk. In addition, acquiring speech samples raises the possibility that conversations intended to be private could one day be made public; moreover, obtaining real-time psychosocial risk information prompts ethical questions regarding how these data should be used for medical, commercial, and personal purposes. Although assessing stress using speech thus has enormous potential, there are critical validation, privacy, and ethical issues that must be addressed.

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**Identifier (keyword):** digital health, ethics, Life stress, privacy, **speech**, **voice**

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## **VOCALIC MARKERS OF COGNITIVE LOAD DERIVED FROM AUTOMATED VERBAL NEUROPSYCHOLOGICAL ASSESSMENT AND MACHINE LEARNING IN A LARGE SCALE REMOTE SAMPLE**

**Author:** Taptiklis, Nick 1 ; Su, Merina 1 ; Barnett, Jennifer H. 2 ; Cormack, Francesca K. 1

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P162. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Detection of cognitive impairment may enable early detection of neurodegenerative disease. However high-functioning individuals may perform in the normal range despite significant pathology. Previous research has identified changes in **voice** features in AD and MCI, suggesting potential novel **biomarkers**. Here, we aim to detect cognitive effort in the context of a verbal cognitive task, using automated **voice** analysis and **machine learning**. Methods: 2,868 participants aged 17-86 years (M=34.5, SD=12.32) completed a web-based implementation of verbal digit-span backwards, scored using automated **speech** recognition. Participants' responses were analysed to assess performance and **vocal** qualities on a trial-by-trial basis. Analysis was limited to correct responses. Cognitive load was calculated for each response relative to the participant's overall performance in the task. For example a span of three would be labelled as 'high load' in a participant with a maximum span of 4, but 'low load' if the participant achieved a maximum span of 8. Acoustic features relating to spectral characteristics, pitch and energy were extracted using a 10 msec sliding window, and aggregated across each trial. Within-subject normalisation of **voice** features was carried out, encoding changes in **voice** related to task difficulty. Furthermore, participants were exclusively assigned to train, test or validation sets to prevent learning of participants-specific **voice** features. Five different models (logistic regression, naive bayes, **support vector machine**, random forest and gradient boost) were trained to predict the cognitive load score based on acoustic features. Once trained, models were validated on a dataset consisting of utterances of a single span (four) to ensure the model was not fitting to features related to span length. Results: Participants achieved an average backward span of 6.34 (SD=1.36). From the five prediction models tested, the gradient boost model and the random forest model achieved the best classification accuracies on the validation set (89% and 88% respectively). Conclusions: These results suggest that **vocalic** information could enrich automatically administered verbal cognitive tests with data relating to mental effort. Future work aims to extend these findings in patients with neurodegenerative disease, and examine the potential of these digital **biomarkers** in increasing sensitivity to the presence of pathology.

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**Subject:** Embase;biological marker;adolescent;adult;aged;automatic speech recognition (major);Bayesian learning;cognitive defect;conference abstract +;controlled study;degenerative disease;female;human;major clinical study;male;pitch;prediction;random forest;support vector machine;voice analysis

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Document 245

## **AUTOMATIC ASSESSMENT OF CONVENTIONAL COGNITIVE TESTS FOR DIFFERENTIATING MILD COGNITIVE IMPAIRMENT: A PROOF OF CONCEPT STUDY OF THE DIGIT SPAN TASK**

**Author:** Asgari, Meysam 1 ; Gale, Robert 1 ; Kaye, Jeffrey A. 1 ; Dodge, Hiroko H. 1

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P437. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Current conventional cognitive assessments are limited in their efficiency and sensitivity, often relying on a single score such as the total items correct. Typically, multiple features of response go uncaptured. The use of digital technologies allows for these response characteristics to be readily captured and automatically analyzed thus increasing the potential power of assessments. As a proof of this concept, we analyzed the Digit Span (DS) task where conventionally, total number of correctly recalled digits in both forward DS (FDS) and backward DS (BDS) tasks across test items constructs the test score. This scoring method pays equal attention to all presented items and ignores the count of incorrectly recalled digits. Additionally, the length of prompts adds to the complexity of test performance. Our objective in this study is to explore a new set of automatically derived **biomarkers** from DS test that address some of the drawbacks in the conventional scoring and are also useful for distinguishing subjects with MCI from those with intact cognition. Methods: Audio-recordings of DS tests administered to 85 subjects (22 MCI and 63 healthy controls, mean age 90.2 yrs) were transcribed using an automatic **speech** recognition (ASR) system. Next, five "count-based" **biomarkers** were generated from Levenshtein distance analysis of responses: number correct, incorrect, deleted, inserted, and substituted words compared to the target prompt. These per-item features were aggregated across all prompts for both FDS and BDS tasks using summary statistical functions, constructing a global feature vector representing the detailed assessment of each subject's response. A **support vector machine** classifier distinguished MCI from cognitively intact participants. Results: Conventional total DS scores did not differentiate MCI participants from controls. The automated multi-feature DS-derived metric achieved 73% on AUC-ROC of the **SVM** classifier, independent of additional clinical features (78% when combined with demographic features of subjects); well above chance, 50%. Conclusions: ASR analysis of conventional cognitive tests such as the DS expanded by additional automated feature assessment can increase the sensitivity of detection of MCI.

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**Conference country:** United States

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**Subject:** Embase;biological marker;aged;attention;audio recording;automatic speech recognition;clinical feature;conference abstract +;controlled study;demography;female;genetic transcription;human;human experiment;major clinical study;male;proof of concept (major);receiver operating characteristic;support vector machine;task performance;very elderly

**Updates:** 2019-10-21

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Document 246

## **STORY TIME: COMPUTATIONAL ANALYSIS OF RAW-SPEECH TO AID THE DETECTION OF PRECLINICAL ALZHEIMER'S DISEASE**

**Author:** Atreya, Alankar 1 ; Lancaster, Claire L. 1 ; Koychev, Ivan G. 1 ; Chinner, Amy 1 ; Blane, Jasmine 1 ; Chatham, Chris 2 ; Taylor, Kirsten I. 3 ; Hinds, Chris 1

1 University of Oxford, Oxford, United Kingdom [claire.lancaster@bdi.ox.ac.uk](mailto:claire.lancaster@bdi.ox.ac.uk) 2 Roche Pharmaceuticals, Basel, Switzerland 3 Roche Pharmaceuticals, Basel, Switzerland, University of Basel, Basel, Switzerland

**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P1556. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Mild Alzheimer's disease is characterised by subtle language impairment; processing of rich, naturalistic speech may further facilitate early detection of preclinical pathology. Story Time, deployed within the Mezurio smartphone app, records spontaneous speech in a narration and long-term memory task. Here, raw speech data from a longitudinal sub-cohort of 'PREVENT' was analysed using an in-depth selection of computational techniques. Methods: 25 healthy adults (aged 40-59 years), self-selected to be at elevated familial risk of dementia, completed daily Story Time tasks for a week, with ongoing data collection at 6- and 12-months. They were asked to narrate a short, daily comic strip aloud from pictorial cues and retell the story from memory immediately and 24-hours later. Digital outcomes are validated against 'gold-standard'

neuropsychological assessment. Results: Automated computational methods extracted acoustic (e.g. fundamental frequency, harmonics to noise ratio), prosodic (pauses, articulation rate) and linguistic **speech** features, alongside story similarity scores at memory test. Initial outcomes from Story Time free-recall tasks correlated as expected with delayed narrative and description recall scores from the COGNITO computerised battery. Conclusions: The combination of **machine-learning** and linguistic analysis techniques used here provides a feasible, automated approach for the analysis of spontaneous **speech**, with the incorporation of measurement within a remote, digital tool promoting scalable preclinical assessment. Preliminary support for the construct validity of Story Time behavioural outcomes justifies ongoing validation of **speech** markers against traditional Alzheimer's disease **biomarkers**.

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**Author e-mail address:** claire.lancaster@bdi.ox.ac.uk

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**Subject:** Embase;**biological marker**;adult;Alzheimer disease (major);clinical article;cohort analysis;conference abstract +;construct validity;controlled study;female;gold

standard;human;language disability;machine learning;male;memory;memory  
test;narrative;noise;preclinical study (major);speech (major)

**Updates:** 2019-10-18

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Document 247

## **WORK IN PROGRESS: AN INDUSTRY-CLINICAL-ACADEMIC PARTNERSHIP FOR DIGITAL AND PERSISTENT ASSESSMENT OF MOTOR AND COGNITIVE-LINGUISTIC OUTCOMES**

**Author:** Berisha, Visar 1 ; Liss, Julie 1 ; Jones, Daniel 2 ; Hahn, Shira 2 ; Rutkove, Seward 3 ; Shelton, Kerisa 4 ; Au, Rhoda 5 ; Shefner, Jeremy 4

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P165. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Remote and digital assessment of neurological health has the potential for earlier detection of decline and more sensitive tracking of neurological health. The implications of this are considerable. More sensitive outcome measures can lead to digital tools for early diagnosis or can help to power clinical trials with fewer samples. Speech is an important modality in this context because it is easy to collect and taxes both the cognitive and motor systems. Aural Analytics (A2) has a platform for monitoring motor and cognitive-linguistic outcomes both at-home and in-clinic using automated speech analytics. In this work we describe the important role that speech analysis plays as a part of a more complete brain monitoring platform and highlight a use-case from large-scale home-monitoring studies. Methods: Participants download the application on their Android or iOS devices and are guided through a set of speech-elicitation tasks. A suite of back-end algorithms extracts outcome measures from the collected speech samples to generate a battery of clinically-interpretable outcome measures related to motor control, cognition, and mood/affect. Constellations of these features are relevant as outcome measures for different neurological diseases. The technology has been validated in different contexts in collaboration with clinical and academic partners. This work focuses on ongoing studies in collaboration with Barrow Neurological Institute. Amyotrophic lateral sclerosis (ALS) patients with and without frontotemporal dementia download the application on their personal device and provide periodic speech samples. In addition, they are also evaluated using clinically-standard motor and cognition rating scales. We use generalized linear models (GLMs) to evaluate the relationship between the digital battery and the clinically-standard outcome measures. Results: Preliminary analysis using a GLM reveals that the digital battery outcomes are strongly predictive of the ALS-functional rating scale. In addition, post-hoc analysis reveals that changes in the digital battery precede clinically-detectable changes.

Conclusions: The results highlight the potential of **speech** analytics as a robust means of tracking motor and cognitive health. Current on-going studies include preclinical Alzheimer's disease centered on identifying cognitive **voice biomarkers**.

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**Author e-mail address:** visar@asu.edu

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**Subject:** Embase;**biological marker**;adult;Alzheimer disease;amyotrophic lateral sclerosis;clinical evaluation;conference abstract +;controlled study;frontotemporal dementia;home monitoring;human;mood;motor control;motor system;neuromonitoring;post hoc analysis;preclinical study;rating scale;**speech analysis**;tax;**voice**

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Document 248

## COMPARISON OF A SPEECH-BASED DIGITAL BIOMARKER WITH THE MOCA IN A NATURALISTIC COHORT OF SENIORS

**Author:** Simpson, William 1 ; Kaufman, Liam 2 ; Balagopalna, Aparna 2 ; Novikova, Jekaterina 2

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P1523. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Computerized analysis of speech can be used to measure cognitive impairment and detect the presence of psychiatric and neurological disorders(1). For example, changes in speech rate, sentence length, word frequency, pronoun usage, repetitions, word finding difficulties, and number of ideas expressed are highly characteristic of Alzheimer's disease (AD)(2). The aim of this study was to compare markers extracted from computational analysis of speech against MoCA scores in a naturalistic cohort of seniors. Methods: Participants were 111 seniors recruited from the community and independent living facilities in Canada and the US. Participants completed a tablet-based speech assessment, which included a picture description task. Verbal responses were recorded, transcribed and analyzed to produce more than 500 individual speech and language markers. From these markers, 7 aggregate scores, chosen for their previous association to AD(2), were produced describing: discourse, information units, word finding difficulty, syntax, coherence (global and local), and sentiment. Results: Spearman correlations between total MoCA scores and individual aggregate measures ranged from poor (sentiment, rho=0.09) to strong (information units, rho=0.53). Information units (0.53) and word finding difficulty (-0.48) showed the highest absolute degree of correlation. A linear regression model including each aggregate measure as a term explained 35.7% of the variance and identified information units and word finding difficulty as significant predictors of MoCA score. A simplified model using only those 2 significant aggregates explained 34.5% of the variance in MoCA. Conclusions: These preliminary results support previous work, indicating that markers derived from computational analysis of speech correlate with established measures of cognitive status. These results support the use and further development of speech-based biomarkers of cognition for use as screening and tracking tools in this population. References: [1] Fraser C, Meltzer A, and Rudzicz F. Linguistic Features Identify Alzheimer's Disease in Narrative Speech. Journal of Alzheimer's Disease: JAD 49 (2): 407–22, 2016. [2] Slegers A, Filiou RP, Montembeault M, et al. Connected Speech Features from Picture Description in Alzheimer's Disease: A Systematic Review. Journal of Alzheimer's Disease: JAD 65 (2): 519–42, 2018.

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**Author e-mail address:** bill@winterlightlabs.com

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**Subject:** Embase;biological marker (major);adult;Alzheimer disease;Canada;conference abstract +;controlled study;female;genetic transcription;human;independent living;language;linear regression analysis;male;Montreal cognitive assessment;narrative;preliminary data;speech (major);systematic review;tablet

**Updates:** 2019-10-21

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Document 249

## **UTILITY OF SPEECH-BASED DIGITAL BIOMARKERS FOR EVALUATING DISEASE PROGRESSION IN CLINICAL TRIALS OF ALZHEIMER'S DISEASE**

**Author:** Simpson, William 1 ; Kaufman, Liam 2 ; Detke, Mike 3 ; Lynch, Casey 3 ; Butler, Adam 2 ; Dominy, Steve 3

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 15.7: P1524. Elsevier Inc. (Jul 2019)

**Abstract (summary):** Background: Recent clinical trials in Alzheimer's disease have been overwhelmingly negative, spurring development of novel **biomarkers** which might capture changes in cognitive function with greater precision. Computational analysis of **speech** and language represent one such group of **biomarkers**(1,2). The objective of this study was to examine the utility of a **speech-based digital biomarker** for tracking disease progression and treatment response to investigational treatment COR388 in a group of patients with Alzheimer's disease. Methods: The study was a small, double-blind placebo-controlled Phase 1b trial (NCT03418688) of COR388 with a cohort of nine (9) individuals with Alzheimer's disease. Participants were randomized to receive COR388 or placebo in a 2:1 fashion, BID for 28 days. A tablet-based **speech** and language assessment was administered at Days 1, 15 and 28. Participants were asked to complete 2 picture description tasks and verbal responses were analyzed. Five aggregate markers, chosen for their previous association to AD(1,2), were computed: discourse, syntactic complexity, lexical complexity, information units and word finding difficulty (WFD). Results: Previous analysis of single outcomes showed significant improvement in the quality of picture descriptions for COR388 patients relative to placebo (increase in unique object content units,  $p=0.016$  and prepositions,  $p=0.0011$ ). Positive trends, but no significant differences in MMSE scores were observed(3). For aggregate markers, mean baseline to endpoint comparisons showed statistically significant ( $p<0.05$ ) improvements in syntactic complexity, lexical complexity and information units in those treated with COR388. No significant within-subject differences were observed for placebo. Baseline to endpoint COR388 information unit differences remained significant post Bonferroni correction ( $p=0.002$ ). Between-group analysis of information unit change scores (Day 28 vs. Day 1) revealed a 10-point increase for COR388 vs. a 5-point change for placebo but this numerical difference was not significant ( $p=0.21$ ). Conclusions: In this preliminary trial, patients treated with COR388 showed signs of significant improvement relative to placebo as measured by a **speech-based, digital biomarker**. No significant changes in MMSE were observed suggesting that **digital biomarkers** may represent sensitive tools for tracking changes in cognition in small trials. The study also highlights the potential therapeutic benefit of COR388, though additional studies of sufficient power are needed.

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**Author e-mail address:** bill@winterlightlabs.com

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**Subject:** Embase;biological marker (major);placebo;adult;Alzheimer disease (major);clinical evaluation (major);cohort analysis;conference abstract +;controlled study;disease course (major);double blind procedure;experimental therapy;female;human;major clinical study;male;Mini Mental State Examination;phase 1 clinical trial;randomized controlled trial;speech and language assessment (major);tablet;treatment response

**Updates:** 2019-10-21

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Document 250

## **Automated tongue-twister phrase-based screening for Cerebellar Ataxia using Vocal tract Biomarkers**

**Author:** Kashyap, Bipasha; Pathirana, Pubudu N.; Horne, Malcolm; Power, Laura; Szmulewicz, David

**Publication info:** Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual International Conference 2019 : 7173-7176. NLM (Medline). (Jul 1, 2019)

**Abstract (summary):** Cerebellar Ataxia (CA) is a neurological condition that leads to uncoordinated muscle movements, even affecting the production of speech. Effective biomarkers are necessary to produce an objective decision-making support tool for early diagnosis of CA in non-clinical environments. This paper investigates the reliability and effectiveness of vocal tract acoustic biomarkers for assessing CA speech. These features were tested on a database consisting of 52 clinically rated tongue-twister phrase 'British Constitution' and its 4 consonant-vowel (CV) excerpts /ti/, /ti/, /tu/, /tion/ acquired from 30 ataxic patients and 22 healthy controls. Such a marker could be applied to objectively assess the severity of CA from a simple speaking test, contributing to the possibility of being translated into a computer based automatic module to screen the disease from the speech. All the vocal tract features explored in this study were statistically significant using

Kolmogorov-Smirnov test at 5% level in distinguishing healthy and CA **speech**. Several **machine learning** classifiers with 5-fold cross-validations were implemented on the **vocal** features. It was observed that the intensity ratios corresponding to the 4 C-V excerpts in CA group showed an increased variability and produced the best classification accuracy of 84.6% using KNN classifier. Results motivate the use of **vocal** tract features for monitoring CA **speech**.

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**Subject:** MEDLINE;**biological marker**;cerebellar ataxia -- diagnosis;human;reproducibility;**speech** (major);**speech analysis** (major);**voice**

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Document 251

### **Speech-based markers for posttraumatic stress disorder in US veterans**

**Author:** Marmar, Charles R. 1 ; Brown, Adam D. 2 ; Qian, Meng 1 ; Laska, Eugene 1 ; Siegel, Carole 1 ; Li, Meng 1 ; Abu-Amara, Duna 1 ; Tsiartas, Andreas 3 ; Richey, Colleen 3 ; Smith, Jennifer 3 ; Knoth, Bruce 3 ; Vergyri, Dimitra 3

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**Publication info:** Depression and Anxiety 36.7: 607-616. Blackwell Publishing Inc. (Jul 2019)

**Abstract (summary):** Background: The diagnosis of posttraumatic stress disorder (PTSD) is usually based on clinical interviews or self-report measures. Both approaches are subject to under- and over-reporting of symptoms. An objective test is lacking. We have developed a classifier of PTSD based on objective **speech**-marker features that discriminate PTSD cases from controls. Methods: **Speech** samples were obtained from warzone-exposed veterans, 52 cases with PTSD and 77 controls, assessed with the Clinician-Administered PTSD Scale. Individuals with major depressive disorder (MDD) were excluded. Audio recordings of clinical interviews were used to obtain 40,526 **speech** features which were input to a random forest (RF) algorithm. Results: The selected RF used 18 **speech** features and the receiver operating characteristic curve had an area under the curve (AUC) of 0.954. At a probability of PTSD cut point of 0.423, Youden's index was 0.787, and overall correct classification rate was 89.1%. The probability of PTSD was higher for markers that indicated slower, more monotonous **speech**, less change in tonality, and less activation. Depression symptoms, alcohol use disorder, and TBI did not meet statistical tests to be considered confounders. Conclusions: This study demonstrates that a **speech**-based algorithm can objectively differentiate PTSD cases from controls. The RF classifier had a high AUC. Further validation in an independent sample and appraisal of the classifier to identify those with MDD only compared with those with PTSD comorbid with MDD is required.

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**Author e-mail address:** Charles.Marmar@nyulangone.org

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**Correspondence author:** Marmar, Charles R. Department of Psychiatry, New York University School of Medicine, New York, NY, United States.

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**Grant:** TATRC. Telemedicine and Advanced Technology Research Center.

This study was supported by the US Army Medical Research & Acquisition Activity (USAMRAA), the Telemedicine and Advanced Technology Research Center (TATRC), W81XWH-11-C-0004, and grants from the Steven A. and Alexandra M. Cohen Foundation, Inc. and Cohen Veterans Bioscience Inc. (CVB) to NYU Langone School of Medicine.

**Identifier (keyword):** biomarkers, diagnostics, feature extraction, military, posttraumatic stress disorder, speech-based assessment, veterans

**Language:** English

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**Subject:** Embase;MEDLINE;biological marker (major);adult;age distribution;alcoholism;anxiety assessment (major);Article;audio recording;classifier;clinical feature;Clinician Administered PTSD Scale +;controlled study;depression;differential diagnosis;disease classification;disease marker;female;human;interview;major clinical study;male;mental disease assessment;posttraumatic stress disorder -- diagnosis (major);priority journal;probability;random forest;receiver operating characteristic;sampling;sex difference;speech (major);speech rate;traumatic brain injury;United States;veteran (major);war;Youden index

**Updates:** 2019-07-102019-07-152019-07-242019-11-12

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Document 252

## Using Speech Markers to Diagnose PTSD

**Author:** Abbasi, Jennifer

**Publication info:** JAMA 321.22: 2155. NLM (Medline). (Jun 11, 2019)

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**Subject:** MEDLINE;biological marker;automatic speech recognition (major);human;posttraumatic stress disorder -- diagnosis;speech (major)

**Updates:** 2019-07-012019-07-23

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Document 253

## **Using Acoustic and Linguistic Markers From Spontaneous Speech to Predict Scores on the Montreal Cognitive Assessment (MoCA)**

**Author:** Balagopalan, Aparna 1 ; Yancheva, Maria 2 ; Novikova, Jekaterina 2 ; Simpson, William 3

1 Winterlight Labs, University of Toronto 2 Winterlight Labs 3 McMaster University

**Publication info:** Biological Psychiatry, suppl. Supplement 85.10: S313. Elsevier USA. (May 15, 2019)

**Abstract (summary):** Background: Recent clinical trials in Alzheimer's disease have been overwhelmingly negative. This has spurred development of composite metrics and novel biomarkers with the intent of more accurately capturing changes in cognitive function. Computational analysis of speech and language represents one such group of biomarkers. The objective of this study was to examine the construct validity of speech and language markers by using them to predict scores on the MoCA. Methods: 94 individuals, aged 55-95, were recruited from the community and senior care facilities. A picture description task and a MoCA were administered by a trained psychometrist. Audio samples and transcripts were analyzed to generate markers pertaining to acoustics, syntax and grammar (among others). Feature selection and linear regression with 10-fold cross validation were used to generate an estimated MoCA score (total and subscales). Results: Numerous speech and

language markers relating to complexity, coherence and level of detail reported in picture descriptions were significantly correlated with MoCA scores. Feature selection identified 55 variables which were most predictive of total MoCA score. Regression produced a MoCA estimate with a mean error of 3.4 points (11% of total score) which explained 18.4% ( $R^2$ ) of the variance. Regression to MoCA subscales produced estimates with 6.5% (Orientation) to 34.7% (Delayed Recall) error. Conclusions: The low error in total score prediction suggests that **speech** and language variables map to the constructs measured by the MoCA. This supports the further development of novel, **speech** based markers, and composite metrics for assessing cognitive status. Keywords: Computational Neuroscience, **Machine Learning**, Cognition, MOCA, Psychometrics

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**Conference end date:** 2019-05-18

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**Subject:** Embase;adult;aged;Alzheimer disease;conference abstract +;construct validity;controlled study;**feature selection**;female;genetic transcription;grammar;human;human experiment;language;linear regression analysis;**machine learning**;major clinical study;male;middle aged;Montreal cognitive assessment (major);neuroscience;prediction;psychometry;recall;**speech** (major)

**Updates:** 2019-10-04

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Document 254

## **Depression Screening from Voice Samples of Patients Affected by Parkinson's Disease**

**Author:** Ozkanca, Yasin 1 ; Göksu Öztürk, Miraç 2 ; Ekmekci, Merve Nur 1 ; Atkins, David C. 3 ; Demiroglu, Cenk 1 ; Hosseini Ghomi, Reza 4

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**Publication info:** Digital Biomarkers 3.2: 72-82. S. Karger AG. (May 1, 2019)

**Abstract (summary):** Depression is a common mental health problem leading to significant disability worldwide. It is not only common but also commonly co-occurs with other mental and neurological illnesses. Parkinson's disease (PD) gives rise to symptoms directly impairing a person's ability to function. Early diagnosis and detection of depression can aid in treatment, but diagnosis typically requires an interview with a health provider or a structured diagnostic questionnaire. Thus, unobtrusive measures to monitor depression symptoms in daily life could have great utility in screening depression for clinical treatment. **Vocal biomarkers** of depression are a potentially effective method of assessing depression symptoms in daily life, which is the focus of the current research. We have a database of 921 unique PD patients and their self-assessment of whether they felt depressed or not. **Voice** recordings from these patients were used to extract paralinguistic features, which served as inputs to **machine learning** and **deep learning** techniques to predict depression. The results are presented here, and the limitations are discussed given the nature of the recordings which lack language content. Our models achieved accuracies as high as 0.77 in classifying depressed and nondepressed subjects accurately using their **voice** features and PD severity. We found depression and severity of PD had a correlation coefficient of 0.3936, providing a valuable feature when predicting depression from **voice**. Our results indicate a clear correlation between feeling depressed and PD severity. **Voice** may be an effective digital **biomarker** to screen for depression among PD patients.

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**Author e-mail address:** rezahg@uw.edu

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**Document type:** Article

**DOI:** <http://dx.doi.org/10.1159/000500354>

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**Identifier (keyword):** Audio features, Deepneural networks, Depression screening, Feature selection, Parkinson?s disease, Voicebiomarkers, Voice technology

**Language:** English

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**Number of references:** 32

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**Subject:** Embase;biological marker (major);aged;Article;deep learning;deep neural network;depression -- diagnosis (major);diagnostic accuracy;diagnostic test accuracy study;disease severity;early diagnosis;feature extraction;feature selection;feature selection algorithm;female;human;major clinical study;male;mental disease assessment (major);paralanguage;Parkinson disease (major);priority journal;random forest;recording;self evaluation;support vector machine;Unified Parkinson Disease Rating Scale;voice analysis (major)

**Updates:** 2019-06-252019-09-122019-09-172021-09-30

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Document 255

## **Multi-Source Ensemble Learning for the Remote Prediction of Parkinson's Disease in the Presence of Source-Wise Missing Data**

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**Publication info:** IEEE Transactions on Biomedical Engineering 66.5: 1402-1411. IEEE Computer Society. (May 2019)



**Abstract (summary):** As the collection of mobile health data becomes pervasive, missing data can make large portions of datasets inaccessible for analysis. Missing data has shown particularly problematic for remotely diagnosing and monitoring Parkinson's disease (PD) using smartphones. This contribution presents multi-source ensemble learning, a methodology which combines dataset deconstruction with ensemble learning and enables participants with incomplete data (i.e., where not all sensor data is available) to be included in the training of **machine learning** models and achieves a 100% participant retention rate. We demonstrate the proposed method on a cohort of 1513 participants, 91.2% of which contributed incomplete data in tapping, gait, **voice**, and/or memory tests. The use of multi-source ensemble learning, alongside **convolutional neural networks (CNNs)** capitalizing on the amount of available data, increases PD classification accuracy from 73.1% to 82.0% as compared to traditional techniques. The increase in accuracy is found to be partly caused by the use of multi-channel **CNNs** and partly caused by developing models using the large cohort of participants. Furthermore, through bootstrap sampling we reveal that feature selection is better performed on a large cohort of participants with incomplete data than on a small number of participants with complete data. The proposed method is applicable to a wide range of wearable/remote monitoring datasets that suffer from missing data and contributes to improving the ability to remotely monitor PD via revealing novel methods of accounting for symptom heterogeneity.

**Accession number:** 624801428

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**Correspondence author:** Prince, John Department of Engineering Sciences, Institute of Biomedical Engineering, University of Oxford, Oxford, United Kingdom.

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**Device trade name:** Device trade name Name: iPhone; Manufacturer: Apple; Country: United States;

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RCUK Digital Economy Programme under Grant EP/G036861/1 (Oxford Centre for Doctoral Training in Healthcare Innovation).

**Identifier (keyword):** bootstrap statistics, convolutional neural networks, ensemble learning, feature selection, Missing data, mobile-Health, Parkinson's disease, multi-source learning

**Language:** English

**Language of abstract:** English

**Number of references:** 40

**Publication date:** May 2019

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**Publisher:** IEEE Computer Society

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**Subject:** Embase;MEDLINE;biological marker (major);iPhone +;smartphone;Article;classifier;cohort analysis;controlled study;convolutional neural network +;diagnostic accuracy;diagnostic test accuracy study;gait;human;machine learning (major);major clinical study;memory test;multi source ensemble learning + (major);Parkinson disease -- diagnosis (major);prediction;remote sensing (major);voice

**Updates:** 2018-11-132018-11-232019-05-072019-05-132019-05-15

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Document 256

## **A Single-channel EEG-based approach to detect mild cognitive impairment via speech-evoked brain responses**

**Author:** Khatun, Saleha 1 ; Morshed, Bashir I. 1 ; Bidelman, Gavin M. 2

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**Publication info:** IEEE Transactions on Neural Systems and Rehabilitation Engineering 27.5: 1063-1070. Institute of Electrical and Electronics Engineers Inc. (May 2019)

**Abstract (summary):** Mild cognitive impairment (MCI) is the preliminary stage of dementia, which may lead to Alzheimer's disease (AD) in the elderly people. Therefore, early detection of MCI has the potential to minimize the risk of AD by ensuring the proper mental health care before it is too late. In this paper, we demonstrate a single-channel EEG-based MCI detection method, which is cost-

effective and portable, and thus suitable for regular home-based patient monitoring. We collected the scalp EEG data from 23 subjects, while they were stimulated with five auditory **speech** signals. The cognitive state of the subjects was evaluated by the Montreal cognitive assessment test (MoCA). We extracted 590 features from the event-related potential (ERP) of the collected EEG signals, which included time and spectral domain characteristics of the response. The top 25 features, ranked by the random forest method, were used for classification models to identify subjects with MCI. Robustness of our model was tested using leave-one-out cross-validation while training the classifiers. Best results (leave-one-out cross-validation accuracy 87.9%, sensitivity 84.8%, specificity 95%, and F score 85%) were obtained using **support vector machine (SVM)** method with radial basis kernel (RBF) ( $\sigma = 10/\text{cost} = 10^2$ ). Similar performances were also observed with logistic regression (LR), further validating the results. Our results suggest that single-channel EEG could provide a robust **biomarker** for early detection of MCI.

**Accession number:** 627606888

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**Copyright:** Copyright 2019 Elsevier B.V., All rights reserved.

**Correspondence author:** Khatun, Saleha Department of Electrical and Computer Engineering (EECE), University of Memphis, Memphis, TN, 38152, United States.

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**First available:** 2019-05-20

**Identifier (keyword):** Electroencephalography, event-related potential, mild cognitive impairment, **speech**-evoked brain responses

**Language:** English

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**Number of references:** 50

**Publication date:** May 2019

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**Publisher:** Institute of Electrical and Electronics Engineers Inc.

**Publisher location:** United States

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**Subject:** Embase;MEDLINE;biological marker;accuracy;adult;aged;algorithm;Alzheimer disease;Article;auditory stimulation;auditory system;clinical article;cognition;cognitive aging;controlled study;dementia;electroencephalogram;electroencephalography (major);event related potential;evoked cortical response (major);female;human;male;mental health;middle aged;mild cognitive impairment -- diagnosis (major);Montreal cognitive assessment;patient monitoring;random forest;sensitivity and specificity;skin conductance;speech (major);support vector machine;time factor;very elderly

**Updates:** 2019-05-202019-05-222019-05-24

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Document 257

## **Protocol for a conversation-based analysis study: PREVENT-ED investigates dialogue features that may help predict dementia onset in later life**

**Author:** de la Fuente Garcia, Sofia 1 ; Ritchie, Craig W 2 ; Luz, Saturnino 1

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**Publication info:** BMJ open 9.3: e026254. (Mar 27, 2019)

### **Abstract (summary): INTRODUCTION**

Decreasing the incidence of Alzheimer's disease (AD) is a global public health priority. Early detection of AD is an important requisite for the implementation of prevention strategies towards this goal. While it is plausible that patients at the early stages of AD may exhibit subtle behavioural signs of neurodegeneration, neuropsychological testing seems unable to detect these signs in preclinical AD. Recent studies indicate that spontaneous speech data, which can be collected frequently and naturally, provide good predictors for AD detection in cohorts with a clinical diagnosis. The potential of models based on such data for detecting preclinical AD remains unknown.

### **METHODS AND ANALYSIS**

The PREVENT-Elicitation of Dialogues (PREVENT-ED) study builds on the PREVENT Dementia project to investigate whether early behavioural signs of AD may be detected through dialogue interaction. Participants recruited through PREVENT, aged 40-59 at baseline, will be included in this study. We will use speech processing and machine learning methods to assess how well speech and visuospatial markers agree with neuropsychological, biomarker, clinical, lifestyle and genetic data from the PREVENT cohort.

## ETHICS AND DISSEMINATION

There are no expected risks or burdens to participants. The procedures are not invasive and do not raise significant ethical issues. We only approach healthy consenting adults and all participants will be informed that this is an exploratory study and therefore has no diagnostic aim. Confidentiality aspects such as data encryption and storage comply with the General Data Protection Regulation and with the requirements from sponsoring bodies and ethical committees. This study has been granted ethical approval by the London-Surrey Research Ethics Committee (REC reference No: 18/LO/0860), and by Caldicott and Information Governance (reference No: CRD18048). PREVENT-ED results will be published in peer-reviewed journals.

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**Correspondence author:** de la Fuente Garcia, Sofia Usher Institute of Population Health Sciences and Informatics, University of Edinburgh School of Molecular Genetic and Population Health Sciences, Edinburgh, UK.

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MR/N013166/1. Medical Research Council. United Kingdom.

**Identifier (keyword):** computational paralinguistics, dialogue analysis, psycholinguistics, **speech** processing, dementia prevention, dialogue analysis, early detection of Alzheimer's disease, screening

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Adult;Cognitive Dysfunction -- diagnosis;Dementia -- diagnosis (major);Dementia -- psychology;Early Diagnosis;Female;Humans;Language Disorders -- diagnosis (major);**Machine Learning**;Male;Middle Aged;Neuropsychological Tests -- standards (major);**Speech** (major)

**Notes:** Competing interests: None declared.;; Publication model: Electronic;; Cited medium:Internet

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**Publisher location:** ENGLAND

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Document 258

### **Tracking ALS progression in clinical trials with a mobile app measuring speech**

**Author:** Hahn, Shira 1 ; Stegmann, Gabriela 1 ; Berisha, Visar 2 ; Liss, Julie M. 2 ; Cockroft, Bettina M. 3 ; Malik, Fady I. 3 ; Meng, Lisa 3 ; Rudnicki, Stacy 3 ; Wolff, Andrew A. 3 ; Shefner, Jeremy 4

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**Publication info:** Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, suppl. Supplement 1 20 : 267. Taylor and Francis Ltd. (2019)

**Abstract (summary):** Background: Current clinical trials for ALS have several limitations: First, the number of clinic visits needed to track disease progression may restrict participation and contribute to early attrition. Second, clinical ratings for ALS (ALSFRS-R, a 5-point Likert scale) lack sensitivity to small changes in function. Third, clinicians cannot track a participant's ALS progression in their home setting. Tracking neurological health with a biomarker easily measured at home could help address these limitations. We utilized an app-enabled digital biomarker to measure and track patients' speech, both in clinic and at home, in FORTITUDE-ALS. The recordings may provide a sensitive measure of the dysarthria caused by involvement of bulbar musculature in ALS. Objectives: Aural Analytics developed a mobile app allowing participants to record speech samples. This speech app can provide value to clinical trials by increasing the frequency of data collection in a minimally invasive way. Our goal is to determine whether the speech app is a viable and valid way of tracking ALS progression in participants. Methods: In FORTITUDE-ALS, participants were randomized to receive placebo, 150 mg, 300 mg, or 450 mg bid riluzole. The mobile app was used to record speech samples designed to assess function of the physiological subsystems used in speech production at screening, baseline (Day 1), Weeks 2, 4, 8, 12, and follow-up visits. In addition, recordings were performed weekly at home. Recordings take 3-5 minutes to complete and upload to the cloud for subsequent analysis. Speech is deconstructed into components that are linked to the function of each physiological subsystem. These components are generated for each recording session and can be used to track participants' change in speaking ability over time. For patients who had a complete set

of components in clinic visits, composite scores for **voice** attributes were explored. Percent change from baseline of the composites were analyzed using a pre-specified Mixed Model Repeated Measures method. Results: The treatment of reldesemtiv had a trend to slow the decline (p-value) in the **vocal** control composite by -38.7% (0.097), -37.2% (0.11), -28.5% (0.22) for 150 mg, 300 mg, and 450 mg bid relative to placebo, respectively. Discussion and conclusions: The **speech** app may have detected a trend of a treatment effect early in a 12-week course of study. Missing data due to recording quality and disease progression indicated that validation of the **voice** components by comparing home measures and cross-validation using other outcome measures such ALSFRS-R scores are warranted. The **speech** app helps track participants' progress and facilitates more frequent assessment than would be possible at clinic visits, resulting in more precise estimates of rates of change.

**Accession number:** 631518014

**Author e-mail address:** shira.hahn@auralanalytics.com

**Conference country:** Australia

**Conference end date:** 2019-12-06

**Conference location:** Perth, WA

**Conference start date:** 2019-12-04

**Conference title:** 30th International Symposium on ALS/MND

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**Correspondence author:** Hahn, Shira Aural Analytics, Scottsdale, AZ, United States.

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**DOI:** <http://dx.doi.org/10.1080/21678421.2019.1646997>

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**Identifier (keyword):** ALSFRS-R, Disease progression

**Language:** English

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**Publication date:** 2019

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**Publisher:** Taylor and Francis Ltd

**Publisher location:** Netherlands

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**Subject:** Embase;biological marker;placebo;reldesemtiv;adult;clinical trial;conference abstract;controlled study;cross validation;drug therapy;dysarthria (major);female;follow up;human;male;mobile application (major);nervous system;outcome assessment;randomized controlled trial;speech analysis;voice

**Substance:** Substance Substance: reldesemtiv; CAS: 1345410-31-2;

**Updates:** 2020-04-22

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Document 259

### Validated automatic speech biomarkers in primary progressive aphasia

**Author:** Nevler, Naomi 1 ; Ash, Sharon 1 ; Irwin, David J 1 ; Liberman, Mark 2 ; Grossman, Murray 1

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**Publication info:** Annals of Clinical and Translational Neurology 6.1: 4-14. Wiley-Blackwell. (Jan 2019)

**Abstract (summary):** Objective: To automatically extract and quantify specific disease biomarkers of prosody from the acoustic properties of speech in patients with primary progressive aphasia. Methods: We analyzed speech samples from 59 progressive aphasic patients (non-fluent/agrammatic = 15, semantic = 21, logopenic = 23; ages 50–85 years) and 31 matched healthy controls (ages 54–89 years). Using a novel, automated speech analysis protocol, we extracted acoustic measurements of prosody, including fundamental frequency and speech and silent pause durations, and compared these between groups. We then examined their relationships with clinical tests, gray matter atrophy, and cerebrospinal fluid analytes. Results: We found a narrowed range of fundamental frequency in patients with non-fluent/agrammatic variant aphasia (mean  $3.86 \pm 1.15$  semitones) compared with healthy controls ( $6.06 \pm 1.95$  semitones;  $P < 0.001$ ) and patients with semantic variant aphasia ( $6.12 \pm 1.77$  semitones;  $P = 0.001$ ). Mean pause rate was significantly increased in the non-fluent/agrammatic group (mean  $61.4 \pm 20.8$  pauses per minute) and the logopenic group ( $58.7 \pm 16.4$  pauses per minute) compared to controls. In an exploratory analysis, narrowed fundamental frequency range was associated with atrophy in the left inferior frontal cortex. Cerebrospinal level of phosphorylated tau was associated with an acoustic classifier combining fundamental frequency range and pause rate ( $r = 0.58$ ,  $P = 0.007$ ). Receiver operating characteristic analysis with this combined classifier distinguished non-fluent/agrammatic speakers from healthy controls (AUC = 0.94) and from semantic variant patients (AUC = 0.86). Interpretation: Restricted



fundamental frequency range and increased pause rate are characteristic markers of **speech** in non-fluent/agrammatic primary progressive aphasia. These can be extracted with automated **speech** analysis and are associated with left inferior frontal atrophy and cerebrospinal phosphorylated tau level.

**Accession number:** 625141992

**Author e-mail address:** naomine@penntmedicine.upenn.edu, mgrossma@penntmedicine.upenn.edu

**Copyright:** Copyright 2019 Elsevier B.V., All rights reserved.

**Correspondence author:** Nevler, Naomi Penn Frontotemporal Degeneration Center, Department of Neurology, University of Pennsylvania, Philadelphia, PA, United States.

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Institute of Aging.

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**Publication date:** Jan 2019

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**Publisher:** Wiley-Blackwell

**Publisher location:** United States

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**Subject:** Embase;amyloid beta protein -- endogenous compound;biological marker -- endogenous compound;tau protein -- endogenous compound;adult;aged;Article;atrophy;automatic speech recognition (major);cerebrospinal fluid;clinical feature;disease duration;dysarthria;female;gray matter;human;imaging;male;nuclear magnetic resonance imaging;pathology;phenotype;primary progressive aphasia (major);protein phosphorylation;receiver operating characteristic;speech analysis;speech disorder;validation process (major);very elderly

**Substance:** Substance Substance: amyloid beta protein; CAS: 109770-29-8;

**Updates:** 2018-11-292019-01-242019-02-06

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Document 260

### **MildInt: Deep learning-based multimodal longitudinal data integration framework**

**Author:** Lee, Garam 1 ; Kang, Byungkon 2 ; Nho, Kwangsik 3 ; Sohn, Kyung-Ah 2 ; Kim, Dokyoon 4

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**Publication info:** Frontiers in Genetics 10.JUN Frontiers Media S.A. (2019)

**Abstract (summary):** As large amounts of heterogeneous biomedical data become available, numerous methods for integrating such datasets have been developed to extract complementary knowledge from multiple domains of sources. Recently, a deep learning approach has shown promising results in a variety of research areas. However, applying the deep learning approach requires expertise for constructing a deep architecture that can take multimodal longitudinal data.

Thus, in this paper, a **deep learning**-based python package for data integration is developed. The python package **deep learning**-based multimodal longitudinal data integration framework (MildInt) provides the preconstructed **deep learning** architecture for a classification task. MildInt contains two learning phases: learning feature representation from each modality of data and training a classifier for the final decision. Adopting deep architecture in the first phase leads to learning more task-relevant feature representation than a linear model. In the second phase, linear regression classifier is used for detecting and investigating **biomarkers** from multimodal data. Thus, by combining the linear model and the **deep learning** model, higher accuracy and better interpretability can be achieved. We validated the performance of our package using simulation data and real data. For the real data, as a pilot study, we used clinical and multimodal neuroimaging datasets in Alzheimer's disease to predict the disease progression. MildInt is capable of integrating multiple forms of numerical data including time series and non-time series data for extracting complementary features from the multimodal dataset.

**Accession number:** 628500515

**Author e-mail address:** kasohn@ajou.ac.kr, dokyoon.kim@penncmedicine.upenn.edu

**Copyright:** Copyright 2019 Elsevier B.V., All rights reserved.

**Correspondence author:** Kim, Dokyoon Biomedical and Translational Informatics Institute, Geisinger, Danville, PA, United States.

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The support for this research was provided by NLM R01 LM012535, NIA R03 AG054936, and the Pennsylvania Department of Health (#SAP 4100070267). The department specifically disclaims responsibility for any analyses, interpretations, or conclusions. This work was also supported by the National Research Foundation of Korea grant funded by the Korea government (MSIT) (no. NRF-2019R1A2C1006608).

**Identifier (keyword):** Alzheimer's disease, Data integration, Gated recurrent unit, Multimodal **deep learning**, Python package

**Language:** English

**Language of abstract:** English

**Number of references:** 16

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**Publication type:** Journal

**Publisher:** Frontiers Media S.A.

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**Subject:** Embase;biological marker;Alzheimer disease (major);Article;conceptual framework;deep learning (major);disease exacerbation;feature extraction;human;linear regression analysis;longitudinal study;mild cognitive impairment;natural language processing;neuroimaging;single nucleotide polymorphism;speech discrimination;support vector machine;time series analysis

**Updates:** 2019-07-232019-07-29

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Document 261

## **Detecting Apathy in Older Adults with Cognitive Disorders Using Automatic Speech Analysis**

**Author:** König, Alexandra 1 ; Linz, Nicklas 2 ; Zeghari, Radia 3 ; Klinge, Xenia 2 ; Tröger, Johannes 2 ; Alexandersson, Jan 2 ; Robert, Philippe 3

1 CoBTeK (Cognition-Behaviour-Technology) Lab, Memory Center CHU, Université Côte d'Azur, Nice, France, INRIA Stars Team, Sophia Antipolis, Valbonne, France, France 2 German Research Center for Artificial Intelligence (DFKI), Saarbrücken, Germany, Germany 3 CoBTeK (Cognition-Behaviour-Technology) Lab, Memory Center CHU, Université Côte d'Azur, Nice, France, France

**Publication info:** Journal of Alzheimer's disease : JAD 69.4: 1183-1193. (2019)

### **Abstract (summary): BACKGROUND**

Apathy is present in several psychiatric and neurological conditions and has been found to have a severe negative effect on disease progression. In older people, it can be a predictor of increased dementia risk. Current assessment methods lack objectivity and sensitivity, thus new diagnostic tools and broad-scale screening technologies are needed.

### **OBJECTIVE**

This study is the first of its kind aiming to investigate whether automatic speech analysis could be used for characterization and detection of apathy.

## METHODS

A group of apathetic and non-apathetic patients (n=60) with mild to moderate neurocognitive disorder were recorded while performing two short narrative **speech** tasks. Paralinguistic markers relating to prosodic, formant, source, and temporal qualities of **speech** were automatically extracted, examined between the groups and compared to baseline assessments. **Machine learning** experiments were carried out to validate the diagnostic power of extracted markers.

## RESULTS

Correlations between apathy sub-scales and features revealed a relation between temporal aspects of **speech** and the subdomains of reduction in interest and initiative, as well as between prosody features and the affective domain. Group differences were found to vary for males and females, depending on the task. Differences in temporal aspects of **speech** were found to be the most consistent difference between apathetic and non-apathetic patients. **Machine learning** models trained on **speech** features achieved top performances of AUC=0.88 for males and AUC=0.77 for females.

## CONCLUSIONS

These findings reinforce the usability of **speech** as a reliable **biomarker** in the detection and assessment of apathy.

**Accession number:** 31127764

**Correspondence author:** König, Alexandra CoBTek (Cognition-Behaviour-Technology) Lab, Memory Center CHU, Université Côte d'Azur, Nice, France. , INRIA Stars Team, Sophia Antipolis, Valbonne, France.

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**DOI:** <http://dx.doi.org/10.3233/JAD-181033>

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**Identifier (keyword):** Apathy, assessment, **machine learning**, neuropsychiatric symptoms, **speech** analysis, **voice** analysis

**Language:** English

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**Medline document status:** MEDLINE

**MeSH:** Aged;Apathy (major);Cognition Disorders -- diagnosis;Cognition Disorders -- psychology (major);Environmental Biomarkers;Female;Humans;Machine Learning;Male;Speech;Speech Production Measurement -- methods (major)

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**Substance:** Substance Substance: Environmental Biomarkers; CAS: 0;

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Document 262

### **Comparing a speech-based digital biomarker to the montreal cognitive assessment (MOCA) for tracking cognition over a 6 month period in a naturalistic cohort of older adults**

**Author:** Simpo, W. 1 ; Balagopalan, A. 2 ; Kaufman, L. 2 ; Yancheva, M. 2

1 McMaster University, Hamilton, Canada, Winterlight Labs, Toronto, Canada 2 Winterlight Labs, Toronto, Canada

**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 6 : S129-S130. Springer. (2019)

**Abstract (summary):** Background: A lack of precision in quantifying cognitive performance is a key pillar in the overwhelmingly negative results obtained from clinical trials in Alzheimer's Disease (AD). For example, both the ADAS-Cog (1) and MMSE (2) have well established limitations, including floor/ceiling effects, practice effects and poorer psychometric properties for milder forms of impairment. This can lead to masking or false amplification of clinically relevant treatment effects particularly within the short time frame of a clinical trial. Computerized cognitive assessment batteries have ameliorated some issues but are also far from perfect (3). Effective use of language reflects intact cognitive processing through the coordinated use of working memory, semantic memory and attention. Language performance can therefore be a proxy for the strength of these underlying cognitive capabilities (4). In AD, changes in speech rate, utterance length, word-frequency, pronoun usage, repetitions, word finding difficulties, content units and efficiency are notable language specific disease characteristics 5. These changes are progressive and detectable years before a clinical

diagnosis is made (6). **Speech**, therefore, represents an excellent, novel input for a digital **biomarker**. It has a stable, linear association with AD severity (7) and is simple to collect, requiring minimal equipment and rater training. **Speech**-based digital **biomarkers** developed using natural language processing and **machine learning** could significantly reduce measurement variance by producing objective, consistent estimates, thereby yielding greater precision and greater sensitivity to change compared to existing gold standards. Objectives: The objective of this study was to compare how cognition changed over a 6 month period in a naturalistic cohort of older adults when measured via a gold standard brief cognitive assessment and **speech**-based digital **biomarker**. Methods: Participants were 111 older adults (aged 55-90), recruited from the community and independent living facilities in Canada and the US. Participants completed a tablet-based **speech** assessment which included two picture description tasks at Baseline, 1 month and 6 month timepoints. At baseline and 6 months, a MoCA was administered by a trained psychometrist. The MoCA was chosen for its superior detection of milder forms of cognitive impairment relative to the MMSE. Verbal responses were recorded, transcribed and analyzed to produce more than 500 individual **speech** and language markers. From these markers, 7 aggregate scores, chosen for their previous association to AD (5), were produced describing: discourse, information units, word finding difficulty, syntax, coherence (global and local), and sentiment. Baseline to endpoint changes were evaluated using a non-parametric, within-subjects T-test. Threshold p-values were set using a Bonferroni correction. Results: A total of 59 individuals completed baseline and 6-month assessments. Spearman correlations between total MoCA scores and individual aggregate measures ranged from none (discourse mapping,  $\rho=-0.02$ ) to moderate (word finding difficulty,  $\rho=-0.4$ ). Syntactic complexity (0.34), local coherence (0.36) and word finding difficulty (-0.40) showed the highest absolute degree of correlation. Using a Bonferroni adjusted threshold  $p = 0.0025$ , within-subjects analysis showed a small non-significant increase in MoCA total score (mean change = + 0.79,  $p=0.003$ ). Significant baseline to endpoint reductions were seen in global coherence and information units (both  $p<0.000001$ ) while a significant increase was seen in syntactic complexity ( $p=0.0017$ ). Conclusions: This preliminary study highlights statistically significant reductions in two components of language previously associated with AD severity (coherence and information units) over a 6 month period, with no accompanying reductions in cognitive status as measured by the MoCA. These data provide preliminary support for the use of **speech**-based digital **biomarkers** as sensitive tools for detecting subtle changes in cognition within clinical trials. Replication with larger cohorts, followed for >6 months is required.

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**Conference country:** United States

**Conference end date:** 2019-12-07

**Conference location:** San Diego, CA

**Conference start date:** 2019-12-04

**Conference title:** 12th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** Simpo, W. McMaster University, Hamilton, Canada.

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**Subject:** Embase; **biological marker** (major); adult; aged; Alzheimer disease; attention (major); Canada; cohort analysis (major); conference abstract; controlled study; female; genetic transcription; gold standard; human; independent living; **machine learning**; major clinical study; male; masking; middle aged; Mini Mental State Examination; Montreal cognitive assessment (major); natural language processing; null result; semantic memory; **speech rate** (major); tablet computer (major); working memory

**Updates:** 2020-06-01

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Document 263

## **Enabling early detection and continuous monitoring of Parkinson's disease**

**Author:** Oates, Christopher 1 ; Triantafyllopoulos, Andreas 1 ; Schuler, Björn 2

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**Publication info:** Technology and Disability, suppl. Supplement 1 31 : S84-S85. IOS Press. (2019)

**Abstract (summary):** Background: Parkinson's disease (PD) currently affects 6.3 million people worldwide, and with an aging European population, this number is set to rise. People with this



incurable disease suffer from weakness, tremor, and rigidity. **Biomarkers** of the disease have yet to be fully investigated, and so expensive and time-consuming clinical assessments are required but all too often never carried out. Early detection of the disease and continuous monitoring of its progression can greatly aid in the application of therapies to delay further symptoms and help patients and family manage it both mentally and physically. As symptoms of PD manifest in the **voice**, we are working towards automatic recognition and monitoring of Parkinson's disease directly from the **voice**. Through embedded sensors, PD tests can be carried out at ultra-low-cost, are highly scalable, do not require a visit to a clinic, and can generate high-frequency monitoring data. Our study focuses on differentiating between healthy and diseased individuals, and predicting the severity of a patient's disease. Method: Using openSMILE, our large space feature extraction toolkit, we analysed audio samples collected from a clinical trial featuring 20 patients in various stages of the disease along with a control group of 30 subjects of the same age range. We were also provided with UPDRS Scores which denote the severity of each patient's condition on a scale from 0-199 (worst). The audio samples contain extended vowel utterances "aah", successive consonant-vowel utterances "pa-ta-ka", read **speech**, and free **speech**. Several thousand direct and derived audio features were evaluated w.r.t. their correlation with the test subjects. **Support vector machine (SVM)** classification models were used to differentiate between patients and healthy subjects, and linear regression models were implemented to predict the patients' severity of the disease. For this part of the study, only the extended vowel and successive consonant-vowel utterances were utilized. Key results: Several audio features have been shown to correlate well with our binary classification tasks. In the case of extended vowel utterances, features which showed strong correlation were MFCC coefficients, Jitter, F0 and Harmonic-to-noise ratio. In particular, F0 variations and discontinuities proved to be the most useful. Our algorithms were able to provide a clean separation between healthy subjects and patients with PD, with an average unweighted accuracy of 91% on subject independent folds using a combination of consonant-vowel and vowel sounds. In addition, the UPDRS scores were predicted with a Pearson correlation of 0.55 using only the successive consonant-vowel sounds. Conclusion: We have successfully integrated the openSMILE technology in low-resource embedded systems like smartphones, but more importantly, in low-energy wearable sensors such as smartwatches. This is crucial since it enables the continuous monitoring of a patient's condition through a minimally invasive device placed on the patient themselves. This device would monitor the patient's normal **speech** in everyday life. More accurate measurements could be frequently obtained through structured **voice** tests (such as extended vowel utterances), performed on a smart-phone by any health care assistant.

**Accession number:** 630725997

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**Conference country:** Italy

**Conference end date:** 2019-08-30

**Conference location:** Bologna

**Conference start date:** 2019-08-27

**Conference title:** 15th International Conference of the Association for the Advancement of Assistive Technology in Europe, AAATE 2019

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**Correspondence author:** Oates, Christopher AudEERING GmbH, Gilching, Germany.

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**Identifier (keyword):** OpenSMILE, Parkinson's disease, Wearable sensors

**Language:** English

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**Subject:** Embase;adult;binary classification (major);clinical article;conference abstract;consonant;controlled clinical trial;controlled study;feature extraction;female;human;human tissue;linear regression analysis;male;noise;Parkinson disease (major);sensor (major);smartphone;speech;support vector machine;Unified Parkinson Disease Rating Scale;voice;vowel

**Updates:** 2020-01-30

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Document 264

### **Validated automatic speech biomarkers in primary progressive aphasia**

**Author:** Nevler, Naomi 1 ; Ash, Sharon 1 ; Irwin, David J 1 ; Liberman, Mark 2 ; Grossman, Murray 1

1 Penn Frontotemporal Degeneration Center Department of Neurology University of Pennsylvania Philadelphia Pennsylvania 2 Linguistic Data Consortium Department of Linguistics University of Pennsylvania Philadelphia Pennsylvania

**Publication info:** Annals of clinical and translational neurology 6.1: 4-14. (Nov 24, 2018)

## **Abstract (summary): Objective**

To automatically extract and quantify specific disease **biomarkers** of prosody from the acoustic properties of **speech** in patients with primary progressive aphasia.

## **Methods**

We analyzed **speech** samples from 59 progressive aphasic patients (non-fluent/agrammatic = 15, semantic = 21, logopenic = 23; ages 50-85 years) and 31 matched healthy controls (ages 54-89 years). Using a novel, automated **speech** analysis protocol, we extracted acoustic measurements of prosody, including fundamental frequency and **speech** and silent pause durations, and compared these between groups. We then examined their relationships with clinical tests, gray matter atrophy, and cerebrospinal fluid analytes.

## **Results**

We found a narrowed range of fundamental frequency in patients with non-fluent/agrammatic variant aphasia (mean  $3.86 \pm 1.15$  semitones) compared with healthy controls ( $6.06 \pm 1.95$  semitones;  $P < 0.001$ ) and patients with semantic variant aphasia ( $6.12 \pm 1.77$  semitones;  $P = 0.001$ ). Mean pause rate was significantly increased in the non-fluent/agrammatic group (mean  $61.4 \pm 20.8$  pauses per minute) and the logopenic group ( $58.7 \pm 16.4$  pauses per minute) compared to controls. In an exploratory analysis, narrowed fundamental frequency range was associated with atrophy in the left inferior frontal cortex. Cerebrospinal level of phosphorylated tau was associated with an acoustic classifier combining fundamental frequency range and pause rate ( $r = 0.58$ ,  $P = 0.007$ ). Receiver operating characteristic analysis with this combined classifier distinguished non-fluent/agrammatic speakers from healthy controls (AUC = 0.94) and from semantic variant patients (AUC = 0.86).

## **Interpretation**

Restricted fundamental frequency range and increased pause rate are characteristic markers of **speech** in non-fluent/agrammatic primary progressive aphasia. These can be extracted with automated **speech** analysis and are associated with left inferior frontal atrophy and cerebrospinal phosphorylated tau level.

**Accession number:** 30656179

**Correspondence author:** Nevler, Naomi Penn Frontotemporal Degeneration Center Department of Neurology University of Pennsylvania Philadelphia Pennsylvania.

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**Language:** English

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**MeSH:** Aged;Aged, 80 and over;Aphasia, Primary Progressive -- cerebrospinal fluid;Aphasia, Primary Progressive -- diagnosis (major);Aphasia, Primary Progressive -- pathology;Aphasia, Primary Progressive -- psychology (major);Biomarkers;Brain -- diagnostic imaging;Brain -- pathology;Female;Humans;Linguistics;Male;Middle Aged;Pattern Recognition, Automated;Sensitivity and Specificity;Speech (major);Speech Acoustics;Speech Production Measurement -- methods;tau Proteins -- cerebrospinal fluid

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Document 265

## **Deep language space neural network for classifying mild cognitive impairment and Alzheimer-type dementia**

**Author:** Orimaye, Sylvester Olubolu 1 ; Wong, Jojo Sze-Meng 2 ; Wong, Chee Piau 3

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**Publication info:** PLoS ONE 13.11 Public Library of Science. (Nov 2018)

**Abstract (summary):** It has been quite a challenge to diagnose Mild Cognitive Impairment due to Alzheimer's disease (MCI) and Alzheimer-type dementia (AD-type dementia) using the currently available clinical diagnostic criteria and neuropsychological examinations. As such we propose an automated diagnostic technique using a variant of **deep neural networks** language models (DNNLM) on the verbal utterances of affected individuals. Motivated by the success of DNNLM on natural language tasks, we propose a combination of **deep neural network** and **deep** language models (D2NNLM) for classifying the disease. Results on the DementiaBank language transcript clinical dataset show that D2NNLM sufficiently learned several linguistic **biomarkers** in the form of higher order n-grams to distinguish the affected group from the healthy group with reasonable accuracy on very sparse clinical datasets.

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**Author e-mail address:** orimaye@etsu.edu

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10.1371/journal.pone.0214103. 2001700910.

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**Subject:** Embase;MEDLINE;biological marker -- endogenous compound;Alzheimer disease (major);area under the curve;Article;clinical article;cognition;controlled study;diagnostic procedure;disease classification;human;information processing;language ability;language test;linguistics;longitudinal study;mild cognitive impairment (major);nerve cell network (major);neuropsychological test;speech analysis;task performance

**Updates:** 2018-11-152018-11-192018-11-202019-03-262019-04-30

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Document 266

### **Early development of a unified, speech and language composite to assess clinical severity of frontotemporal lobar degeneration (FTLD)**

**Author:** Balagopalan, A. 1 ; Kaufman, L. 1 ; Novikova, J. 1 ; Siddiqui, O. 2 ; Paul, R. 2 ; Ward, M. 2 ; Simpson, W. 3

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**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 6 : S122-S123. Springer. (2019)

**Abstract (summary):** Background: Frontotemporal Lobar Degeneration (FTLD) is a progressive neurodegenerative disorder that presents in a heterogeneous manner depending on the localization and molecular basis of the underlying neuropathology. Clinical syndromes include behavioural variant Frontotemporal Dementia (bvFTD), and the primary progressive aphasia; semantic (svPPA), non-fluent (nfvPPA) and logopenic (lpPPA), supranuclear palsy and corticobasal syndrome. The heterogeneous presentation of the disease can make diagnosis, clinical staging and longitudinal tracking of decline challenging. Some specialized scales have been developed and are useful in research settings (e.g. CDR® plus NACC FTLD 1,2), though in routine clinical practice, many use a patchwork of assessments examining cognition, activities of daily living, and neuroanatomical data to stage and subtype FTLD 3. A valid measure of severity must have good construct validity, test-retest reliability and be highly sensitive to change over time. In FTLD, this measure has the added requirement of being sensitive across distinct clinical presentations (such as bvFTD and PPA) while still maintaining reasonable specificity. The pronounced language deficits observed in PPA suggest that a detailed, computational analysis of speech may be a suitable approach for developing such a metric. Previously, our group used natural language processing (NLP) and machine learning (ML) algorithms to evaluate whether extracted speech and language variables could be used to distinguish

between PPA subtypes. We found that these variables could reliably distinguish svPPA and nfvPPA from controls with >95% accuracy and svPPA from nfvPPA with 80% accuracy 4. **Speech** and language variables identified using similar approaches could be used to derive a '**speech** assay' of FTLD which may serve as an accurate **marker** of clinical severity. Objectives: Our primary objective was to examine which computationally derived characteristics of **speech** were correlated with aphasia severity, using a large academic database. Our secondary objective was to assess the test-retest reliability of these variables alone and when combined into a composite score in healthy individuals and those with FTLD (bvFTD and PPA). Methods: More than 500 acoustic and linguistic variables were extracted using Winterlight's linguistic analytic software from samples of spontaneous **speech**. To determine which variables were most relevant to aphasia, we analyzed picture descriptions from the AphasiaBank (<https://aphasia.talkbank.org/>) corpus. AphasiaBank is a large academic database of multimedia files from patients with Transmotor, Broca's, Wernicke's, Anomic, and Conduction aphasias and is therefore a good test dataset to examine which **speech** and language variables may be most relevant. We selected Winterlight-extracted variables which exceeded a Spearman ( $\rho$ ) correlation of 0.5 with the Spontaneous **Speech** Score, Object Naming Score or Fluency Score from the Western Aphasia Battery (WAB). Using picture descriptions from two prospective cohort studies (Healthy older adults ( $n=111$ ) and FTLD ( $n=19$ )), we then examined: the sensitivity of the selected variables for detection of? FTLD and test-retest reliability. Results: Of the ~500 variables produced by the Winterlight software, 42 exceeded  $\rho=0.5$ . These variables related to syntactic complexity, discourse mapping, coherence, lexical complexity, pauses and fundamental frequency of **speech**. In comparing the healthy and FTLD cohorts, 31 variables (73.8%) (20 (47.6%) after Bonferroni correction) were significantly different between the two groups. Test-retest reliability for individual variables in the FTLD cohort was modest, with 17 variables (40.5%) exceeding a  $\rho$  value of 0.7. To examine test-retest reliability of a composite of these 42 variables, we used them as inputs for a ridge regression model to estimate the WAB score. The computed WAB model had a Mean Absolute Error (MAE) of 17.9% and demonstrated excellent test-retest reliability ( $\rho=0.87$ ,  $p<0.00001$ ). Conclusions: Preliminary results indicate that computationally derived **speech** and language variables extracted from spontaneous **speech** correlate with overall aphasia severity and can separate healthy from FTLD individuals. Test-retest of individual variables was variable, but a simple composite measure showed excellent test-retest reliability. This suggests that these variables could be useful for building a unified language composite score for FTLD which would be easier to measure and more objective than existing clinical instruments. Future work should focus on further verifying the selected variables in larger FTLD samples with longer observation windows.

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**Correspondence author:** Balagopalan, A. Winterlight Labs, Toronto, Canada.

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**Subject:** Embase;aged;algorithm;anomia;ataxic aphasia;clinical assessment tool;clinical practice;cohort analysis;conduction aphasia;conference abstract;construct validity;controlled study;cortical sensory aphasia;daily life activity;female;frontal variant frontotemporal dementia (major);human;human tissue;machine learning;major clinical study;male;multimedia;natural language processing (major);preliminary data;prospective study;software;speech (major);test retest reliability;Western aphasia battery

**Updates:** 2020-06-01

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Document 267

### **Tracking bulbar impairment using the Beiwe smartphone app**

**Author:** Connaghan, Kathryn 1 ; Green, Jordan 1 ; Paganoni, Sabrina 2 ; Chan, James 3 ; Weber, Harli 4 ; Collins, Ella 4 ; Richburg, Brian 1 ; Eshghi, Marziye 1 ; Onnela, Jp 5 ; Berry, James 2

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**Publication info:** Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, suppl. Supplement 1 20 : 297-298. Taylor and Francis Ltd. (2019)

**Abstract (summary):** Background: Early identification of bulbar dysfunction and accurate monitoring of **speech** changes in ALS is crucial to appropriate treatment planning and for establishing response to treatment in either clinical or trial settings. Longitudinal **speech** data collected frequently and conveniently can inform ALS disease prognosis, facilitate timely intervention, and can be leveraged to determine responsiveness to treatment (1). Due to their ubiquity, smartphones can be used to reduce barriers to acquiring **speech** recordings for quantitative analysis from people with ALS. The Beiwe platform provides a flexible smartphone-based app for Android and iOS devices for acquiring active and passive **digital** data, including high quality audio recordings. Objectives: We have established the feasibility of using the Beiwe platform for smartphone-based **digital** phenotyping in ALS across multiple domains (2). The current study extends that work to investigate the utility of Beiwe for identifying and tracking **speech** decline in ALS. We explored its feasibility for the frequent collection of **speech** recordings and self-ratings for the purposes of identifying the onset of bulbar symptoms and monitoring ALS progression (3, 4). Methods: Twelve people with ALS participated over a multi-week period. Participants completed the Revised ALS Functional Rating Scale (ALSFRS-R) and recorded themselves reading the Bamboo passage weekly. Three **speech** acoustic measures (ie, speaking rate, articulation rate and percent pause) were automatically extracted offline. Participants were grouped based on baseline speaking rate into those presenting with (Bulbar) and without (No-Bulbar) bulbar signs. Multiple t-tests were conducted to examine ALSFRS-R (Bulbar, **Speech** subscores) and acoustic (articulation rate, percent pause) group differences at baseline. Separate linear mixed-effects (LME) models were further conducted on these variables to evaluate group differences in the rate of bulbar decline. Results: Baseline ALSFRS-R (Bulbar, **Speech**) scores and articulation rate were significantly lower for Bulbar than No-Bulbar participants ( $p < .05$ ). Further, the Bulbar group demonstrated faster rate of decline of these measures ( $p < .01$ ). Discussion and conclusions: Successful implementation of the Beiwe platform for collection of **speech** recordings for quantitative analysis provides a promising new paradigm for diagnostic screening and ALS progression monitoring. The convenience of recording the **speech** signal for use as a **bio-marker** can reduce barriers, such as travel, and thereby promote adherence to clinical and research protocols.

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**Author e-mail address:** kconnaghan@mghihp.edu

**Conference country:** Australia

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**Conference start date:** 2019-12-04

**Conference title:** 30th International Symposium on ALS/MND

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**Correspondence author:** Connaghan, Kathryn MGH Institute of Health Professions, Boston, MA, United States.

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**Subject:** Embase;**biological marker**;adult;audio recording;bamboo;conference abstract;controlled study;feasibility study;female;human;human experiment;male;nonhuman;phenotype;quantitative analysis;rating scale;smartphone (major);**speech rate** (major);travel

**Updates:** 2020-04-22

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Document 268

### **Novel digitalized **markers** for screening, cognitive assessments and disease trajectory tracking in clinical trials**

**Author:** König, A. 1 ; Linz, N. 2 ; Tröger, J. 2 ; Guerchouche, R. 3 ; Radia, Z. 4 ; Inez, R. 5 ; Pauline, A. 5 ; Philipp, P. 5

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**Publication info:** Journal of Prevention of Alzheimer's Disease, suppl. Supplement 1 6 : S130-S131. Springer. (2019)

**Abstract (summary):** The current procedures for selecting participants for (pharmaceutical) trials developing drugs for Alzheimer's (AD) are lengthy, costly, invasive and characterized by a very high exclusion rate - only one of ten initial candidates is selected. Moreover, patients living in rural areas rarely onboard into trials due to limited access to assessments and long travel times to clinical sites. Today, there is an increasing need for harmonization and innovation of outcome measures in AD trials; ecologically valid and sensitive methods are required to improve accessibility as frontline screening in the general population for clinical trials as well as remote disease tracking. Smart digital technologies may serve as additional noninvasive and/or cost-effective tools, allowing identification of subjects in the early clinical stages who could be suitable as well as more continuous monitoring of the disease trajectory. Additionally, more standardized measures could lead to a reduction in errors due to human annotations facilitating better data comparisons across clinical sites. Implementation of such new measurement methods may facilitate early diagnostics and potentially more effective preventative strategies and treatment of dementia. However, before applying them in clinical practice and trials, these tools should be examined in ongoing large cohorts. Hinging on existing **speech**-based neurocognitive tests (today done in expert-participant f2f setting with manual test score evaluation), the DeepSpa project will render this procedure in a telecommunication-based service (video-call or telephone) using **artificial intelligence (AI)** and automatic **speech**, language and image analysis. This will allow to cut down costs: previous research shows that a telephone-based **AI** empowered system is able to discriminate with up to 90% accuracy between AD vs. healthy controls and mild-cognitive impairment. The resulting remote service can be either operated entirely autonomous (dialogue system operating on phone) or semi-automatic with trained personnel. The project explores two use cases with a clinical study for each in a different setting; the first one assesses the feasibility, usability and further refinement of a phone-based neurocognitive assessment tool for patient pre-screening at the Alzheimer Center in Maastricht University, Netherlands. Furthermore, the predictive potential (sensitivity/ specificity) for differential/prognostic diagnosis is examined based on information extracted from the participant's **speech** in cognitive **vocal** and narrative **speech** tasks and its usefulness for remote pre-screening and monitoring. Longitudinal data is collected and results extracted remotely validated against face-to-face results. We will prospectively include 120 new pre-clinical patients from an ongoing cohort with a minimal dataset consisting of clinical data and a cognitive assessment. In addition, a MRI of the brain, and blood samples and CSF samples (optional) are collected for biobanking purpose. Additionally, to these procedures, after 6 and 15 months patients will be called for a brief (30 min) remote follow up evaluation on the phone. A research nurse or researcher will introduce and guide the assessment session in which **speech** parameters will be collected through a semi-automatic phone-based interface. The assessment consists of a short interview on how the patients perceive their memory and overall mental state, a verbal memory task, digit span and fluency tasks, being comparable to the baseline assessment e.g. care as usual. In addition, the regular cognitive assessments at baseline and 12 month will be audio-recorded. The second use case will test the use of a tele-conference system (including video) for remote cognitive testing and monitoring of isolated elderly in rural areas in South of France (Digne-les-bains). The system uses automatic **speech** and image analysis for a precise and potentially more timely detection of cognitive decline. In order to assess how the systems performs in such a context, a

beta version will be evaluated for its feasibility and usability. A hundred of volunteers with memory complaints will be included from the Dignes-les-bains region in the protocol. The aim for this first full-scale study is to carry out a battery of clinical interview and tests (visual memory, attention, language, and mood - 80 min) through the system and compare to face to face results in order to assess its reliability for potential remote diagnosis, with support from Nice University Hospital and Memory Clinics specialists. **Speech** features as well as information on facial expressions and posture are extracted automatically and compared to classical assessment scales. Moreover, these variables might help indicating levels of engagement, stress, fatigue or mood. User experience on the participant as well as on the clinician side will be assessed with the help of extensive qualitative interviews and satisfaction questionnaires. The protocols are submitted to the ethical committees and first results can be expected after the summer. A demo of the system for both use cases will be presented at the conference.

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**Conference country:** United States

**Conference end date:** 2019-12-07

**Conference location:** San Diego, CA

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**Conference title:** 12th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** König, A. INRIA, Cobtek (Cognition, Behaviour, Technology) Lab, University Côte d'azur, Nice, France.

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**Document type:** Conference Abstract

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**First available:** 2020-06-01

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**Subject:** Embase;aged;Alzheimer disease;artificial intelligence;body position;cancer staging;cerebrospinal fluid;clinical practice;cohort analysis;conference abstract;controlled study;facial expression;fatigue;feasibility study;female;follow up;France;human;image analysis;interview;language;major clinical study;male;mental health;mild cognitive impairment;mood;narrative;Netherlands;nuclear magnetic resonance imaging;nurse;outcome assessment;preclinical study;questionnaire;reliability;rural area;satisfaction;sensitivity and specificity;speech test;stress;summer;teleconference;tediagnosis;telephone;travel;verbal memory test;videorecording;visual attention;visual memory;voice parameter

**Updates:** 2020-06-01

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Document 269

## **Smartphone motor testing to distinguish idiopathic REM sleep behavior disorder, controls, and PD**

**Author:** Arora, Siddharth 1 ; Baig, Fahd 1 ; Lo, Christine 1 ; Barber, Thomas R 1 ; Lawton, Michael A 1 ; Zhan, Andong 1 ; Rolinski, Michal 1 ; Ruffmann, Claudio 1 ; Klein, Johannes C 1 ; Rumbold, Jane 1 ; Louvel, Amandine 1 ; Zaiwalla, Zenobia 1 ; Lennox, Graham 1 ; Quinnell, Tim 1 ; Dennis, Gary 1 ; Wade-Martins, Richard 1 ; Ben-Shlomo, Yoav 1 ; Little, Max A 1 ; Hu, Michele T 1

1 From the Oxford Parkinson's Disease Centre (OPDC) (S.A., F.B., C.L., T.R.B., M.R., C.R., J.C.K., J.R., A.L., R.W.-M, M.T.H.), University of Oxford, UK; Engineering and Applied Science (S.A., M.A.L.), Aston University, Birmingham, UK; Somerville College (S.A.), University of Oxford, UK; Nuffield Department of Clinical Neurosciences (F.B., C.L., T.R.B., M.A.L., M.T.H.), University of Oxford, UK; Population Health Sciences (M.A.L.), University of Bristol, UK; and Department of Computer Science (A.Z.), Johns Hopkins University, Baltimore; Department of Neurology and Neurophysiology (Z.Z., G.L., M.T.H.), Oxford University Hospitals NHS Trust, UK; Respiratory Support and Sleep Centre (T.Q.), Papworth Hospital, Cambridge, UK; Department of Neurology (G.D.), Royal Hallamshire Hospital, Sheffield, UK; and Media Lab (M.A.L.), Massachusetts Institute of Technology, Cambridge, MA, MA Michele.hu@ndcn.ox.ac.uk

**Publication info:** Neurology 91.16: e1528-e1538. (Oct 16, 2018)

### **Abstract (summary): OBJECTIVE**

We sought to identify motor features that would allow the delineation of individuals with sleep study-confirmed idiopathic REM sleep behavior disorder (iRBD) from controls and Parkinson disease (PD) using a customized smartphone application.

## **METHODS**

A total of 334 PD, 104 iRBD, and 84 control participants performed 7 tasks to evaluate **voice**, balance, gait, finger tapping, reaction time, rest tremor, and postural tremor. Smartphone recordings were collected both in clinic and at home under noncontrolled conditions over several days. All participants underwent detailed parallel in-clinic assessments. Using only the smartphone sensor recordings, we sought to (1) discriminate whether the participant had iRBD or PD and (2) identify which of the above 7 motor tasks were most salient in distinguishing groups.

## RESULTS

Statistically significant differences based on these 7 tasks were observed between the 3 groups. For the 3 pairwise discriminatory comparisons, (1) controls vs iRBD, (2) controls vs PD, and (3) iRBD vs PD, the mean sensitivity and specificity values ranged from 84.6% to 91.9%. Postural tremor, rest tremor, and **voice** were the most discriminatory tasks overall, whereas the reaction time was least discriminatory.

## CONCLUSIONS

Prodromal forms of PD include the sleep disorder iRBD, where subtle motor impairment can be detected using clinician-based rating scales (e.g., Unified Parkinson's Disease Rating Scale), which may lack the sensitivity to detect and track granular change. Consumer grade smartphones can be used to accurately separate not only iRBD from controls but also iRBD from PD participants, providing a growing consensus for the utility of **digital biomarkers** in early and prodromal PD.

**Accession number:** 30232246

**Author e-mail address:** Michele.hu@ndcn.ox.ac.uk

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**Correspondence author:** Arora, Siddharth From the Oxford Parkinson's Disease Centre (OPDC) (S.A., F.B., C.L., T.R.B., M.R., C.R., J.C.K., J.R., A.L., R.W.-M, M.T.H.), University of Oxford, UK; Engineering and Applied Science (S.A., M.A.L.), Aston University, Birmingham, UK; Somerville College (S.A.), University of Oxford, UK; Nuffield Department of Clinical Neurosciences (F.B., C.L., T.R.B., M.A.L., M.T.H.), University of Oxford, UK; Population Health Sciences (M.A.L.), University of Bristol, UK; and Department of Computer Science (A.Z.), Johns Hopkins University, Baltimore; Department of Neurology and Neurophysiology (Z.Z., G.L., M.T.H.), Oxford University Hospitals NHS Trust, UK; Respiratory Support and Sleep Centre (T.Q.), Papworth Hospital, Cambridge, UK; Department of Neurology (G.D.), Royal Hallamshire Hospital, Sheffield, UK; and Media Lab (M.A.L.), Massachusetts Institute of Technology, Cambridge, MA.

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**MeSH:** Aged;Female;Fingers -- physiopathology;Gait;Humans;Male;Middle Aged;Parkinson Disease -  
- diagnosis (major);Parkinson Disease -- psychology;Postural Balance;Psychomotor  
Performance;REM Sleep Behavior Disorder -- diagnosis (major);REM Sleep Behavior Disorder --  
psychology;Reaction Time;Reproducibility of Results;Sensitivity and Specificity;Smartphone  
(major);Tremor -- diagnosis;Tremor -- psychology;Voice

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092020-03-112021-01-102022-07-16

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Document 270

**A comprehensive digital biomarker active testing and passive monitoring suite for the remote and frequent assessment of motor symptom progression in Parkinson's disease**

**Author:** Taylor, K. 1 ; Postuma, R. 1 ; Boess, F. 1 ; Lipsmeier, F. 1 ; Kilchenmann, T. 1 ; Verselis, L. 1 ; Soto, J. 1 ; Koller, M. 1 ; Gossens, C. 1 ; Post, A. 1 ; Sevigny, J. 1 ; Lindemann, M. 1

1 , Basel, Switzerland

**Publication info:** Movement Disorders, suppl. Supplement 2 33 : S668. John Wiley and Sons Inc. (Oct 2018)

**Abstract (summary):** Objective: We present the development and design of a comprehensive **digital biomarker** smartphone application (app) for remote and frequent assessments of motor symptom severity and progression in Parkinson's disease (PD). Background: PD symptoms vary within and across patients over time, complicating the benchmarking of symptom severity at infrequent clinic visits. Our previous studies with 44 PD patients and 35 controls demonstrated that daily testing with smartphone apps generates reliable, clinically valid, and sensitive symptomatic data in PD patients. We built upon these initial learnings to develop a smartphone app that comprehensively measures the core signs of PD remotely, continuously (i.e., daily) and objectively (i.e., via smartphone sensors). Methods: The app design was based on our initial learnings, the available literature, analyses of longitudinal PPMI MDS-UPDRS item data, and consultation with movement disorders neurologists and patients. Tests of the cardinal signs of PD which were both amenable to smartphone testing and declined most in the first year of de novo PD (PPMI) were identified. Neurologists reviewed these tests and selected a final set based on estimated fidelity of clinical signs during unsupervised, in-home testing. Tests were programmed on the app. Finally, the app was reviewed by patients to ensure they understood and could complete all tasks. Results: The testing suite encompasses the following active tests: sustained **phonation**, postural tremor, and rest tremor (tremor); reading and free **speech**, shape drawing, finger-tapping and pronation/supination (bradykinesia); balance and U-turn tests (rigidity/postural instability); and a modified version of the digit-symbol modalities test. Passive monitoring via smartphone and smartwatch estimated the effect of PD on daily motor behavior. Finally, the Timed Up and Go and short Berg Balance Scale are performed with the smartphone at clinic visits. Conclusions: The present smartphone app relies on direct symptom measurement via smartphone sensors while patients perform a comprehensive suite of active and passive activities in an ecologically valid environment. Thus, this app should provide measures of symptom severity and progression that are complementary to established clinical outcome measures.

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**Conference end date:** 2018-10-09

**Conference location:** Wanchai

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**Conference title:** 22nd International Congress of Parkinson's Disease and Movement Disorders, MDS 2018

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**Correspondence author:** Taylor, K. , Basel, Switzerland.

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**Document type:** Conference Abstract

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**Subject:** Embase;biological marker (major);adult;balance impairment;Berg Balance Scale;bradykinesia;clinical article;clinical outcome;conference abstract +;consultation;controlled study;disease course (major);drawing;female;finger;human;learning;locomotion;male;monitoring (major);neurologist;outcome assessment;Parkinson disease (major);phonation;pronation;rest;rigidity;sensor;smartphone;supination;symbol digit modalities test;timed up and go test;tremor;Unified Parkinson Disease Rating Scale

**Updates:** 2018-10-29

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Document 271

## **Acoustic analysis and subjective vocal perception of Parkinson's disease patients and healthy control and the relation to depression and quality of life**

**Author:** Manor, Y. 1 ; Naor, S. 1 ; Shpunt, D. 1 ; Diamant, N. 1 ; Zivion, N. 1 ; Hayat, L. 1 ; Yaron, A. 1 ; Hillel, A. 1 ; Ezra, A. 1 ; Opher, I. 1 ; Hauptman, Y. 1 ; Aloni-Lavi, R. 1 ; Faust-Socher, A. 1 ; Gurevich, T. 1

1 , Tel Aviv, Israel

**Publication info:** Movement Disorders, suppl. Supplement 2 33 : S825. John Wiley and Sons Inc. (Oct 2018)

**Abstract (summary):** Objective: To assess the acoustic differences between PD patients and healthy control (HC), the participants' perception of their vocal characteristics and the relation of the acoustic characteristics to depression and quality of life (QOL). Background: Vocal characteristics associated with Parkinson's disease (PD) are part of hypokinetic dysarthria. Acoustic correlates of PD have a potential to provide biomarkers for depression. Methods: The study included 26 PD patients (8

females) and 13 HC. All participants underwent the Montreal Cognitive Assessment (MoCA), the voice handicapped index (VHI) and the Beck depression inventory (BDI). The PD patients underwent the Parkinson's disease quality of life questionnaire (PDQ8), Hoehn &Yahr scale (H&Y), and the researchers assessed the participants' voice quality using the Grade, Roughness, Breathiness, Asthenia &strain (GRBAS) score. All participants were recorded while performing a long /A/, reading a phonetically balanced paragraph and during spontaneous speech. An acoustic analysis that included pitch and Root Mean Square (RMS) was performed using digital signal processing. Results: PD patients' mean Hoehn&Yahr 2.8±0.97; disease duration 7.84±5.36 and PDQ8 11.5±6.55. Mean age of PD/HC 67.26±11.28/ 68.70 ±4.47 respectively; MoCA, VHI, BDI and GRBAS mean score of PD/HC 20.73±5.76/ 27.15±1.95; 37.07± 32.8/5.07±3.87; 4.46±4.32/ 0.69±1.06 1.38±0.92/0±0 (p<0.001) respectively. Significant difference was noted in RMS MAX between PD patients 29.04±14.61 and HC 5.07±0.96. A positive correlation was noted between PD patients' BDI, PDQ8 and VHI scores (p<0.05). A positive tendency was observed between PDQ8 score and RMS 378.68 ±346.85 in spontaneous speech (p=0.06). No correlation was noted between BDI and acoustic measurements. In the HC group a positive correlation was noted between pitch (1.06±0.13) and GRBAS (0±0; p<0.05) score during reading. Conclusions: The vocal characteristics of PD patients perceived by the patients and examiners was worse than the HC. Patients with greater variability in acoustic energy seemed to have better QOL. Acoustic characteristics were not correlated with depression scale in this pilot study.

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**Conference country:** Hong Kong

**Conference end date:** 2018-10-09

**Conference location:** Wanchai

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**Conference title:** 22nd International Congress of Parkinson's Disease and Movement Disorders, MDS 2018

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**Subject:** Embase;acoustic analysis (major);aged;asthenia;Beck Depression Inventory;clinical article;conference abstract +;controlled study;depression (major);disabled person;disease course;female;human;male;Montreal cognitive assessment;Parkinson disease (major);perception (major);pilot study;pitch;quality of life (major);questionnaire;scientist;signal processing;speech;voice

**Updates:** 2018-10-29

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Document 272

## **Semantic and syntactic analysis of speech in patients at ultra-high-risk for psychosis: A proof of concept study**

**Author:** Bazziconi, Pierre-François 1 ; Lemey, Christophe 1 ; Kim-Duffor, D.H. 1 ; Bleton, Laure 1 ; Walter, Michel 1

1 CHRU BREST, Psychiatry, France

**Publication info:** Early Intervention in Psychiatry, suppl. Supplement 1 12 : 175. Blackwell Publishing. (Oct 2018)

**Abstract (summary):** In the early psychosis detection field, the challenge is to identify a predictive marker of transition to schizophrenia. Language disorders, could be one of these markers. Computerized speech analysis techniques such as Latent Semantic Analysis (LSA) have already proven their reliability in schizophrenia (Elvevag, 2007, Schizophrenia research). One study showed that a combination of semantic and syntactic analysis would accurately predict the psychotic transition (Bedi G, 2015, NPJ Schizophrenia). The aim of our study is to validate this model in French language as well as identifying specific linguistic markers of the psychotic transition. Patients will be recruited during two years from the early psychosis detection centers in Brest, Paris and in Lausanne. The initial report, including the Comprehensive Assessment of At-Risk Mental States will be completed with an audio recording from the initial medical interview. The recording will be transcribed and analyzed by computer following the method of LSA. An analysis of the grammatical function (number of words, rate of the various grammatical functions) will also be performed. With this first analysis, linguistic markers correlated to transition to psychosis, can be identified. Then, we will use these markers and the global coherence index to construct a predictive model for transition to schizophrenia. Finally this model will be tested through machine learning, where each new inclusion will enrich the algorithmic model. Our study leads to demonstrate that language abnormalities may be

predictive **markers** of the psychotic transition in high-risk psychotic patients, using a model based on automatize semantic and syntactic analysis.

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**Conference location:** Boston, MA

**Conference start date:** 2018-10-07

**Conference title:** IEPA 11th International Conference on Early Intervention in Mental Health - "Prevention and Early Intervention: Broadening the Scope"

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**Correspondence author:** Bazziconi, Pierre-François CHRU BREST, Psychiatry, France.

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**Subject:** Embase;adult;anamnesis;audio recording;conference abstract +;congenital malformation;France;French (language);genetic transcription;human;**machine learning**;mental health;proof of concept (major);psychosis (major);risk assessment;**speech** (major)

**Updates:** 2018-10-15

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Document 273

## **Automated **speech** analysis to predict development of psychosis: A novel endpoint in a randomized, phase II trial of BI 409306 in attenuated psychosis syndrome**

**Author:** Mota, Natalia 1 ; Copelli, Mauro 2 ; Ribeiro, Sidarta 1 ; Berisha, Visar 3 ; Slezak, Diego Fernandez 4 ; Daniels, Kristen 5 ; Sand, Michael 5

1 Brain Institute, Federal University of Rio Grande Do Norte, Brazil 2 Physics Department, Federal University of Pernambuco, Brazil 3 Department of Speech and Hearing Science, School of Electrical Computer and Energy Engineering, Arizona State University, United States 4 Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Computación, Brazil, CONICET-Universidad de Buenos Aires, Instituto de Investigación en Ciencias de la Computación (ICC), Brazil 5 Boehringer Ingelheim Pharmaceuticals Inc., Brazil

**Publication info:** Early Intervention in Psychiatry, suppl. Supplement 1 12 : 186. Blackwell Publishing. (Oct 2018)

**Abstract (summary):** Although individuals with attenuated psychosis syndrome (APS) can be identified, reliable prediction of frank psychosis onset among them remains elusive. Improving the capacity to predict those at highest risk for conversion to psychosis would have important ramifications for early identification and preventive intervention, potentially critically altering the long-term life trajectory of people with emergent psychotic disorders. Subtle disorganization in **speech** has consistently been identified as predictive of psychosis (i.e., with classification accuracy of ~60%) among young people identified as clinically high-risk. BI 409306, a potent and selective phosphodiesterase-9 inhibitor that improves NMDA signaling, is under development for early intervention in APS. An ongoing multinational, double-blind, parallel-group study will assess the efficacy, safety, and tolerability of BI 409306 in patients with APS (16-30 years of age). Patients will be randomized (300 planned, 1:1) to BI 409306 or placebo for 52 weeks. The primary endpoint is time to first episode psychosis. Secondary endpoints will assess functional capacity, cognition, and disease symptoms. Novel automated **speech** analysis, an exploratory **biomarker** of brain plasticity, will also be assessed. Patients will participate in audio-recorded interviews (baseline, Weeks 18, 42, 52). Audio recordings and transcripts will be analyzed to extract acoustic parameters and generate **speech** graphs and semantic features. Classifiers will be applied to determine the optimal combination of acoustic, graph-theoretical, and semantic features to predict psychosis. This novel **speech** analysis, as part of a clinical trial, may provide valuable data to aid early detection of APS. Recruitment is ongoing.

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**Conference country:** United States

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**Conference location:** Boston, MA

**Conference start date:** 2018-10-07

**Conference title:** IEPA 11th International Conference on Early Intervention in Mental Health - "Prevention and Early Intervention: Broadening the Scope"

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**Correspondence author:** Mota, Natalia Brain Institute, Federal University of Rio Grande Do Norte, Brazil.

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**Document type:** Conference Abstract

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**Language:** English

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**Subject:** Embase;biological marker;endogenous compound;phosphodiesterase;placebo;adult;audio recording;classifier;comparative effectiveness;conference abstract +;controlled study;double blind procedure;drug efficacy;drug safety;early intervention;female;functional status;genetic transcription;human;interview;major clinical study;male;multicenter study;nerve cell plasticity;parallel design;phase 2 clinical trial;psychosis (major);randomized controlled trial;signal transduction;speech;speech analysis (major);syndrome (major);theoretical study;visually impaired person

**Substance:** Substance Substance: phosphodiesterase; Enzyme comm: EC 3.1.4;

**Updates:** 2018-10-15

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Document 274

**Harnessing the power of big data and technology innovations to advance Alzheimer's disease clinical development**

**Author:** Uspenskaya-Cadoz, Olga 1 ; Nigmatullina, Yuliya 2 ; Stanley, Kenneth 3 ; Alamuri, Chaitanya 2 ; Randall, Penny 1 ; Khinda, Sam 3 ; Wang, Lanhui 2 ; Yang, Mengting 2 ; Rubel, Carolina 3 ; Hughes, Lynne 3 ; Cao, Tao 2 ; O'Keefe, Michelle 2 ; Kayal, Nikhil 2

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**Publication info:** Journal of Prevention of Alzheimer's Disease 5.1: S155-S156. Springer. (Oct 2018)

**Abstract (summary):** Introduction: The traditional approach for patient enrollment in prodromal Alzheimer's Disease (AD) population is to identify patients through direct-to-patient outreach and to target healthcare professionals (HCPs) who have historically treated AD patients who then identify potential patients from within their database. However, patients with early stages of AD can be simply missed or not even be on the radar of the AD-treating HCPs. In addition, targeting patients at early AD stages increases the pool of potential patients, which increases the demand and the need for the dementia specialist clinical evaluations and conduction of expensive and/or invasive diagnostic tests (PET, LPs). The use of big data and innovative technology solutions will provide new opportunities to optimize the clinical development process including patient enrolment/retention and ongoing trial management. Objective: The objective of this abstract is to trigger discussion into innovative approaches for optimising the clinical development process in AD with specific focus into early stages of the disease. The innovative approaches include: • Use of **machine learning** predictive analytics for identifying non-diagnosed prodromal AD patients in general population and support new referral networks; • Use of patient insights to optimize protocol design and increase **biomarker** collection acceptability in AD trials; • Deployment of virtual trials in AD for a more patient-centric clinical trial management approach. Discussion: Big data and recent technology innovations are critical in allowing development of solutions that can help combat key issues in clinical development for AD. One of these solutions is the **machine learning** predictive model that may ingest data from various sources including claims, prescription, EMR, familial history, patient digital devices (e.g. apps sensors) to identify at risk of prodromal AD patient populations. These identified patient populations can then be linked to their HCPs for identification of the sites and physicians where these patients could be reached (see Figure 1). In addition, a predictive analytics screening tool can be embedded at the provider site to support direct screening of patients for the clinical trial. The disease risk score can be generated and viewed directly by the physician, which helps in making the decision on whether the patients should be referred for additional diagnostic tests. Additional data collected through the diagnostic tests acts as a feedback loop to validate and further train the predictive model, improving its accuracy and decreasing screening failure rate. The insights generated by the predictive model on the location of the prodromal AD patients allows for expanding AD investigator site networks by implementation recruitment strategies that are study- and site- specific. Recent innovations in app and digital device technology may provide digital **biomarkers** that will further screen the at-risk prodromal AD patient population. These digital **biomarkers** may arise from various sources to generate a longitudinal profile of patient behaviour: • App interactions to test cognitive ability e.g. Peak, CogniSense, BrainTest. • Wearables to monitor motion, gait, sleep, heart rate and other behavioural factors; • Social media patterns to observe changes in network activities; • Smart devices interaction including **voice** sampling, handwriting analysis, password recall etc; • In home monitoring e.g. time in

social areas, food preparation, sedentary time. Once validated, the data collected by digital **biomarker** apps/ devices can be fed into the predictive model to further improve the precision of prodromal patient identification and support patient diagnosis. Highly complex, lengthy and burdensome AD disease modification trials have a strong potential to benefit from both the insights provided by study participants and from virtual trial platforms which allow study staff and study partners to bring some of the trial-related procedures directly to the patient in his or her home, including e-consent, phlebotomy, and shipping of study drug. By listening to patient feedback we can design trials that are more acceptable to participants which in turn should improve enrolment and retention rates. Additionally, endpoint data may be collected directly from the patient at home through connected devices and ePROs. Where studies typically require clinician-based assessments, bidirectional High Definition video capability can be integrated into the platform facilitating virtual interviews and ratings of subjects by a small cadre of highly trained clinicians/raters. Conclusion: Rapid technology advancements and emergence of predictive disease models using big data will significantly change clinical trial space in the nearest in several ways: • Allow accurate and much earlier prodromal AD diagnosis already in the primary care setting with timely referral to expert sites for **biomarker** assessment and diagnosis confirmation; • Better patient and HCP engagement (early interventions on AD risk factors, accurate early diagnosis, improved treatment plans and timely initiation of disease modifying drugs should such become available); • Unburden patients/caregivers/sites involved in complex AD clinical trials through leveraging patient insights and implementation of virtual trial platform; • Collect meaningful real-world data with emerging digital **biomarkers** allowing better understanding of long-term outcomes of disease modifying treatments. (Figure Presented) .

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**Conference country:** Spain

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**Conference title:** 11th Conference Clinical Trials Alzheimer's Disease

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**Correspondence author:** Uspenskaya-Cadoz, Olga IQVIA CNS Center of Excellence, United States.

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**Subject:** Embase;biological marker;adult;Alzheimer disease (major);big data (major);caregiver;clinical assessment;clinician;conference abstract +;controlled study;diagnosis;diagnostic test accuracy study;early diagnosis;early intervention;feedback system;female;food processing;gait;genetic marker;handwriting;health care personnel;heart rate;home monitoring;human;interview;machine learning;male;motion;patient identification;patient referral;phlebotomy;population;prescription;primary medical care;recall;risk assessment;risk factor;sampling;sedentary time;sensor;shipping;sleep;social media;staff;videorecording;voice

**Updates:** 2019-05-16

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Document 275

## **Now we're talking: bringing a voice to digital medicine**

**Author:** Steinhubl, Steven R 1 ; Topol, Eric J 1

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**Publication info:** The Lancet 392.10148: 627. Lancet Publishing Group. (Aug 25, 2018 - Aug 31, 2018)

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**Language:** English

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**Publication type:** Journal

**Publisher:** Lancet Publishing Group

**Publisher location:** United Kingdom

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**Subject:** Embase;biological marker;digital computer (major);smartphone;accuracy;Alzheimer disease;coronary artery disease;depression;diabetes mellitus;digital medicine + (major);facial expression;gesture;health care;health care delivery;health care need;human;human computer interaction (major);interpersonal communication;medical care;medical information;medical record;medical research;medicine (major);mental disease;Note;Parkinson disease;patient monitoring;priority journal;respiratory tract disease;visual impairment;voice (major);voice analysis;voice based coaching +

**Updates:** 2018-08-282018-09-062021-02-09

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Document 276

## **Evaluation of smartphone-based testing to generate exploratory outcome measures in a phase 1 Parkinson's disease clinical trial**

**Author:** Lipsmeier, Florian 1 ; Taylor, Kirsten I. 1 ; Kilchenmann, Timothy 1 ; Wolf, Detlef 1 ; Scotland, Alf 1 ; Schjodt-Eriksen, Jens 1 ; Cheng, Wei-Yi 1 ; Fernandez-Garcia, Ignacio 1 ; Siebourg-Polster, Juliane 1 ; Jin, Liping 1 ; Soto, Jay 2 ; Verselis, Lynne 1 ; Boess, Frank 1 ; Koller, Martin 2 ; Grundman, Michael 3 ; Monsch, Andreas U. 4 ; Postuma, Ronald B. 5 ; Ghosh, Anirvan 1 ; Kremer, Thomas 1 ; Czech, Christian 1 ; Gossens, Christian 1 ; Lindemann, Michael 1

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**Publication info:** Movement Disorders 33.8: 1287-1297. John Wiley and Sons Inc. (Aug 2018)

**Abstract (summary):** Background: Ubiquitous digital technologies such as smartphone sensors promise to fundamentally change biomedical research and treatment monitoring in neurological diseases such as PD, creating a new domain of digital biomarkers. Objectives: The present study assessed the feasibility, reliability, and validity of smartphone-based digital biomarkers of PD in a clinical trial setting. Methods: During a 6-month, phase 1b clinical trial with 44 Parkinson participants, and an independent, 45-day study in 35 age-matched healthy controls, participants completed six daily motor active tests (sustained phonation, rest tremor, postural tremor, finger-tapping, balance, and gait), then carried the smartphone during the day (passive monitoring), enabling assessment of, for example, time spent walking and sit-to-stand transitions by gyroscopic and accelerometer data. Results: Adherence was acceptable: Patients completed active testing on average 3.5 of 7 times/week. Sensor-based features showed moderate-to-excellent test-retest reliability (average intraclass correlation coefficient = 0.84). All active and passive features significantly differentiated PD from controls with  $P < 0.005$ . All active test features except sustained phonation were significantly related to corresponding International Parkinson and Movement Disorder Society–Sponsored UPDRS clinical severity ratings. On passive monitoring, time spent walking had a significant ( $P = 0.005$ ) relationship with average postural instability and gait disturbance scores. Of note, for all smartphone active and passive features except postural tremor, the monitoring procedure detected abnormalities even in those Parkinson participants scored as having no signs in the corresponding International Parkinson and Movement Disorder Society–Sponsored UPDRS items at the site visit. Conclusions: These findings demonstrate the feasibility of smartphone-based digital biomarkers and indicate that smartphone-sensor technologies provide reliable, valid, clinically meaningful, and highly sensitive phenotypic data in Parkinson's disease. © 2018 The Authors. Movement Disorders published by Wiley Periodicals, Inc. on behalf of International Parkinson and Movement Disorder Society.

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**Identifier (keyword):** clinical trial, digitalbiomarkers, digital health, Parkinson's disease, remote patient monitoring

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**Subject:** Embase;MEDLINE;biological marker (major);smartphone (major);accelerometry;adult;Article;body equilibrium;clinical article;clinical evaluation;clinical feature;concurrent validity;controlled study;data processing;disease severity;female;finger tapping test;gait;gait disorder;human;male;motor active test +;motor activity;motor function test;observational study;outcome assessment;Parkinson disease (major);patient compliance;patient monitoring;phase 1 clinical trial;phonation;priority journal;program feasibility;telemedicine;test retest reliability;treatment duration;tremor;Unified Parkinson Disease Rating Scale;walking

**Updates:** 2018-09-252018-09-272018-10-032018-10-092018-10-232019-09-10

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Document 277

## **Vocal biomarker predicts long term survival among heart failure patients**

**Author:** Maor, E. 1 ; Mazin, I. 1 ; Tel-Zur, D. 2 ; Taiblum, N. 2 ; Luz, Y. 2 ; Perry, D. 2 ; Levanon, Y. 2 ; Koren, G. 3 ; Shalev, V. 3

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**Publication info:** European Heart Journal, suppl. Supplement 1 39 : 876. Oxford University Press. (Aug 2018)

**Abstract (summary):** Home telemedicine holds the potential to reduce costs and improve outcome among patients with congestive heart failure (CHF). We recently reported a possible relationship between **vocal biomarkers** and coronary artery disease. The purpose of the current study was to test the hypothesis that **vocal biomarkers** are associated with long term survival among CHF patients. Methods: Study cohort included 2,282 patients who were registered to a large HMO's call center of patients suffering from chronic conditions including CHF. 940 acoustic features were extracted from 20 secs of **speech** for each of the patients. A **biomarker** was then developed based on a train cohort (N=1,391) using **machine learning** techniques optimized according to an age cutoff of 75. The **biomarker** was then tested on a final mutually exclusive CHF study cohort (N=891). The **biomarker** was evaluated as a continuous variable, as well as dichotomized to two groups: high (upper quartile) and low. Results: Mean age of the CHF study population was 74±12, 67% were men. During an average follow-up of 32±15 months, 246 (28%) patients died. Kaplan Meier survival analysis showed significantly higher cumulative probability of death among subjects in the higher **vocal biomarker** group (41%±19% vs. 30%±20%, p<0.001; FIGURE). Consistently, cox regression analysis of the **vocal biomarker** as a continuous variable in the model, and with adjustment to known predictors of poor survival, demonstrated that each standard deviation increase in the **vocal biomarker** was associated with a significant 15% increased risk of death during follow-up (95% CI 1.02 - 1.3, p=0.02). Conclusions: This is the first study to document a relationship between a **vocal biomarker** and long-term survival among CHF patients. The results have important clinical implications for telemedicine and CHF patient care. (Figure Presented).

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**Conference title:** European Society of Cardiology Congress, ESC 2018

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**Correspondence author:** Maor, E. Chaim Sheba Medical Center, Tel Hashomer, Israel.

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**Subject:** Embase;biological marker (major);aged;call center;chronic disease;cohort analysis;conference abstract +;congestive heart failure (major);controlled study;coronary artery disease;death;female;follow up;human;long term survival (major);machine learning;major clinical study;male;mortality;patient care;probability;speech;telemedicine

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Document 278

## **NOVEL DIGITAL VOICE BIOMARKERS OF DEMENTIA FROM THE FRAMINGHAM STUDY**

**Author:** Stück, David 1 ; Signorini, Alessio 1 ; Al Hanai, Tuka 2 ; Sandoval, Maggie 1 ; Lemke, Christine 1 ; Glass, Jim 2 ; Hardy, Spencer 3 ; Lavallee, Maria 3 ; Wasserman, Brynna 3 ; Alvin Ang, Ting Fang 4 ; Nowak, Christina 3 ; Au, Rhoda 5

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 14.7: P778-P779. Elsevier Inc. (Jul 2018)

**Abstract (summary):** Background: Effective treatments for Alzheimer's disease (AD) remain elusive and the heterogeneity of the disease's behavioral symptoms in its earliest stages make it difficult to detect those on a neurodegenerative trajectory with high degree of accuracy. Beginning in 2005, digital audio recordings of spoken responses to neuropsychological tests administered to the Offspring cohort of the Framingham Heart Study were collected. We leveraged this unique database

of audio recordings to test the feasibility of identifying **voice biomarkers** of dementia/AD. Methods: From a pool of 7000+ recordings obtained between 2005-2016, we selected a subset that included those diagnosed with dementia by consensus review (n=107) and a control group that was not demented (n=35). The audio files were diarized (separating tester's **speech** from that of the subject) and transcribed semi-automatically, and a set of acoustic and language-based features were computed on the annotated text. We posed the **machine learning** task as a classification problem and trained a random forest classifier using mean area under the receiver operating curve (AUC) scores across a 10-fold cross validation scheme as the performance metric. Results: Table 1 shows performance and Confidence Intervals (CI) of the random forest classifier built on various subsets of the features. Using only context-agnostic acoustic features the model obtains an average AUC of 0.76. Adding natural language processing (NLP) based features boosts the value to 0.91. Conclusions: While these results are preliminary, simple acoustic and language features computed over **speech** segments show promise for the development of accurate digital **biomarkers** of cognitive impairment. Future work will involve a bigger sample size and aim to determine whether these **biomarkers** can serve as a low-cost, scalable screening tool to accurately identify individuals-at-risk among the general population. [Figure presented]

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**Author e-mail address:** rhodaau@bu.edu

**Conference country:** United States

**Conference end date:** 2018-07-26

**Conference location:** Chicago, IL

**Conference start date:** 2018-07-22

**Conference title:** Alzheimer's Association International Conference 2018

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**Subject:** Embase;biological marker (major);adult;Agnostic;classifier;cognitive defect (major);conference abstract +;controlled study;diagnosis;female;genetic transcription;human;major clinical study;male;natural language processing;population;random forest;sample size;speech;validation study;voice (major)

**Updates:** 2018-10-26

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Document 279

## **AUTOMATIC DETECTION OF LINGUISTIC INDICATORS AS A MEANS OF EARLY PREDICTION OF ALZHEIMER'S AND OF RELATED DEMENTIAS: A CROSS-LINGUISTICS ANALYSIS**

**Author:** Rentoumi, Vassiliki 1 ; Paliouras, George 1 ; Arfani, Dimitra 2 ; Fragkopoulou, Katerina 2 ; Varlokosta, Spyridoula 2 ; Garrard, Peter 3

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 14.7: P1302. Elsevier Inc. (Jul 2018)

**Abstract (summary):** Background: Alzheimer's disease (AD) and other types of dementia are associated with changes in spoken language, but the impact of these changes on different languages has not been extensively examined or compared. In this direction iASiS intends to pave the way towards personalized medicine for AD patients integrating and analyzing data from various sources and languages. In the present study which is performed within the context of iASiS we analysed samples obtained from native speakers of Greek and English who were at mild and moderate stages of probable Alzheimer's disease. Methods: We evaluated differences in spoken language between AD patients and normal controls using novel quantitative methods. We searched for the most important sources of variation between the groups in the two languages. Most importantly, we tried to identify AD-induced language characteristics that are either cross-linguistic or language-specific. We adopted a computational approach for the comparison of morpho-syntactic complexity and lexical variety in digitised transcripts of speech produced by AD patients at various stages and by age-matched cognitively normal controls (NC). We used text classification approaches to assign the samples to one of the two groups. The classifiers were tested using various features: morpho-syntactic, lexical as well as complex statistical characteristics. Results: Preliminary findings indicate that syntactic and lexical complexity can be markers of linguistic change in both languages. The method succeeded in finding linguistic characteristics which differentiated AD patients from NC in mild stages in both languages. Conclusions: The cross-linguistic comparison can contribute to a deeper understanding of language



deficits in Alzheimer's disease, potentially leading to the development of a cross-linguistic diagnostic tool.

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**Conference start date:** 2018-07-22

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+;controlled study;genetic transcription;human;linguistics (major);prediction (major);quantitative  
analysis;speech

**Substance:** Substance Substance: morphine; CAS: 52-26-657-27-2;

**Updates:** 2018-10-26

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Document 280

## The **Voice** of the Heart: Vowel-Like Sound in Pulmonary Artery Hypertension

**Author:** Elgendi, Mohamed 1 ; Bobhate, Prashant 2 ; Jain, Shreepal 2 ; Guo, Long 2 ; Rutledge, Jennifer 3 ; Coe, Yashu 4 ; Zemp, Roger 5 ; Schuurmans, Dale 6 ; Adatia, Ian 4

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**Publication info:** Diseases (Basel, Switzerland) 6.2 (Apr 13, 2018)

**Abstract (summary):** Increased blood pressure in the pulmonary artery is referred to as pulmonary hypertension and often is linked to loud pulmonic valve closures. For the purpose of this paper, it was hypothesized that pulmonary circulation vibrations will create sounds similar to sounds created by **vocal** cords during **speech** and that subjects with pulmonary artery hypertension (PAH) could have unique sound **signatures** across four auscultatory sites. Using a digital stethoscope, heart sounds were recorded at the cardiac apex, 2nd left intercostal space (2LICS), 2nd right intercostal space (2RICS), and 4th left intercostal space (4LICS) undergoing simultaneous cardiac catheterization. From the collected heart sounds, relative power of the frequency band, energy of the sinusoid formants, and entropy were extracted. PAH subjects were differentiated by applying the linear discriminant analysis with leave-one-out cross-validation. The entropy of the first sinusoid formant decreased significantly in subjects with a mean pulmonary artery pressure (mPAp)  $\geq$  25 mmHg versus subjects with a mPAp <25 mmHg with a sensitivity of 84% and specificity of 88.57%, within a 10-s optimized window length for heart sounds recorded at the 2LICS. First sinusoid formant entropy reduction of heart sounds in PAH subjects suggests the existence of a vowel-like pattern. Pattern analysis revealed a unique sound **signature**, which could be used in non-invasive screening tools.

**Accession number:** 29652794

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Document 281

## **Dysprosody markers in PPA**

**Author:** Nevler, Naomi 1 ; Ash, Sharon 1 ; Irwin, David 1 ; Liberman, Mark 1 ; Grossman, Murray 1

1 University of Pennsylvania, Philadelphia, PA, United States

**Publication info:** Neurology, suppl. Supplement 1 90.15 Lippincott Williams and Wilkins. (Apr 2018)

**Abstract (summary):** Objective: To quantify objective markers of dysprosody in Primary Progressive Aphasia (PPA) and relate them to specific clinico-anatomic features. Background: Most research in prosody has relied on subjective assessments, often focusing on emotional elements. We developed an automated technique of speech analysis, the Speech Activity Detector (SAD), to examine the

prosodic characteristics of **speech** in patients with PPA. We hypothesized distinct acoustic **markers** of dysprosody in variants of PPA. Design/Methods: We analyzed semistructured, digitized **speech** samples from 49 aphasic patients (naPPA=14, svPPA=18, lvPPA=17; age range 50-85 years, 43% males) and 31 matched healthy controls (age range 54-89 years, 36% males). We implemented an automated, **speech** analysis protocol, and extracted acoustic measurements of fundamental frequency (f0) and **speech** and pause durations. We then calculated f0 range and pause rate per minute and compared these between the groups and examined their relationships with clinical tests, grey matter atrophy, and CSF levels of phosphorylated tau. Results: We found narrowed f0 range in patients with naPPA (mean  $3.96 \pm 1.14$  semitones) compared with healthy controls ( $6.06 \pm 1.95$  semitones;  $p=0.003$ ) and patients with svPPA ( $5.85 \pm 1.96$  semitones;  $p=0.023$ ). Mean pause rate was significantly increased in naPPA (mean  $58.7 \pm 21.4$  pauses per minute). ROC curve analysis for a combined classifier (pause-rate/f0-range) gave an AUC of 93% for detection of naPPA versus healthy controls and 84% for distinguishing naPPA from svPPA. Regression analysis associated f0 range in non-fluent patients with cortical atrophy in their left premotor and middle temporal cortices. In a subset of patients, CSF level of phosphorylated tau was associated with abnormal acoustic features of **speech**. Conclusions: This study validates the implementation of SAD in the clinical evaluation of patients with variants of PPA, and suggests that this tool may provide effective and inexpensive means for screening and monitoring disease in PPA.

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**Conference end date:** 2018-04-27

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**Conference start date:** 2018-04-21

**Conference title:** 70th Annual Meeting of the American Academy of Neurology, AAN 2018

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**Correspondence author:** Nevler, Naomi University of Pennsylvania, Philadelphia, PA, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Language:** English

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**Publication type:** Journal

**Publisher:** Lippincott Williams and Wilkins

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;endogenous compound;tau protein;adult;aged;aphasia;brain cortex atrophy;classifier;clinical article;clinical evaluation;conference abstract +;controlled study;female;gene expression;gray matter;human;human tissue;male;middle aged;monitoring;protein expression;receiver operating characteristic;regression analysis;speech analysis;temporal cortex

**Updates:** 2018-05-29

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Document 282

## **Language disturbance as a predictor of psychosis onset in youth at enhanced clinical risk**

**Author:** Corcoran, Cheryl 1 ; Carrillo, Facundo 2 ; Slezak, Diego Fernández 2 ; Klim, Casimir 3 ; Bedi, Gillinder 4 ; Javitt, Daniel 5 ; Bearden, Carrie 6 ; Cecchi, Guillermo 7

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**Publication info:** Schizophrenia Bulletin, suppl. Supplement 1 44 : S43-S44. Oxford University Press. (Apr 2018)

**Abstract (summary):** Background: Language offers a privileged view into the mind; it is the basis by which we infer others' thoughts. Subtle language disturbance is evident in schizophrenia prior to psychosis onset, including decreases in coherence and complexity, as measured using clinical ratings in familial and clinical high-risk (CHR) cohorts. Bearden et al previously used manual linguistic analysis of baseline speech transcripts in CHR to show that illogical and referential thinking, and poverty of content, predict later psychosis onset. Then, Bedi et al used automated natural language processing (NLP) of CHR transcripts to show that decreased semantic coherence and reduction in syntactic complexity predicted psychosis onset. To determine validity and reproducibility, we have applied automated NLP methods, with machine learning, to Bearden's original CHR transcripts to identify a language profile predictive of psychosis. Methods: Participants in the Bearden UCLA cohort include 59 CHR, of whom 19 developed psychosis (CHR+) within 2 years, whereas 40 did not (CHR-), as well as 16 recent-onset psychosis and 21 healthy individuals, similar in demographics; speech was

elicited using Caplan's 'Story Game. Participants in the Bedi NYC cohort include 34 CHR (29 CHR+), with **speech** elicited using open-ended interview. **Speech** was audiotaped, transcribed, de-identified and then subjected to latent semantic analysis to determine coherence and part-of-**speech** tagging to characterize syntactic structure and complexity. A **machine-learning speech** classifier of psychosis onset was derived from the UCLA CHR cohort, and then applied both to the NYC CHR cohort and to the UCLA psychosis/control comparison, with convex hull (three-dimension depiction of model) and receiver operating characteristics analyses. Correlational analyses with demographics, symptoms and manual linguistic features were also done. Results: A four-factor model language classifier derived from the UCLA CHR cohort that comprised three semantic coherence variables and one syntax (usage of possessive pronouns) predicted psychosis with accuracy of 83% (intra-protocol) for UCLA CHR, 79% (cross-protocol) for NYC CHR, and 72% for discriminating psychosis from normal **speech** (UCLA psychosis/control). Convex hulls were defined as the smallest space containing all datapoints within a set for CHR- or healthy controls: these convex hulls showed substantial overlap, with CHR+ and psychosis **speech** datapoints largely outside these convex hulls. Coherence was associated with age, but **speech** variables did not vary by gender, race, or socioeconomic status in this study. While automated text features were unrelated to prodromal symptom severity, they were highly correlated with manual text features ( $r = 0.7, p < .000001$ ). Discussion: In this small preliminary study, we identified and cross-validated a robust language classifier of psychosis risk that comprised measures of semantic coherence (flow of meaning in language) and syntactic usage (usage of possessive pronouns). This classifier had utility in discriminating **speech** in individuals with recent-onset psychosis from the norm. It demonstrated concurrent validity in that it was highly correlated with manual linguistic features previously identified by Bearden et al, important as automated methods are fast and inexpensive. Automated language features were unrelated to sex, ethnicity or social class in these small samples, and semantic coherence increased with age, consistent with prior studies of normal language development. Of interest, overlapping convex hulls could be defined for groups of individuals without psychosis (UCLA CHR-, NYC CHR- and UCLA healthy), suggesting a constrained hull of normal language in respect to syntax and semantics, from which pre-psychosis and psychosis **speech** deviates. The RDoC linguistic corpus-based variables of semantic coherence and syntactic structure hold promise as **biomarkers** of psychosis risk and expression, with initial validation and reproducibility. Next steps in **biomarker** development include larger multisite studies with standardization of protocols for **speech** elicitation, test-retest, and attention to traction/feasibility, acceptability, cost, and utility. Mechanistic studies can also yield neural and physiological correlates of abnormal semantic coherence and syntax.

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**Conference country:** Italy

**Conference end date:** 2018-04-08

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**Conference start date:** 2018-04-04

**Conference title:** 6th Biennial Schizophrenia International Research Society Conference, SIRS 2018

**Copyright:** Copyright 2018 Elsevier B.V., All rights reserved.

**Correspondence author:** Corcoran, Cheryl Icahn School of Medicine at Mount Sinai, Los Angeles, United States.

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**Document type:** Conference Abstract

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**Subject:** Embase;biological marker;adult;age;attention;classifier;clinical article;cohort analysis;concurrent validity;conference abstract +;ethnicity;feasibility study;female;gender;human;interview;juvenile (major);language development (major);male;natural language processing;nervous system;prodromal symptom;psychosis (major);race;receiver operating characteristic;reproducibility;semantics;social class;speech;standardization;traction therapy;validation process

**Updates:** 2018-05-04

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Document 283

## **Electronic monitoring in bipolar disorder**

**Author:** Faurholt-Jepsen, Maria 1

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**Publication info:** Danish Medical Journal 65.3 Danish Medical Association. (Mar 2018)

**Abstract (summary):** Major reasons for the insufficient effects of current treatment options in bipolar disorder include delayed intervention for pro-dromal depressive and manic symptoms and decreased adherence to psychopharmacological treatment. The reliance on subjective information and clinical evaluations when diagnosing and assessing the severity of depressive and manic symptoms calls for less biased and more objective **markers**. By using electronic devices, fine-grained data on complex psychopathological aspects of bipolar disorder can be evaluated unobtrusively over the long term. Moreover, electronic data could possibly represent candidate **markers** of diagnosis and illness activity in bipolar disorder and allow for early and individualized intervention for prodromal symptoms outside clinical settings. The present dissertation concerns the use of electronic monitoring as a **marker** and treatment intervention in bipolar disorder and investigated the scientific literature and body of evidence within the area, which includes ten original study reports and two systematic reviews, one of which included a meta-analysis, conducted by the author of the dissertation. Taken together, the literature presented in this dissertation illustrates that 1) smartphone-based electronic self-monitoring of mood seems to reflect clinically assessed depressive and manic symptoms and enables the long-term characterization of mood instability in bipolar disorder; 2) preliminary results suggest that smartphone-based automatically generated data (e.g. the number of text messages sent/day; the number of incoming and outgoing calls/day; the number of changes in cell tower IDs/day; and **voice** features) seem to reflect clinically assessed depressive and manic symptoms in bipolar disorder; 3) smartphone-based electronic self-monitoring had no effects on the severity of depressive and manic symptoms in bipolar disorder, according to a randomized controlled trial; and 4) electronic monitoring of psychomotor activity and heart rate variability seems to reflect illness activity in bipolar disorder and differentiate between patients with bipolar disorder and healthy control individuals. These findings point toward the usefulness of electronic monitoring as a **marker** of illness in bipolar disorder. Using electronic monitoring as a treatment intervention could provide innovative and novel interventions on-demand with a potential global reach, filling the gap between availability and the need for treatment. However, future studies using rigorous methodology and more randomized controlled trials that carefully investigate the positive effects and possible harmful effects of electronic monitoring in bipolar disorder are needed. In addition, patient safety, privacy issues, data security and legal aspects are major concerns that must be considered and addressed when using electronic monitoring.

**Accession number:** 621085192

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**Correspondence author:** Faurholt-Jepsen, Maria Department O, Psychiatric Center Copenhagen, Rigshospitalet, University of Copenhagen, Denmark.

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**Date created:** 2018-08-24

**Document status:** Revised

**Document type:** Article



**Embase document status:** Embase; MEDLINE

**First available:** 2018-03-13

**Language:** English

**Language of abstract:** English

**Number of references:** 327

**Publication date:** Mar 2018

**Publication type:** Journal

**Publisher:** Danish Medical Association

**Publisher location:** Denmark

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**Subject:** Embase;MEDLINE;smartphone;Article;bipolar disorder (major);clinical assessment;depression;disease severity;heart rate variability;human;intention to treat analysis;machine learning;mania;mental health;mental instability;meta analysis (topic);monitoring (major);mortality;outcome assessment;patient care;prevalence;psychomotor activity;quality of life;randomized controlled trial (topic);scoring system;self monitoring;sensitivity and specificity;systematic review (topic)

**Updates:** 2018-03-132018-03-272018-09-11

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Document 284

## **Combining speech sample and feature bilateral selection algorithm for classification of Parkinson's disease**

**Author:** Zhang, Xiaoheng 1 ; Wang, Lirui 2 ; Cao, Yao 2 ; Wang, Pin 2 ; Zhang, Cheng 2 ; Yang, Liuyang 2 ; Li, Yongming 3 ; Zhang, Yanling 4 ; Cheng, Oumei 5

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**Publication info:** Sheng wu yi xue gong cheng xue za zhi = Journal of biomedical engineering = Shengwu yixue gongchengxue zazhi 34.6: 942-948. NLM (Medline). (Feb 1, 2018)

**Abstract (summary):** Diagnosis of Parkinson's disease (PD) based on speech data has been proved to be an effective way in recent years. However, current researches just care about the feature extraction and classifier design, and do not consider the instance selection. Former research

by authors showed that the instance selection can lead to improvement on classification accuracy. However, no attention is paid on the relationship between **speech** sample and feature until now. Therefore, a new diagnosis algorithm of PD is proposed in this paper by simultaneously selecting **speech** sample and feature based on relevant feature weighting algorithm and multiple kernel method, so as to find their synergy effects, thereby improving classification accuracy. Experimental results showed that this proposed algorithm obtained apparent improvement on classification accuracy. It can obtain mean classification accuracy of 82.5%, which was 30.5% higher than the relevant algorithm. Besides, the proposed algorithm detected the synergy effects of **speech** sample and feature, which is valuable for **speech marker** extraction.

**Accession number:** 630491123

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**Copyright:** This record is sourced from MEDLINE/PubMed, a database of the U.S. National Library of Medicine

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**First available:** 2020-01-08

**Identifier (keyword):** bilateral hybrid **speech** feature selection, classification, multiple kernel learning, Parkinson's disease, synergy effects

**Language:** Chinese

**Language of abstract:** English

**Publication date:** Feb 1, 2018

**Publication type:** Journal

**Publisher:** NLM (Medline)

**Publisher location:** China

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**Subject:** MEDLINE;algorithm;article;attention;extraction;**feature selection** (major);human;**kernel method**;learning (major);Parkinson disease (major);**speech analysis** (major)

**Updates:** 2020-01-08

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Document 285

## **The ALS mobile analyzer: Monitor disease progression using a mobile app**

**Author:** Snir, Yehuda 1 ; Davis, Noa 1 ; Ron, Idit 1 ; Rishoni, Shay 1

1 Prize4life, Ramat Hasharon, Israel ndavis@prize4life.org

**Publication info:** Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, suppl. Supplement 1 19 : 297. Taylor and Francis Ltd. (2018)

**Abstract (summary):** Background: The rapidly evolving mobile technology offers a unique opportunity for the development of much needed novel tools for continuous, accurate and accessible monitoring of ALS patients in their home environment. Such tools will generate large-scale functional data for ALS research, facilitate better and more responsive clinical care for patients and accelerate ALS drug development by supporting faster, smaller and more efficient clinical trials. Objectives: We aimed to use the widely available smartphone mobile technology to develop an application that collects objective, detailed and frequently sampled information about patients' clinical and functional status. The collected data can be used to better characterize disease course and to develop novel **digital biomarkers** of disease progression. Methods: The ALS Analyzer mobile app was launched in November 2015 and is available as a free mobile app for Android and iOS platforms. A new and improved version was released on June 2018. The app includes a self-reported **digital** version of the ALSFRS-R questionnaire and a series of tasks that estimate patients' functional abilities in all relevant functional domains: breathing capacity tests, **speech** tests to evaluate **dysarthria**, line tracing and finger tapping tests (fine motor skills), arm gross motor test and walking test. All relevant demographic information and self-reported ALSFRS-R scores are also collected through the app. A clinical validation study was initiated on June 2018, aimed to study the correlation between the standard questionnaire and the scores given by the app. Results: Over 400 ALS patients and 500 controls used the app since its launch. The accumulated data are used to find thresholds separating patients from controls and to detect different levels of dysfunction in ALS patients. Discussion and conclusions: The ALS mobile Analyzer harnesses the latest technology to collect large scale real world functional data from ALS patients worldwide and to create novel ALS disease progression **digital biomarker**. These objective, frequently collected, sensitive **digital** measurements could revolutionize ALS research, clinical care and clinical trials.

**Accession number:** 625667300

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**Conference country:** United Kingdom

**Conference end date:** 2018-12-09

**Conference location:** Glasgow

**Conference start date:** 2018-12-07

**Conference title:** 29th International Symposium on ALS/MND

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**Correspondence author:** Davis, Noa Prize4life, Ramat Hasharon, Israel.

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**DOI:** <http://dx.doi.org/10.1080/21678421.2018.1510580>

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**First available:** 2018-12-31

**Identifier (keyword):** Disease progression, Mobile app, Monitoring

**Language:** English

**Language of abstract:** English

**Publication date:** 2018

**Publication type:** Journal

**Publisher:** Taylor and Francis Ltd

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;adult;analyzer (major);breathing;conference abstract +;controlled study;disease exacerbation (major);dysarthria;finger tapping test;functional status;human;human cell;human tissue;in vitro study;mobile application (major);monitoring (major);motor performance;questionnaire;smartphone;speech test;validation study;walk test

**Updates:** 2018-12-31

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Document 286

### **Use of **speech** analyses within a mobile application for the assessment of cognitive impairment in elderly people**

**Author:** König, Alexandra 1 ; Satt, Aharon 2 ; Sorin, Alex 2 ; Hoory, Ran 2 ; Derreumaux, Alexandre 3 ; David, Renaud 4 ; Robert, Phillippe H. 4

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Sophia Antipolis, Nice, France, Centre Mémoire de Ressources et de Recherche, CHU de Nice, Nice, France, Association Innovation Alzheimer, Nice, France

**Publication info:** Current Alzheimer Research 15.2: 120-129. Bentham Science Publishers B.V. (2018)

**Abstract (summary):** Background: Various types of dementia and Mild Cognitive Impairment (MCI) are manifested as irregularities in human **speech** and language, which have proven to be strong predictors for the disease presence and progression. Therefore, automatic **speech** analytics provided by a mobile application may be a useful tool in providing additional indicators for assessment and detection of early stage dementia and MCI. Method: 165 participants (subjects with subjective cognitive impairment (SCI), MCI patients, Alzheimer's disease (AD) and mixed dementia (MD) patients) were recorded with a mobile application while performing several short **vocal** cognitive tasks during a regular consultation. These tasks included verbal fluency, picture description, counting down and a free **speech** task. The **voice** recordings were processed in two steps: in the first step, **vocal markers** were extracted using **speech** signal processing techniques; in the second, the **vocal markers** were tested to assess their 'power' to distinguish between SCI, MCI, AD and MD. The second step included training automatic classifiers for detecting MCI and AD, based on **machine learning** methods, and testing the detection accuracy. Results: The fluency and free **speech** tasks obtain the highest accuracy rates of classifying AD vs. MD vs. MCI vs. SCI. Using the data, we demonstrated classification accuracy as follows: SCI vs. AD = 92% accuracy; SCI vs. MD = 92% accuracy; SCI vs. MCI = 86% accuracy and MCI vs. AD = 86%. Conclusions: Our results indicate the potential value of **vocal** analytics and the use of a mobile application for accurate automatic differentiation between SCI, MCI and AD. This tool can provide the clinician with meaningful information for assessment and monitoring of people with MCI and AD based on a non-invasive, simple and low-cost method.

**Accession number:** 620867073

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**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2018-03-08

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**Document type:** Article

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This study was supported by grants from the FP7 Dem@care project, (grant number 288199) by the Innovation Alzheimer association, by the IBM Speech Lab in Haifa, Israel. The CoBTeK (Cognition-Behaviour-Technology) Research Unit from the Nice Sophia-Antipolis University (UNS) located at the Institut Claude Pompidou in the Edmond and Lilly Safra research center, the Nice CHU Memory Center (platform of the CIU-S). Thank to the foundation Claude Pompidou for providing such facilities. Final great thanks to all participants of the study.

**Identifier (keyword):** Algorithm, Alzheimer, Assessment, Audio analysis, Dementia, Machine learning, MCI, Speech

**Language:** English

**Language of abstract:** English

**Number of references:** 50

**Publication date:** 2018

**Publication type:** Journal

**Publisher:** Bentham Science Publishers B.V.

**Publisher location:** P.O. Box 294, 1400 AG, Netherlands

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**Subject:** Embase;MEDLINE;accuracy;aged;Alzheimer disease;Article;cognitive defect (major);dementia;disease classification;female;human;machine learning;major clinical study;male;mild cognitive impairment;Mini Mental State Examination;mixed dementia +;mobile application (major);priority journal;speech analysis (major);subjective cognitive impairment +

**Updates:** 2018-03-062018-03-092018-11-232019-03-12

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Document 287

## **Machine learning using speech utterances for parkinson disease detection**

**Author:** Klempíř, Ondřej 1 ; Krupička, Radim 1

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**Publication info:** Lekar a Technika 48.2: 66-71. Czech Medical Association J.E. Purkyne. (2018)

**Abstract (summary):** Pathophysiological recordings of patients measured from various testing methods are frequently used in the medical field for determining symptoms as well as for probability prediction for selected diseases. There are numerous symptoms among the Parkinson's disease (PD)

population, however changes in **speech** and articulation are potentially the most significant **biomarker**. This article is focused on PD diagnosis classification based on their **speech** signals using pattern recognition methods (AdaBoost, Bagged trees, Quadratic **SVM** and k-NN). The dataset investigated in the article consists of 30 PD and 30 healthy controls (HC) individuals **voice** measurements, with each individual being represented with 2 recordings within the dataset. Training signals for PD and HC underwent an extraction of relatively well-discriminating features relating to energy and spectral **speech** properties. Model implementations included a 5-fold cross validation. The accuracy of values obtained by employing the models was calculated using a confusion matrix. The average value of the overall accuracy = 82.3% and averaged AUC = 0.88 (min. AUC = 0.86) on the available data.

**Accession number:** 625146644

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**Date created:** 2018-12-04

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This study was supported by the Grant no. SGS18/102/OHK4/1T/17 "The Application of Data Mining Techniques to Heterogeneous Biomedical Sources", Grant Agency of the Czech Technical University in Prague. Further thanks to the Department of Neurology, 1st Faculty of Medicine, Charles University and Faculty of Electrical Engineering, CTU in Prague, namely Jan Ruzs, Ph.D., for providing the research dataset.

**Identifier (keyword):** Classification, Digital **biomarker**, **Machine learning**, Parkinson's disease, **Speech**

**Language:** English

**Language of abstract:** English

**Number of references:** 20

**Publication date:** 2018

**Publication type:** Journal

**Publisher:** Czech Medical Association J.E. Purkyne

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**Subject:** Embase;biological marker (major);adaboost +;area under the curve;Article;audio recording;automated pattern recognition;bagged tree +;clinical article;controlled study;decision tree;diagnostic accuracy;feature extraction;human;k nearest neighbor;kernel method;machine learning (major);male;Parkinson disease -- diagnosis (major);quadratic support vector machine +;speech analysis (major);speech disorder;support vector machine;voice analysis

**Updates:** 2018-11-292018-12-05

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Document 288

## **The ALS mobile analyzer: Monitoring ALS disease progression via smartphone app and identifying novel digital biomarkers**

**Author:** Bronfeld, M. 1 ; Ron, I. 1 ; Rishoni, S. 1

1 Prize4Life, Haifa, Israel ndavis@prize4life.org

**Publication info:** Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, suppl. Supplement 2 18 : 269-270. Taylor and Francis Ltd. (Nov 2017)

**Abstract (summary):** Background: The rapidly evolving mobile technology offers a unique opportunity for the development of much needed novel tools for continuous, accurate and accessible monitoring of ALS patients in their home environment. Such tools will generate large scale functional data for ALS research, facilitate better and more responsive clinical care for patients and accelerate ALS drug development by supporting faster, smaller and more efficient clinical trials. Objectives: We aimed to use the widely available smartphone mobile technology to develop an application that collects objective, detailed and frequently sampled information about patients' clinical and functional status. The collected data can be used to better characterize disease course and to develop novel digital biomarkers of disease progression. Methods: The ALS Analyzer mobile app was launched in November 2015 and is available as a free mobile app for Android and iOS platforms. The app includes a self-reported digital version of the ALSFRS-R questionnaire and a series of tasks that estimate patients' functional abilities in all relevant functional domains: breathing capacity tests, speech tests to evaluate dysarthria, line tracing and finger tapping tests (fine motor skills), arm gross motor test and walking test. All relevant demographic information and self-reported ALSFRS-R scores are also collected through the app. The app's tasks can be completed by patients anytime, anywhere and require none or minimal assistance. All functional data is recorded via the phone's built-in sensors with no additional devices needed, making the app readily available for use by patients all over the



world with only the click of a button. A range of task-specific performance parameters are recorded, allowing the development of in-depth informative analysis schemes. Results: Over 200 ALS patients and 300 controls used the app since its launch, roughly a quarter of them using it repeatedly. Unique algorithms were developed to analyze performance in each functional task. The accumulated data was used to find thresholds separating patients from controls and to detect different levels of dysfunction in ALS patients. Discussion and conclusions: The ALS Analyzer mobile app harnesses the latest technology to collect large scale real world functional data from ALS patients worldwide and to create a novel ALS disease progression **digital biomarker**. These objective, frequently collected, sensitive **digital** measurements could revolutionize ALS research, clinical care and clinical trials.

**Accession number:** 619349690

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**Conference country:** United States

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**Conference start date:** 2017-12-08

**Conference title:** 28th International Symposium on ALS/MND

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**Correspondence author:** Bronfeld, M. Prize4Life, Haifa, Israel.

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**Identifier (keyword):** Clinical assessment, **Digital** health, Disease progression

**Language:** English

**Language of abstract:** English

**Publication date:** Nov 2017

**Publication type:** Journal

**Publisher:** Taylor and Francis Ltd

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker (major);adult;analyzer (major);breathing;clinical trial;controlled clinical trial;controlled study;disease course (major);dysarthria;female;finger tapping test;functional status;human;human cell;human tissue;in vitro study;major clinical study;male;mobile application;monitoring (major);motor performance;questionnaire;sensor;smartphone (major);speech test;walk test

**Updates:** 2017-11-24

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Document 289

## **Toward clinical application of landmark-based speech analysis: Landmark expression in normal adult speech**

**Author:** Ishikawa, Keiko 1 ; MacAuslan, Joel 2 ; Boyce, Suzanne 3

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**Publication info:** The Journal of the Acoustical Society of America 142.5: EL441. (Nov 2017)

**Abstract (summary):** The goal of clinical speech analysis is to describe abnormalities in speech production that affect a speaker's intelligibility. Landmark analysis identifies abrupt changes in a speech signal and classifies them according to their acoustic profiles. These acoustic markers, called landmarks, may help describe intelligibility deficits in disordered speech. As a first step toward clinical application of landmark analysis, the present study describes expression of landmarks in normal speech. Results of the study revealed that syllabic, glottal, and burst landmarks consist of 94% of all landmarks, and suggest the effect of gender needs to be considered for the analysis.

**Accession number:** 29195420

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**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Document type:** Comparative Study, Journal Article, Research Support, N.I.H., Extramural

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R42 AG033523. NIA NIH HHS. United States.

R41 DC005534. NIDCD NIH HHS. United States.

R42 DC005534. NIDCD NIH HHS. United States.

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**Language:** English

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**Medline document status:** MEDLINE

**MeSH:** Acoustics (major);Adult;Female;Humans;Male;Middle Aged;Pattern Recognition, Automated;Sex Factors;Signal Processing, Computer-Assisted (major);Sound Spectrography;Speech Acoustics (major);Speech Intelligibility (major);Speech Production Measurement -- methods (major);Voice Quality (major);Young Adult

**Notes:** Publication model: Print;; Cited medium:Internet

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**Updates:** 2017-12-032017-12-052017-12-152017-12-192017-12-202019-05-242019-07-17

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Document 290

**Special issue on “Bioinspired intelligence for machine learning”**

**Author:** López-de-Ipiña, Karmele 1 ; Barroso, Nora 1

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**Publication info:** Neurocomputing 255 : 1-2. Elsevier B.V. (Sep 13, 2017)

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**Correspondence author:** López-de-Ipiña, Karmele Engineering and Society research group, EleKin, elekin.net, Department of Systems Engineering and Automation, Universidad del País Vasco/Euskal Herriko Unibertsitatea (UPV/EHU), Donostia, Spain.

**Database:** Embase®; 1947 to date (1947 - current)

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**First available:** 2017-04-19

**Language:** English

**Publication date:** Sep 13, 2017

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**Publisher:** Elsevier B.V.

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**Subject:** Embase;biological marker;intelligence (major);machine learning (major);artificial intelligence (major);artificial neural network;bioengineering;biomechanics;biomedicine;biosensor;classification;control system;Editorial;emotionality;human;image processing;mathematical computing;methodology;Parkinson disease;phonation;priority journal;quality control;remote sensing;robotics

**Updates:** 2017-04-192017-06-192017-06-23

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Document 291

## Functional neural circuits that underlie developmental stuttering

**Author:** Qiao, Jianping 1 ; Wang, Zhishun 2 ; Zhao, Guihu 3 ; Huo, Yuankai 2 ; Herder, Carl L 4 ; Sikora, Chamonix O 4 ; Peterson, Bradley S 5

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**Publication info:** PloS one 12.7: e0179255. (Jul 31, 2017)

**Abstract (summary):** The aim of this study was to identify differences in functional and effective brain connectivity between persons who stutter (PWS) and typically developing (TD) fluent speakers, and to assess whether those differences can serve as **biomarkers** to distinguish PWS from TD controls. We acquired resting-state functional magnetic resonance imaging data in 44 PWS and 50 TD controls. We then used Independent Component Analysis (ICA) together with Hierarchical Partner Matching (HPM) to identify networks of robust, functionally connected brain regions that were highly reproducible across participants, and we assessed whether connectivity differed significantly across diagnostic groups. We then used Granger Causality (GC) to study the causal interactions (effective connectivity) between the regions that ICA and HPM identified. Finally, we used a kernel **support vector machine** to assess how well these measures of functional connectivity and granger causality discriminate PWS from TD controls. Functional connectivity was stronger in PWS compared with TD controls in the supplementary motor area (SMA) and primary motor cortices, but weaker in inferior frontal cortex (IFG, Broca's area), caudate, putamen, and thalamus. Additionally, causal influences were significantly weaker in PWS from the IFG to SMA, and from the basal ganglia to IFG through the thalamus, compared to TD controls. ICA and GC indices together yielded an accuracy of 92.7% in classifying PWS from TD controls. Our findings suggest the presence of dysfunctional circuits that support **speech** planning and timing cues for the initiation and execution of motor sequences in PWS. Our high accuracy of classification further suggests that these aberrant brain features may serve as robust **biomarkers** for PWS.

**Accession number:** 28759567

**Correspondence author:** Qiao, Jianping School of Physics and Electronics, Shandong Province Key Laboratory of Medical Physics and Image Processing Technology, Institute of Data Science and Technology, Shandong Normal University, Jinan, China. , Department of Psychiatry, Columbia University, New York, NY, United States of America.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2017-10-17

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**Date revised:** 2018-11-13

**Document status:** Revised

**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1371/journal.pone.0179255>

**First available:** 2017-08-01

**Language:** English

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**Medline document status:** MEDLINE

**MeSH:** Adolescent;Adult;Algorithms;Basal Ganglia -- physiopathology;Brain -- diagnostic imaging (major);Brain -- physiopathology (major);Brain Mapping;Case-Control Studies;Child;Female;Humans;Machine Learning;Magnetic Resonance Imaging;Male;Middle Aged;Motor Cortex -- physiopathology;Nerve Net -- physiopathology (major);Neural Pathways -- physiopathology (major);Principal Component Analysis;Reproducibility of Results;Speech;Stuttering -- diagnostic imaging (major);Stuttering -- physiopathology (major);Young Adult

**Notes:** Publication model: Electronic-eCollection;; Cited medium:Internet

**Publication date:** Jul 31, 2017

**Publication type:** Journal

**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

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Document 292

### **Early detection of cognitive disorders such as dementia on the basis of speech analysis: A crosslinguistic comparison of speech features**

**Author:** Konig, Alexandra 1 ; Rudzicz, Frank 2 ; Fraser, Kathleen C. 3 ; Kaufman, Liam 4 ; Alexandersson, Jan 5 ; Linz, Nicklas 5 ; Tröger, Johannes 5 ; Wolters, Maria 6 ; Bremond, Francois 7 ; Robert, Philippe 8

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**Publication info:** Alzheimer's and Dementia 13.7: P364. Elsevier Inc. (Jul 2017)

**Abstract (summary):** Background: The people best placed to spot early cognitive decline are carers, social workers, and family. But there is a clear lack of affordable, usable screening apps that people without medical training can use to validate these concerns and to provide actionable data for medical professionals. The study aims to validate a new tool for fully-automated, reliable, unobtrusive, self-managed screening for cognitive decline, in particular dementia, and other cognitive disorders based on automatic **speech** analysis. It will allow earlier detection and, through that, more effective interventions resulting in the reduction of overall costs associated with treatment and rehabilitation. For users it will offer the comfort of flexible usage without visiting professional physicians. Methods: At the moment there is an American English corpus of **speech** data used for training the algorithms of the system used by the tool for automatic detection of dementia in the USA and Canada. The main objective of the study will be the first experience in producing such corpus for another language, namely French. The corpus will contain ca. 250 samples of **speech** of patients with various levels of the syndrome, as well as other cognitive and behavioral disorders and ca. 50 samples of healthy people as a control group. All participants will be asked to perform a set of **vocal** tasks such as describing a series of images or perform verbal fluencies. Then, all **speech** samples will be transcribed and annotated by professional clinicians to make the corpus suitable for **machine learning** and identify which features transfer between languages. The processes, tools and experiences will be then presented in the blueprint for transferring the system into a new language. Results: First results of the analysis and cross linguistic comparison of the **speech** features will be presented at the conference. Conclusions: The proposed solution may supplement neuropsychological assessment with sophisticated and unobtrusive natural **biomarkers** extracted from **speech** data that can be collected outside of medical consultations. It can provide rich information about cognitive and emotional characteristics and can be used to inform clinical judgment during consultations, saving time and money.

**Accession number:** 620610517

**Author e-mail address:** akonig03@gmail.com

**Conference country:** United Kingdom

**Conference end date:** 2017-07-20

**Conference location:** London

**Conference start date:** 2017-07-14

**Conference title:** Alzheimer's Association International Conference, AAIC 2017

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**Correspondence author:** Konig, Alexandra Association Innovation Alzheimer, CoBTek - Cognition Behaviour Technology Research Unit, Université Côte d'Azur, Nice, France.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2018-02-13

**Document status:** New

**Document type:** Conference Abstract

**Embase document status:** Embase

**First available:** 2018-02-13

**Language:** English

**Language of abstract:** English

**Publication date:** Jul 2017

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**Publisher:** Elsevier Inc.

**Publisher location:** Netherlands

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**Subject:** Embase; biological marker; adult; behavior disorder; Canada; cognitive defect (major); comfort; conference abstract +; consultation; controlled study; decision making; female; genetic transcription; human; human tissue; language; machine learning; major clinical study; male; money; physician; rehabilitation; speech analysis (major); syndrome

**Updates:** 2018-02-13

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Document 293

## **Improving diagnostic accuracy of Alzheimer's disease from speech analysis using markers of hemispatial neglect**

**Author:** Field, Thalia S. 1 ; Masrani, Vaden 1 ; Murray, Gabriel 2 ; Carenni, Giuseppe 1

1 University of British Columbia, Vancouver, BC, Canada thalia.field@ubc.ca 2 University of the Fraser Valley, Abbotsford, BC, Canada

**Publication info:** Alzheimer's and Dementia 13.7: P157-P158. Elsevier Inc. (Jul 2017)



**Abstract (summary):** Background: Machine learning has been previously used to distinguish patients with Alzheimer's disease (AD) versus healthy controls using transcripts of descriptions of the "Cookie Theft" picture from the Boston Diagnostic Aphasia Exam. Previous work achieved a positive predictive value (PPV) of 0.83 (95% CI 0.79 - 0.87) and negative predictive value (NPV) of 0.81 (0.74 - 0.88) using lexical (e.g. word choice and complexity) and acoustic (e.g. pauses, prosody) features extracted from interviews. Given that language deficits may be associated with other dominant hemisphere findings, we evaluated the diagnostic utility in adding markers of hemispatial neglect to our previous baseline algorithm. Methods: We used the publicly available DementiaBank dataset (257 interviews from 169 AD patients and 242 interviews with 99 healthy controls). In addition to our baseline algorithm, which included 353 lexical and acoustic markers, we evaluated three approaches to dividing the Cookie Theft image: Halves, strips and quadrants, as seen in figure 1. For each given division, we compiled a list of information units (info-units) that are contained in each region (e.g. the info-units "stool" and "mother" are contained by the left and right halves, respectively). For each region we then recorded four measures from a given transcript: 1) Number of info-units mentioned 2) ratio of info-units to all words 3) ratio of unique info-units to all possible info-units in the region 4) ratio of unique info-units to total mentioned info-units (a measure of redundancy). We also included quadratic interaction terms between regions. We then performed a 10-fold cross validation procedure with a correlation-based feature selection preprocessing phase and trained a logistic regression model using each of the halves, strips, and quadrants approach, and compared against baseline. Results: The halves model [PPV 0.84, 95%CI 0.80-0.86, NPV 0.81(0.74 - 0.88)] and strips model [PPV 0.84 (0.77 - 0.91), NPV 0.82 (0.76 - 0.88)] but not the quadrants model [PPV 0.81 (0.74 - 0.87), NPV 0.81 (0.75 - 0.87)] showed a trend towards improvement from baseline. Conclusions: Including markers of hemispatial neglect to a machine learning algorithm analyzing lexical and acoustic speech features may improve diagnostic accuracy of AD versus healthy controls. (Figure Presented).

**Accession number:** 620610180

**Author e-mail address:** thalia.field@ubc.ca

**Conference country:** United Kingdom

**Conference end date:** 2017-07-20

**Conference location:** London

**Conference start date:** 2017-07-14

**Conference title:** Alzheimer's Association International Conference, AAIC 2017

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**Correspondence author:** Field, Thalia S. University of British Columbia, Vancouver, BC, Canada.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document type:** Conference Abstract

**Embase document status:** Embase

**First available:** 2018-02-13

**Language:** English

**Language of abstract:** English

**Publication date:** Jul 2017

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**Publisher:** Elsevier Inc.

**Publisher location:** Netherlands

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**Subject:** Embase;adult;Alzheimer disease (major);conference abstract +;controlled study;cookie;diagnostic accuracy (major);diagnostic test accuracy study;diagnostic value;feces;female;genetic transcription;human;intermethod comparison;interview;language;machine learning;major clinical study;neglect (major);predictive value;speech analysis (major);theft;validation process

**Updates:** 2018-02-13

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Document 294

### **Predicting rapid progression of Parkinson's Disease at baseline patients evaluation**

**Author:** Tsiouris, Kostas M.; Rigas, Georgios; Gatsios, Dimitrios; Antonini, Angelo; Konitsiotis, Spiros; Koutsouris, Dimitrios D.; Fotiadis, Dimitrios I.

**Publication info:** Conference proceedings : ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference 2017 : 3898-3901. (Jul 1, 2017)

**Abstract (summary):** The rate of Parkinson's Disease (PD) progression in the initial post-diagnosis years can vary significantly. In this work, a methodology for the extraction of the most informative features for predicting rapid progression of the disease is proposed, using public data from the Parkinson's Progression Markers Initiative (PPMI) and machine learning techniques. The aim is to determine if a patient is at risk of expressing rapid progression of PD symptoms from the baseline evaluation and as close to diagnosis as possible. By examining the records of 409 patients from the PPMI dataset, the features with the best predictive value at baseline patient evaluation are found to be sleep problems, daytime sleepiness and fatigue, motor symptoms at legs, cognition impairment, early axial and facial symptoms and in the most rapidly advanced cases speech issues, loss of smell and affected leg muscle reflexes.

**Accession number:** 625117819

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**Document type:** Article

**DOI:** <http://dx.doi.org/10.1109/EMBC.2017.8037708>

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**Publication date:** Jul 1, 2017

**Publication type:** Journal

**Publisher location:** United States

**Source attribution:** Embase, © Publisher specific

**Subject:** MEDLINE;cognitive defect;disease exacerbation;fatigue;human;Parkinson disease (major);sleep stage

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Document 295

## **Predicting mild cognitive impairment from spontaneous spoken utterances**

**Author:** Asgari, Meysam 1 ; Kaye, Jeffrey 2 ; Dodge, Hiroko 3

1 Center for Spoken Language Understanding, Oregon Health & Science University (OHSU), Portland, Oregon, United States [asgari@ohsu.edu](mailto:asgari@ohsu.edu) 2 Department of Neurology, Layton Aging and Alzheimer's Disease Center, Oregon Health & Science University (OHSU), Portland, Oregon, United States 3 Department of Neurology, Layton Aging and Alzheimer's Disease Center, Oregon Health & Science University (OHSU), Portland, Oregon, United States, Department of Neurology, Michigan Alzheimer's Disease Center, University of Michigan, Ann Arbor, Michigan, United States

**Publication info:** Alzheimer's and Dementia: Translational Research and Clinical Interventions 3.2: 219-228. Elsevier Inc. (Jun 1, 2017)

**Abstract (summary):** Introduction Trials in Alzheimer's disease are increasingly focusing on prevention in asymptomatic individuals. We hypothesized that indicators of mild cognitive impairment (MCI) may be present in the content of spoken language in older adults and be useful in distinguishing those with MCI from those who are cognitively intact. To test this hypothesis, we performed linguistic analyses of spoken words in participants with MCI and those with intact cognition participating in a clinical trial. Methods Data came from a randomized controlled behavioral clinical trial to examine the effect of unstructured conversation on cognitive function among older adults with either normal cognition or MCI (ClinicalTrials.gov: NCT01571427). Unstructured conversations (but with standardized preselected topics across subjects) were recorded between interviewers and interviewees during the intervention sessions of the trial from 14 MCI and 27 cognitively intact participants. From the transcription of interviewees recordings, we grouped spoken words using Linguistic Inquiry and Word Count (LIWC), a structured table of words, which categorizes 2500 words into 68 different word subcategories such as positive and negative words, fillers, and physical states. The number of words in each LIWC word subcategory constructed a vector of 68 dimensions representing the linguistic features of each subject. We used **support vector machine** and random forest classifiers to distinguish MCI from cognitively intact participants. Results MCI participants were distinguished from those with intact cognition using linguistic features obtained by LIWC with 84% classification accuracy which is well above chance 60%. Discussion Linguistic analyses of spoken language may be a powerful tool in distinguishing MCI subjects from those with intact cognition. Further studies to assess whether spoken language derived measures could detect changes in cognitive functions in clinical trials are warranted.

**Accession number:** 615026262

**Author e-mail address:** asgari@ohsu.edu

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**Correspondence author:** Asgari, Meysam Center for Spoken Language Understanding, Oregon Health & Science University (OHSU), Portland, Oregon, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**DOI:** <http://dx.doi.org/10.1016/j.trci.2017.01.006>

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**First available:** 2017-04-04

**Identifier (keyword):** **Biomarkers**, Conversational interactions, Early identification, Mild cognitive impairment (MCI), Social markers, **Speech** characteristics

**Language:** English

**Language of abstract:** English

**Number of references:** 40

**Publication date:** Jun 1, 2017

**Publication type:** Journal

**Publisher:** Elsevier Inc

**Publisher location:** United States

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**Subject:** Embase;adult;clinical article;clinical trial;controlled clinical trial;controlled study;conversation;disease carrier;DNA transcription;human;language;mild cognitive impairment (major);random forest;randomized controlled trial;speech (major);support vector machine

**Updates:** 2017-04-04

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Document 296

## **Novel techniques of sound wave analysis can detect ventricular assist device thrombosis**

**Author:** Bran Pouyan, M. 1 ; Blazquez Arroyo, L. 2 ; Hersek, S. 1 ; Janmohamed, M. 2 ; De Marco, T. 2 ; Wieselthaler, G.M. 3 ; Selby, V.N. 2 ; Inan, O.T. 1 ; Klein, L. 2

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**Publication info:** Journal of Heart and Lung Transplantation, suppl. Supplement 1 36.4: S110. Elsevier USA. (Apr 2017)

**Abstract (summary):** Purpose: Early identification of ventricular assist device (VAD) thrombosis can improve outcomes. Although VAD sounds can be recorded, it is unknown which sound parameter best detects pump thrombosis. Methods: Patients (one centrifugal, one axial VAD) presented with recurrent abnormal hemolysis markers and power elevations consistent with pump thrombosis and received tissue plasminogen activator (tPA) + iv heparin. Hemolysis parameters and VAD power normalized after each episode of tPA. During each episode, VAD sounds were recorded before and after tPA using a digital stethoscope. The data analytics consisted of 2 steps: (1) extracting features (frequency domain, time-frequency, acoustic/speech features) from the acoustical signals; (2) applying semi-supervised machine-learning algorithms [KODAMA and t-Stochastic Neighbor Embedding (t-SNE)] to visualize differences between acoustic signal features for the 3 classes of data (thrombosis, post-tPA, and no thrombosis). The matrix embedded the data onto a 2D map that was used to visualize and classify the 3 groups. Results: We found that the best separation of data was

obtained using the combination of KODAMA and t-SNE (Figure). This combination overcomes the issues observed with other methods (e.g. harmonic frequency analysis, principal component analysis, conventional clustering). As expected, the pumps had different acoustic patterns, related to their operating speed characteristics (2400 vs. 9000 rpm). The signature patterns were quite different between the normal operating state (no thrombosis), pump thrombosis and post-TPA, and were consistent between the 2 pump types. Interestingly, the post-TPA acoustic characteristics were different than the no thrombosis state, suggesting residual pump thrombosis that is not identified by pump power or **biomarkers**. Conclusion: **Machine-learning** algorithms can identify pump thrombosis from sound wave analysis and may be more accurate than pump power or **biomarkers** warranting evaluation in larger studies (Figure presented).

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**Conference country:** United States

**Conference end date:** 2017-04-08

**Conference location:** San Diego, CA

**Conference start date:** 2017-04-05

**Conference title:** 37th Annual Meeting and Scientific Sessions of the International Society for Heart and Lung Transplantation, ISHLT 2017

**Copyright:** Copyright 2017 Elsevier B.V., All rights reserved.

**Correspondence author:** Bran Pouyan, M. School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA, United States.

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**Subject:** Embase;biological marker;endogenous compound;tissue plasminogen activator;adult;embedding;female;frequency analysis;hemolysis;human;male;principal component analysis;sound (major);speech;stethoscope;stochastic model;supervised machine learning;thrombosis (major);velocity

**Substance:** Substance Substance: tissue plasminogen activator; CAS: 105913-11-9; Enzyme comm: EC 3.4.21.68;

**Updates:** 2017-10-13

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Document 297

## “Is voice a marker for Autism spectrum disorder? A systematic review and meta-analysis”

**Author:** Fusaroli, Riccardo 1 ; Lambrechts, Anna 2 ; Bang, Dan 3 ; Bowler, Dermot M. 2 ; Gaigg, Sebastian B. 2

1 The Interacting Minds Centre, Aarhus University, Aarhus, Denmark Fusaroli@dac.au.dk 2 Autism Research Group, City University London, London, United Kingdom 3 The Interacting Minds Centre, Aarhus University, Aarhus, Denmark, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, London, United Kingdom, Calleva Research Centre for Evolution and Human Sciences, Magdalen College, University of Oxford, Oxford, United Kingdom

**Publication info:** Autism Research 10.3: 384-407. John Wiley and Sons Inc. (Mar 1, 2017)

**Abstract (summary):** Individuals with Autism Spectrum Disorder (ASD) tend to show distinctive, atypical acoustic patterns of speech. These behaviors affect social interactions and social development and could represent a non-invasive marker for ASD. We systematically reviewed the literature quantifying acoustic patterns in ASD. Search terms were: (prosody OR intonation OR inflection OR intensity OR pitch OR fundamental frequency OR speech rate OR voice quality OR acoustic) AND (autis\* OR Asperger). Results were filtered to include only: empirical studies quantifying acoustic features of vocal production in ASD, with a sample size >2, and the inclusion of a neurotypical comparison group and/or correlations between acoustic measures and severity of clinical features. We identified 34 articles, including 30 univariate studies and 15 multivariate machine-learning studies. We performed meta-analyses of the univariate studies, identifying significant differences in mean pitch and pitch range between individuals with ASD and comparison participants (Cohen's d of 0.4–0.5 and discriminatory accuracy of about 61–64%). The multivariate studies reported higher accuracies than the univariate studies (63–96%). However, the methods used and the acoustic features investigated were too diverse for performing meta-analysis. We conclude that multivariate studies of acoustic patterns are a promising but yet unsystematic avenue for establishing ASD markers. We outline three recommendations for future studies: open data, open methods, and

theory-driven research. *Autism Res* 2017, 10: 384–407. © 2016 International Society for Autism Research, Wiley Periodicals, Inc.

**Accession number:** 613143702

**Author e-mail address:** Fusaroli@dac.au.dk

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**Correspondence author:** Fusaroli, Riccardo The Interacting Minds Centre, Aarhus University, Aarhus, Denmark.

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**DOI:** <http://dx.doi.org/10.1002/aur.1678>

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**Identifier (keyword):** acoustic properties, biomarker, machine learning, speech, voice

**Language:** English

**Language of abstract:** English

**Number of references:** 115

**Publication date:** Mar 1, 2017

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc.

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**Subject:** Embase;MEDLINE;biological marker (major);acoustics;autism (major);clinical feature;disease severity;human;machine learning;pitch;Review;systematic review;voice (major)

**Updates:** 2016-11-152017-04-102017-05-032018-05-01

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Document 298



## Portable mTBI Assessment Using Temporal and Frequency Analysis of **Speech**

**Author:** Daudet, Louis 1 ; Yadav, Nikhil 2 ; Perez, Matthew 1 ; Poellabauer, Christian 1 ; Schneider, Sandra 3 ; Huebner, Alan 4

1 Department of Computer Science and Engineering, University of Notre Dame, Notre Dame, IN, 46556, United States ldaudet@nd.edu ; mperez14@nd.edu ; cpoellab@nd.edu 2 Division of Computer Science, Mathematics, and Science, St. John's University, Queens, NY, 11439, United States yadavn@stjohns.edu 3 Department of Communicative Sciences and Disorders, Saint Mary's College, Notre Dame, IN, 46556, United States sschneider@saintmarys.edu 4 Department of Applied and Computational Mathematics and Statistics, University of Notre Dame, Notre Dame, IN, 46556, United States alan.huebner.10@nd.edu

**Publication info:** IEEE Journal of Biomedical and Health Informatics 21.2: 496-506. Institute of Electrical and Electronics Engineers Inc. (Mar 2017)

**Abstract (summary):** This paper shows that extraction and analysis of various acoustic features from **speech** using mobile devices can allow the detection of patterns that could be indicative of neurological trauma. This may pave the way for new types of **biomarkers** and diagnostic tools. Toward this end, we created a mobile application designed to diagnose mild traumatic brain injuries (mTBI) such as concussions. Using this application, data were collected from youth athletes from 47 high schools and colleges in the Midwestern United States. In this paper, we focus on the design of a methodology to collect **speech** data, the extraction of various temporal and frequency metrics from that data, and the statistical analysis of these metrics to find patterns that are indicative of a concussion. Our results suggest a strong correlation between certain temporal and frequency features and the likelihood of a concussion.

**Accession number:** 614853816

**Author e-mail address:** ldaudet@nd.edu, yadavn@stjohns.edu, mperez14@nd.edu, cpoellab@nd.edu, sschneider@saintmarys.edu, alan.huebner.10@nd.edu

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**Identifier (keyword):** Concussions, Portable diagnostics, **Speech** analysis, **Voice** pathology

**Language:** English

**Language of abstract:** English

**Number of references:** 35

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**Publisher:** Institute of Electrical and Electronics Engineers Inc.

**Publisher location:** United States

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**Subject:** Embase;MEDLINE;acoustics;area under the curve;Article;**automatic speech recognition**;concussion;disease assessment (major);frequency analysis (major);measurement accuracy;mobile application (major);**pitch**;predictive value;reading test;receiver operating characteristic;signal noise ratio;**speech analysis** (major);speech perception;speech test;temporal analysis (major);traumatic brain injury (major);**voice change**

**Updates:** 2017-03-272017-03-282019-05-032022-04-14

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Document 299

## **Using **deep learning** to investigate the neuroimaging correlates of psychiatric and neurological disorders: Methods and applications**

**Author:** Vieira, Sandra 1 ; Pinaya, Walter H L 2 ; Mechelli, Andrea 1

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**Publication info:** Neuroscience and biobehavioral reviews 74.Pt A: 58-75. (Mar 2017)

**Abstract (summary):** **Deep learning** (DL) is a family of **machine learning** methods that has gained considerable attention in the scientific community, breaking benchmark records in areas such as **speech** and visual recognition. DL differs from conventional **machine learning** methods by virtue of its

ability to learn the optimal representation from the raw data through consecutive nonlinear transformations, achieving increasingly higher levels of abstraction and complexity. Given its ability to detect abstract and complex patterns, DL has been applied in neuroimaging studies of psychiatric and neurological disorders, which are characterised by subtle and diffuse alterations. Here we introduce the underlying concepts of DL and review studies that have used this approach to classify brain-based disorders. The results of these studies indicate that DL could be a powerful tool in the current search for **biomarkers** of psychiatric and neurologic disease. We conclude our review by discussing the main promises and challenges of using DL to elucidate brain-based disorders, as well as possible directions for future research.

**Accession number:** 28087243

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**Document type:** Journal Article, Review

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**Identifier (keyword):** Autoencoders, **Convolutionalneural networks**, **Deep** belief networks, **Deeplearning**, **Machine learning**, Multilayer **perceptron**, Neuroimaging, Neurologic disorders, Pattern recognition, Psychiatric disorders

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Humans; **Machine Learning**; Mental Disorders (major); Nervous System Diseases (major); **Neural Networks, Computer**; **Neuroimaging**; **Speech**

**Notes:** Indexing method: Curated;; Publication model: Print-Electronic;; Cited medium:Internet

**Publication date:** Mar 2017

**Publication type:** Journal

**Publisher location:** UNITED STATES

**Source attribution:** Medline, © Publisher specific

**Updates:** 2017-01-152017-01-162017-01-232017-01-242017-01-282017-01-312017-02-032017-02-042017-02-102017-04-032017-09-022017-09-252017-10-282018-03-192019-03-192019-10-092022-01-30

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Document 300

## **Automated analysis of connected **speech** reveals early **biomarkers** of Parkinson's disease in patients with rapid eye movement sleep behaviour disorder**

**Author:** Hlavnička, Jan 1 ; Čmejla, Roman 1 ; Tykalová, Tereza 1 ; Šonka, Karel 2 ; Růžička, Evžen 2 ; Ruzs, Jan 3

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**Publication info:** Scientific reports 7.1: 12. (Feb 2, 2017)

**Abstract (summary):** For generations, the evaluation of **speech** abnormalities in neurodegenerative disorders such as Parkinson's disease (PD) has been limited to perceptual tests or user-controlled laboratory analysis based upon rather small samples of human **vocalizations**. Our study introduces a fully automated method that yields significant features related to respiratory deficits, **dysphonia**, imprecise articulation and dysrhythmia from acoustic microphone data of natural connected **speech** for predicting early and distinctive patterns of neurodegeneration. We compared **speech** recordings of 50 subjects with rapid eye movement sleep behaviour disorder (RBD), 30 newly diagnosed, untreated PD patients and 50 healthy controls, and showed that subliminal parkinsonian **speech** deficits can be reliably captured even in RBD patients, which are at high risk of developing PD or other synucleinopathies. Thus, automated **vocal** analysis should soon be able to contribute to screening and diagnostic procedures for prodromal parkinsonian neurodegeneration in natural environments.

**Accession number:** 28144037

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**Correspondence author:** Hlavnička, Jan Czech Technical University in Prague, Faculty of Electrical Engineering, Department of Circuit Theory, Technická 2, 166 27, Prague 6, Czech Republic.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Date revised:** 2019-02-15

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**Document type:** Journal Article, Research Support, Non-U.S. Gov't

**DOI:** <http://dx.doi.org/10.1038/s41598-017-00047-5>

**First available:** 2017-02-01

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Adult;Aged;Aged, 80 and over;Articulation Disorders -- physiopathology (major);Biomarkers;Dysphonia -- physiopathology;Female;Humans;Male;Middle Aged;Parkinson Disease -- diagnosis;Parkinson Disease -- physiopathology (major);Pattern Recognition, Automated -- methods;REM Sleep Behavior Disorder -- physiopathology (major);Respiration

**Notes:** Publication model: Electronic;; Cited medium:Internet

**Publication date:** Feb 2, 2017

**Publication type:** Journal

**Publisher location:** ENGLAND

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**Substance:** Substance Substance: Biomarkers; CAS: 0;

**Updates:** 2017-02-012017-02-022017-05-172017-07-032017-09-072019-02-072019-02-16

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Document 301

## **A Machine Learning Approach to Identifying the Thought Markers of Suicidal Subjects: A Prospective Multicenter Trial**

**Author:** Pestian, John P 1 ; Sorter, Michael 2 ; Connolly, Brian 1 ; Bretonnel Cohen, Kevin 3 ; McCullumsmith, Cheryl 4 ; Gee, Jeffry T 5 ; Morency, Louis-Philippe 6 ; Scherer, Stefan 7 ; Rohlf, Lesley 7

1 Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, USA, USA 2 Division of Psychiatry, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, USA, USA 3 Computational Bioscience Program, University of Colorado School of Medicine, Denver, CO, USA, USA 4 Department of Psychiatry, College of Medicine, University of Cincinnati, Cincinnati, OH, USA, USA 5 Princeton Community Hospital, Princeton, WV, USA, USA 6 Language Technologies Institute, Carnegie Mellon University, Pittsburgh, PA, USA, USA 7 Institute for Creative Technologies, University of Southern California, Los Angeles, CA, USA, USA

**Publication info:** Suicide & life-threatening behavior 47.1: 112-121. (Feb 2017)

**Abstract (summary):** Death by suicide demonstrates profound personal suffering and societal failure. While basic sciences provide the opportunity to understand **biological markers** related to suicide, computer science provides opportunities to understand suicide thought markers. In this novel prospective, multimodal, multicenter, mixed demographic study, we used **machine learning** to measure and fuse two classes of suicidal thought markers: verbal and nonverbal. **Machine learning** algorithms were used with the subjects' words and **vocal** characteristics to classify 379 subjects recruited from two academic medical centers and a rural community hospital into one of three groups: suicidal, mentally ill but not suicidal, or controls. By combining linguistic and acoustic characteristics, subjects could be classified into one of the three groups with up to 85% accuracy. The results provide insight into how advanced technology can be used for suicide assessment and prevention.

**Accession number:** 27813129

**Copyright:** © 2016 The American Association of Suicidology.

**Corporate/institutional author:** STM Research Group

**Correspondence author:** Pestian, John P Division of Biomedical Informatics, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, USA.

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**Date completed:** 2017-10-11

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**Date revised:** 2022-12-07

**Document status:** Revised

**Document type:** Journal Article, Multicenter Study

**DOI:** <http://dx.doi.org/10.1111/sltb.12312>

**First available:** 2016-11-04

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Adolescent;Adult;Artificial Intelligence;Diagnosis, Computer-Assisted -- methods;Female;Humans;Machine Learning (major);Male;Prognosis;Prospective Studies;Suicidal Ideation (major);Suicide (major) -- psychology;Suicide Prevention (major)

**Notes:** Indexing method: Curated;; Publication model: Print-Electronic;; Cited medium:Internet

**Publication date:** Feb 2017

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**Publisher location:** ENGLAND

**Source attribution:** Medline, © Publisher specific

**Updates:** 2016-11-042016-11-052017-02-072017-10-122018-03-172019-03-19

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Document 302

## **Predicting probable Alzheimer's disease using linguistic deficits and biomarkers**

**Author:** Orimaye, Sylvester O 1 ; Wong, Jojo S-M 1 ; Golden, Karen J 2 ; Wong, Chee P 2 ; Soyiri, Ireneous N 3

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**Publication info:** BMC bioinformatics 18.1: 34. (Jan 14, 2017)

### **Abstract (summary): BACKGROUND**

The manual diagnosis of neurodegenerative disorders such as Alzheimer's disease (AD) and related Dementias has been a challenge. Currently, these disorders are diagnosed using specific clinical diagnostic criteria and neuropsychological examinations. The use of several Machine Learning algorithms to build automated diagnostic models using low-level linguistic features resulting from verbal utterances could aid diagnosis of patients with probable AD from a large population. For this

purpose, we developed different **Machine Learning** models on the DementiaBank language transcript clinical dataset, consisting of 99 patients with probable AD and 99 healthy controls.

## RESULTS

Our models learned several syntactic, lexical, and n-gram linguistic **biomarkers** to distinguish the probable AD group from the healthy group. In contrast to the healthy group, we found that the probable AD patients had significantly less usage of syntactic components and significantly higher usage of lexical components in their language. Also, we observed a significant difference in the use of n-grams as the healthy group were able to identify and make sense of more objects in their n-grams than the probable AD group. As such, our best diagnostic model significantly distinguished the probable AD group from the healthy elderly group with a better Area Under the Receiving Operating Characteristics Curve (AUC) using the **Support Vector Machines (SVM)**.

## CONCLUSIONS

Experimental and statistical evaluations suggest that using ML algorithms for learning linguistic **biomarkers** from the verbal utterances of elderly individuals could help the clinical diagnosis of probable AD. We emphasise that the best ML model for predicting the disease group combines significant syntactic, lexical and top n-gram features. However, there is a need to train the diagnostic models on larger datasets, which could lead to a better AUC and clinical diagnosis of probable AD.

**Accession number:** 28088191

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**Correspondence author:** Orimaye, Sylvester O Intelligent Health Research Group, School of Information Technology, Monash University, Jalan Lagoon Selatan, Bandar Sunway, 47500, Malaysia.

**Database:** MEDLINE®; 1946 to date (1946 - current)

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**Date created:** 2017-01-16

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**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1186/s12859-016-1456-0>

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**Grant:** P50 AG005133. NIA NIH HHS. United States.



**Identifier (keyword):** Alzheimer's disease, Clinical diagnostics, Machine learning, Neurolinguistics, Prediction

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Aged;Aged, 80 and over;Algorithms (major);Alzheimer Disease -- diagnosis (major);Alzheimer Disease -- psychology;Biomarkers -- analysis;Humans;Linguistics;Machine Learning (major);Middle Aged;Speech (major)

**Notes:** Indexing method: Curated;; Publication model: Electronic;; Cited medium:Internet

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**Publication type:** Journal

**Publisher location:** ENGLAND

**Source attribution:** Medline, © Publisher specific

**Substance:** Substance Substance: Biomarkers; CAS: 0;

**Updates:** 2017-01-162017-01-192017-01-202017-08-19

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Document 303

## Using speech for the diagnosis of mild traumatic brain injuries

**Author:** Xia, Bryan 1 ; Daudet, Louis; Poellabauer, Christian; Schneider, Sandra

1 University of Notre Dame, United States

**Publication info:** Archives of Physical Medicine and Rehabilitation 97.12: e32. W.B. Saunders. (Dec 2016)

**Abstract (summary):** Research Objectives: While it is well understood that moderate or severe traumatic brain injuries (TBI) directly impact speech production, the impact of milder forms of TBI (mTBI), such as concussions, on speech production and performance remains an area requiring further investigation. The goal is to identify the most significant acoustic features to detect signs of concussions. Design: The project is a case-control study, where changes to acoustic features between two recordings from the same subject are compared for two cohorts: healthy controls and concussed (as diagnosed by athletic trainers or physicians using standard/traditional concussion assessment tools). Baseline recordings are obtained at the beginning of the athletic season. Healthy subjects were randomly selected throughout the sports season for a second recording. Concussed athletes provided a second recording shortly (within a few hours) of their concussion. Setting: The setting is the general community, specifically high school and college students. Participants: We

collected **speech** samples from 580 (high school and college) athletes (95 of them with a diagnosed concussion). All high school and college students participating in one or more sport activities were eligible to participate. Subjects were recruited at the beginning of the athletic season. Interventions: N/A. Main Outcome Measure(s): The main outcome measure is the number of subjects correctly classified as concussed or non-concussed. Results: The analysis of the recordings yielded 24 features with statistical significance (p-value <0.05) out of a total of 102 features, resulting in an AUC of 0.901. Conclusions: **Speech** analysis has a strong potential as a **biomarker** for concussion.

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**Conference country:** United States

**Conference end date:** 2016-11-04

**Conference location:** Chicago, IL

**Conference start date:** 2016-10-30

**Conference title:** 2016 American Congress of Rehabilitation Medicine Annual Conference, ACRM 2016

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**Correspondence author:** Xia, Bryan University of Notre Dame, United States.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document status:** New

**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1016/j.apmr.2016.09.087>

**Embase document status:** Embase

**First available:** 2016-12-21

**Identifier (keyword):** **Machine Learning**, Mobile Apps, **Speech** Analysis

**Language:** English

**Language of abstract:** English

**Publication date:** Dec 2016

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**Publisher:** W.B. Saunders

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;**biological marker**;athlete;athletic trainer;case control study;case report;college student;concussion;controlled clinical trial;controlled study;diagnosis;high school;human;human

tissue;machine learning (major);mobile application (major);physician;randomized controlled trial;season;speech analysis (major);sport;statistical significance;traumatic brain injury (major)

**Updates:** 2016-12-21

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Document 304

## **A computational linguistics approach for prodromal psychosis**

**Author:** Cecchi, Guillermo 1

1 IBM Research, Yorktown Heights, NY, United States

**Publication info:** Neuropsychopharmacology, suppl. Supplement 1 41 : S97-S98. Nature Publishing Group. (Dec 2016)

**Abstract (summary):** Background: We recently presented a pilot study [Bedi et al, NPJ Schizophrenia, 2015] showing that it is possible to identify linguistic features in clinical high risk (CHR) patients that are strongly predictive of conversion to psychosis (CHR+). These features are: (a) the formalization of the concept of 'flight of ideas' using tools from distributed semantics, specifically a measure we call semantic coherence, and (b) the formalization of the concept of 'poverty of speech' using tools from computational probabilistic parsing to measure morpho-syntactic complexity, specifically length of phrases and density of interrogative word determiners ("what", "which"). Applied to transcripts from a cohort of 34 CHR patients who had a baseline open-ended (OE) interview during which they were asked to talk about themselves (~ 1hr), a machine learning model predicted with 100% accuracy the 5 CHR+ patients, validated statistically with multiple approaches. Methods: In collaboration with Carrie Bearden, we conducted a validation/follow-up study using existing retrospective data from previously published work. The experimental setting consisted of a semi-structured baseline interview following the Story Game (SG) protocol [Caplan et al, 1989; Bearden et al, 2011], during which participants had to listen to a story, retell it, and then were asked questions about the narrative. A cohort of 59 CHR patients, of which 19 later converted to psychosis, and 21 healthy age-similar controls, was analyzed using a similar set of linguistic features as in the previous study, encompassing semantic coherence and morpho-syntactic complexity measures. Results: A machine learning ensemble model predicts conversion with a rate of 0.84 for True Positives and 0.17 for False Positives using leave-two-out cross-validation (L2OCV), dropping to 0.81 and 0.18 respectively for L4OCV and L6OCV. This classifier model, applied verbatim to the same linguistic features extracted from the OE data, achieves an accuracy of 0.6 True Positives (3 out of 5,  $p < 0.03$ ) and 0.11 False Positives. A simple Logistic Regression (LR) classifier trained on the entire SG dataset achieves an accuracy of  $AUC = 0.88$ . Moreover, the LR model applied verbatim to the same linguistic features extracted from the OE data, achieves an accuracy of  $AUC = 0.71$ . Conclusions: The high predictive accuracy of the semantic and morpho-syntactic markers on the OE and SG data are a strong indication that psychosis outcome can be predicted computationally, which can lead to high-frequency and remote evaluations that may include voice, facial expressions and written text. The

significant predictive value on the OE data of a model learned on SG, in a very different experimental setting (e.g. low vs. high interviewer intervention), furthermore, supports the idea of a **speech**-and behavior-based naturalistic assessment of mental states that may extend to many other psychiatric and neurologic conditions.

**Accession number:** 613896723

**Conference country:** United States

**Conference end date:** 2016-12-08

**Conference location:** Hollywood, FL

**Conference start date:** 2016-12-04

**Conference title:** 55th Annual Meeting of the American College of Neuropsychopharmacology, ACNP 2016

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**Correspondence author:** Cecchi, Guillermo IBM Research, Yorktown Heights, NY, United States.

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**Document type:** Conference Abstract

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**Subject:** Embase;morphine;**classifier**;controlled study;facial expression;follow up;high risk patient;human;interview;linguistics (major);logistic regression analysis;major clinical study;mental health;model;narrative;nervous system;predictive value;psychosis (major);**speech**;validation process;**voice**

**Substance:** Substance Substance: morphine; CAS: 52-26-657-27-2;

**Updates:** 2017-01-02

## **Innovative voice analytics for the assessment and monitoring of cognitive decline in people with dementia and mild cognitive impairment**

**Author:** König, Alexandra 1 ; Satt, Aharon 2 ; David, Renaud 3 ; Robert, Philippe 4

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**Publication info:** Alzheimer's and Dementia, suppl. Supplement 12.7: P363. Elsevier Inc. (Jul 2016)

**Abstract (summary):** Background: Various types of dementia and Mild Cognitive Impairment (MCI) are manifested as irregularities in human speech and language, which have proven to be strong predictors for the disease presence and progression. Therefore, automatic speech analytics provided by a mobile application may be a useful tool in providing additional indicators for assessment and detection of early stage dementia and MCI. Methods: 165 participants (Healthy elderly subjects (HC), MCI patients and Alzheimer's disease (AD) patients) were recorded with a mobile application while performing several short vocal cognitive tasks during a regular consultation. These tasks included verbal fluency, picture description and counting down. The voice recordings were processed in two steps: in the first step, vocal markers were extracted using speech signal processing techniques; in the second, the vocal markers were tested to assess their 'power' to distinguish between HC, MCI and AD. The second step included training automatic classifiers for detecting MCI and AD, based on machine learning methods, and testing the detection accuracy. Based on previous data collection, the automatic voice analysis software produces a cognitive vocal score ranging from 0-1. Results: High accuracy rates for the continuous 'cognitive vocal score' which was calculated for each participant within the range of 0 - 1 were obtained. The fluency and free speech tasks obtain the highest accuracy rates of classifying AD vs. MCI vs. HC. Using the data, we demonstrated classification accuracy as follows: HC vs AD = 92% accuracy; HC vs. MCI= 86% accuracy; MCI vs. AD = 86% accuracy. Conclusions: Our results indicate the potential value of vocal analytics cognitive and the use of a mobile application for accurate automatic differentiation between HC, MCI and AD. This tool can provide the clinician with meaningful information for assessment and monitoring of people with MCI and AD based on noninvasive, simple and low-cost method. Figure 1 shows a visualisation of Countdown task speech performance (healthy subject below and AD patient above) Figure 2 shows a visualisation of Verbal Fluency task speech performance (healthy subject below and AD patient above).

**Accession number:** 613189020

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**Conference country:** Canada

**Conference end date:** 2016-07-28

**Conference location:** Toronto, ON

**Conference start date:** 2016-07-22

**Conference title:** Alzheimer's Association International Conference 2016

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**Correspondence author:** König, Alexandra School for Mental Health and Neuroscience, Maastricht University, Centre De Recherche- CHU De Nice Institut Claude Pompidou, Nice, France.

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**Date created:** 2016-11-16

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**Document type:** Conference Abstract

**Embase document status:** Embase

**First available:** 2016-12-16

**Language:** English

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**Publication date:** Jul 2016

**Publication type:** Journal

**Publisher:** Elsevier Inc.

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;aged;Alzheimer disease (major);classification;classifier;consultation;controlled study;differentiation;doctor patient relation;human;major clinical study;mild cognitive impairment (major);mobile application;monitoring (major);signal processing;speech test;voice analysis (major)

**Updates:** 2016-12-162017-02-14

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Document 306

### **Multimodal analysis of startle type responses**

**Author:** Ćosić, Krešimir 1 ; Popović, Siniša 1 ; Kukulja, Davor 1 ; Dropuljić, Branimir 1 ; Ivanec, Dragutin 2 ; Tonković, Mirjana 2

1 University of Zagreb, Faculty of Electrical Engineering and Computing, Unska 3, Zagreb, HR-10000, Croatia sinisa.popovic@fer.hr 2 University of Zagreb, Faculty of Humanities and Social Sciences, Ivana Lučića 3, Zagreb, HR-10000, Croatia

**Publication info:** Computer Methods and Programs in Biomedicine 129 : 186-202. Elsevier Ireland Ltd. (Jun 1, 2016)

**Abstract (summary):** Background and objective: This article presents a multimodal analysis of startle type responses using a variety of physiological, facial, and **speech** features. These multimodal components of the startle type response reflect complex brain-body reactions to a sudden and intense stimulus. Additionally, the proposed multimodal evaluation of reflexive and emotional reactions associated with the startle eliciting stimuli and underlying neural networks and pathways could be applied in diagnostics of different psychiatric and neurological diseases. Different startle type stimuli can be compared in the strength of their elicitation of startle responses, i.e. their potential to activate stress-related neural pathways, underlying **biomarkers** and corresponding behavioral reactions. Methods: An innovative method for measuring startle type responses using multimodal stimuli and multimodal feature analysis has been introduced. Individual's multimodal reflexive and emotional expressions during startle type elicitation have been assessed by corresponding physiological, **speech** and facial features on ten female students of psychology. Different startle eliciting stimuli like noise and airblast probes, as well as a variety of visual and auditory stimuli of different valence and arousal levels, based on International Affective Picture System (IAPS) images and/or sounds from International Affective Digitized Sounds (IADS) database, have been designed and tested. Combined together into more complex startle type stimuli, such composite stimuli can potentiate the evoked response of underlying neural networks, and corresponding neurotransmitters and neuromodulators as well; this is referred to as increased power of response elicitation. The intensity and magnitude of multimodal responses to selected startle type stimuli have been analyzed using effect sizes and medians of dominant multimodal features, i.e. skin conductance, eye blink, head movement, **speech** fundamental frequency and energy. The significance of the observed effects and comparisons between paradigms were evaluated using one-tailed t-tests and ANOVA methods, respectively. Skin conductance response habituation was analyzed using ANOVA and post hoc multiple comparison tests with the Dunn-Šidák correction. Results: The results revealed specific physiological, facial and **vocal** reflexive and emotional responses on selected five stimuli paradigms which included: (1) acoustic startle probes, (2) airblasts, (3) IAPS images, (4) IADS sounds, and (5) image-sound-airblast composite stimuli. Overall, composite and airblast paradigms resulted in the largest responses across all analyzed features, followed by sound and acoustic startle paradigms, while paradigm using images consistently elicited the smallest responses. In this context, power of response elicitation of the selected stimuli paradigms can be described according to the aggregated magnitude of the participants' multimodal responses. We also observed a habituation effect only in skin conductance response to acoustic startle, airblast and sound paradigms. Conclusions: This study developed a system for paradigm design and stimuli generation, as well as real-time multimodal signal processing and feature calculation. Experimental paradigms for monitoring individual responses to stressful startle type stimuli were designed in order to compare the response elicitation power across various stimuli. The developed system, applied paradigms and obtained results might be useful in further

research for evaluation of individuals' multimodal responses when they are faced with a variety of aversive emotional distractors and stressful situations.

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**Copyright:** Copyright 2017 Elsevier B.V., All rights reserved.

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**Document type:** Article

**DOI:** <http://dx.doi.org/10.1016/j.cmpb.2016.01.002>

**Embase document status:** Embase; MEDLINE

**First available:** 2016-05-04

**Identifier (keyword):** Airblast, International Affective Digitized Sounds, International Affective Picture System, Multimodal analysis, Physiological, **speech** and facial features, Startle response

**Language:** English

**Language of abstract:** English

**Number of references:** 50

**Publication date:** Jun 1, 2016

**Publication type:** Journal

**Publisher:** Elsevier Ireland Ltd

**Publisher location:** Ireland

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**Subject:** Embase;MEDLINE;neurotransmitter;**biological marker**;analysis of variance;arousal;calculation;clinical article;data base;DNA probe;effect size;electrodermal response;evoked response;face;facies;female;habituation;head movement;human;monitoring;nerve tract;noise;psychology;signal processing;**speech**;startle reflex (major);stimulus;stress;student;Student t test;adult;analytic method (major);Article;**artificial neural network**;auditory stimulation;emotion;eyelid reflex;multimodal analysis + (major);semantics;skin conductance;visual stimulation;white noise

**Updates:** 2016-05-042017-05-292017-05-31



## Investigating voice as a biomarker of LRRK2-associated Parkinson's disease (PD)

**Author:** Arora, S. 1 ; Visanji, N.P. 1 ; Mestre, T.A. 1 ; Ghate, T. 1 ; Lang, A.E. 1 ; Little, M. 1 ; Marras, C. 1

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**Publication info:** Movement Disorders, suppl. Supplement 2 31 : S215. John Wiley and Sons Inc. (Jun 2016)

**Abstract (summary):** Objective: To test for an association between LRRK2 mutation and pathological changes in voice. Background: Voice impairment, characterized by reduced volume, breathiness, roughness and exaggerated vocal tremor, is a common symptom of PD. LRRK2 mutations are associated with increased risk for PD. Although several studies have demonstrated differences in motor and non-motor symptoms between idiopathic PD (iPD) and LRRK2-associated PD, the relationship between LRRK2 mutation and voice impairment has not yet been explored. Subtle changes in voice could be an early motor sign useful in detection of prodromal PD. Methods: Sustained vowel phonations ('aaah') were obtained crosssectionally from individuals with LRRK2-associated PD (n=8); iPD (n=17); non-manifesting carriers (n=19); related controls (first degree relatives) (n=24) and unrelated controls (n=23). To quantify subtle voice changes we extracted a wide range of multiple dysphonia measures and calculated the sensitivity and specificity to distinguish between groups using two independent methods: 1. Random forests: a statistical machine learning technique commonly used to separate generic data into several classes. 2. Chance predictions: randomized determinations. This method tests the null hypothesis that the discrimination results obtained using random forests are no better than chance predictions of group membership. Results: The multiple dysphonia measures had a sensitivity of 81.4% (SD 26.5) and specificity of 78.0% (SD 25.9) in discriminating LRRK2-associated PD from iPD using random forests, whereas chance predictions resulted in a sensitivity of 52.02% (SD 45.40) and specificity of 53.32% (SD 45.66). The sensitivity in discriminating non-manifesting carriers from unrelated controls was 70.97% (SD 26.51) and specificity 75.35% (SD 25.67) using random forests and 50.50% (SD 34.51) and 50.58% (SD 34.47) respectively using chance predictions. Finally, the sensitivity and specificity to discriminate between non-manifesting carriers and unrelated controls was 68.46% (SD 26.46) and 72.38% (SD 25.94) respectively using random forests and 49.58% (SD 34.49) and 49.47% (SD 34.39) using chance predictions. Conclusions: Voice impairment in LRRK2-associated PD may differ to that in iPD. This warrants further investigation. Furthermore, longitudinal studies will determine the potential for voice impairment in nonmanifesting carriers to be predictive of transition to manifesting PD.

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**Conference country:** Germany

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**Conference location:** Berlin

**Conference start date:** 2016-06-19

**Conference title:** 20th International Congress of Parkinson's Disease and Movement Disorders

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**Correspondence author:** Arora, S. , Birmingham, United Kingdom.

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**Publisher:** John Wiley and Sons Inc.

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**Subject:** Embase;biological marker (major);endogenous compound;leucine rich repeat kinase 2 (major);clinical article;controlled clinical trial;controlled study;diagnostic test accuracy study;disease carrier;dysphonia;first-degree relative;gene mutation;genetic susceptibility;human;longitudinal study>null hypothesis;Parkinson disease (major);phonation;prediction;quantitative study;random forest;randomized controlled trial;sensitivity and specificity;symptom;voice change (major);vowel

**Updates:** 2016-09-13

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Document 308

## **Discrimination of Parkinson's disease participants from healthy controls using telephone-quality voice recordings**

**Author:** Arora, S. 1 ; Tsanas, A. 1

1 , Oxford, United Kingdom

**Publication info:** Movement Disorders, suppl. Supplement 2 31 : S266. John Wiley and Sons Inc. (Jun 2016)

**Abstract (summary):** Objective: To test the practicality and efficacy of telephone-quality **voice** recordings to discriminate Parkinson's disease (PD) participants from healthy controls (HC). Background: **Vocal** performance degradation is met in the vast majority of people diagnosed with PD, and may be one of the earliest indicators of disease onset. Using high-quality **voice** recordings, recent studies have developed technologies both to discriminate PD from HC, and also for symptom severity telemonitoring. However, these studies may be limited in scaling massively across the population as they rely on expensive specialized equipment to collect the data, which might not be available in resource-constrained settings. In this study, we investigated whether telephone-quality **voice** recordings collected using readily available standard commercial consumer phones could be used to provide easily accessible, cost-effective means towards accurate PD assessment. Methods: We collected sustained vowel **phonations** ('aaah' sounds, where the subject is requested to keep the pitch and amplitude as steady as possible) through telephone-quality digital audio lines, under realistic, non-lab conditions. The recordings were obtained from the following locations: Argentina, Brazil, Canada, Spain, Mexico, UK and USA. After screening out bad recordings, we used 2799 recordings from 1507 PD participants (mean age: 50.9 years, 45.9% female), and 15486 recordings from 8394 control participants (mean age: 51.1 years, 45.0% female). We extracted and analyzed 309 **dysphonia** measures to quantify subtle changes in the recorded signals, which can differentiate PD from HC voices. We presented the **dysphonia** measures to a random forest classifier, and assessed the efficacy of the model using 10-fold cross-validation with 100 iterations for statistical confidence. Results: Using only the **voice** recordings, we achieved a mean out of sample sensitivity of 63.8% (standard deviation 2.3%) and mean specificity of 67.2% (standard deviation 2.9%) in discriminating PD from HC. Conclusions: The discrimination results obtained are promising and are considerably better than standard naïve benchmarks (or chance). These findings warrant further investigation into the feasibility of using **voice** as a potential **biomarker** of PD, even with low-quality telephonebased recordings.

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**Conference country:** Germany

**Conference end date:** 2016-06-23

**Conference location:** Berlin

**Conference start date:** 2016-06-19

**Conference title:** 20th International Congress of Parkinson's Disease and Movement Disorders

**Copyright:** Copyright 2016 Elsevier B.V., All rights reserved.

**Correspondence author:** Arora, S. , Oxford, United Kingdom.

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**DOI:** <http://dx.doi.org/10.1002/mds.26688>

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**First available:** 2016-09-13

**Language:** English

**Language of abstract:** English

**Publication date:** Jun 2016

**Publication type:** Journal

**Publisher:** John Wiley and Sons Inc.

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;adult;Argentina;Brazil;Canada;classifier;comparative effectiveness;consumer;controlled study;diagnostic test accuracy study;disease assessment;dysphonia;feasibility study;female;human;major clinical study;male;Mexico;middle aged;normal human;Parkinson disease (major);phonation;pitch;quantitative study;random forest;screening;sound;Spain;statistical model;telephone (major);validation process;voice (major);vowel

**Updates:** 2016-09-13

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Document 309

## **New technologies for detecting suicidal risk of psychiatric patients**

**Author:** Lopez-Castroman, J. 1

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**Publication info:** European Psychiatry 33 : S68. Elsevier Masson SAS. (Mar 2016)

**Abstract (summary):** Suicide is a major health issue with considerable human and economic costs. There have been many attempts to develop techniques capable of predicting future suicidal behavior, but known risk factors are insufficiently specific. However, during the last decades, technical developments have made possible the use of new technologies to assess potential clinical markers for psychiatric patients. In many cases the technologies are affordable, wearable and interconnected, multiplying the wealth of data resulting from their use. Quite logically, psychiatrists from all over the world are investing in recently developed devices for their research projects and have consequently started to collaborate with engineering and pattern recognition groups in the study of potential clinical markers. These groups provide the expertise and computational methods required to process this

wealth of data, and can improve the classification accuracy to predict a certain condition using data mining techniques. In the field of suicidal behavior, new devices that capture promising predictors such as electrodermal response activity, some facial expressions or **speech** properties have been developed and are being tested. In view of these facts, during the workshop we will review some of the new methodologies that can be used for the assessment of suicidal risk and how can multidisciplinary and complementary approaches be implemented.

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**Conference country:** Spain

**Conference end date:** 2016-03-15

**Conference location:** Madrid

**Conference start date:** 2016-03-12

**Conference title:** 24th European Congress of Psychiatry, EPA 2016

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**Correspondence author:** Lopez-Castroman, J. CHRU De Nimes, Psychiatry, Nimes, France.

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**Document status:** New

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**First available:** 2016-06-08

**Language:** English

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**Publication date:** Mar 2016

**Publication type:** Journal

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**Subject:** Embase;**marker**;technology (major);risk (major);mental patient (major);human (major);European (major);psychiatry (major);devices;suicidal behavior;psychiatrist;**speech**;facial expression;electrodermal response;**data mining**;risk factor;classification;pattern recognition;workshop;engineering;health;suicide;methodology

**Updates:** 2016-06-08

## Linguistic Features Identify Alzheimer's Disease in Narrative Speech

**Author:** Fraser, Kathleen C 1 ; Meltzer, Jed A 2 ; Rudzicz, Frank 3

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**Publication info:** Journal of Alzheimer's disease : JAD 49.2: 407-22. (2016)

### Abstract (summary): BACKGROUND

Although memory impairment is the main symptom of Alzheimer's disease (AD), language impairment can be an important marker. Relatively few studies of language in AD quantify the impairments in connected speech using computational techniques.

### OBJECTIVE

We aim to demonstrate state-of-the-art accuracy in automatically identifying Alzheimer's disease from short narrative samples elicited with a picture description task, and to uncover the salient linguistic factors with a statistical factor analysis.

### METHODS

Data are derived from the DementiaBank corpus, from which 167 patients diagnosed with "possible" or "probable" AD provide 240 narrative samples, and 97 controls provide an additional 233. We compute a number of linguistic variables from the transcripts, and acoustic variables from the associated audio files, and use these variables to train a machine learning classifier to distinguish between participants with AD and healthy controls. To examine the degree of heterogeneity of linguistic impairments in AD, we follow an exploratory factor analysis on these measures of speech and language with an oblique promax rotation, and provide interpretation for the resulting factors.

### RESULTS

We obtain state-of-the-art classification accuracies of over 81% in distinguishing individuals with AD from those without based on short samples of their language on a picture description task. Four clear factors emerge: semantic impairment, acoustic abnormality, syntactic impairment, and information impairment.

## CONCLUSION

Modern **machine learning** and linguistic analysis will be increasingly useful in assessment and clustering of suspected AD.

**Accession number:** 26484921

**Correspondence author:** Fraser, Kathleen C Department of Computer Science, University of Toronto, Toronto, Canada.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2016-09-12

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**Date revised:** 2022-04-09

**Document status:** Revised

**Document type:** Journal Article, Research Support, N.I.H., Extramural, Research Support, Non-U.S. Gov't

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**First available:** 2015-10-22

**Grant:** AG003705. NIA NIH HHS. United States.

AG005133. NIA NIH HHS. United States.

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**Identifier (keyword):** Automatic data processing, factor analysis, geriatric assessment, heterogeneity, language, statistical

**Language:** English

**Language of abstract:** English

**Medline document status:** MEDLINE

**MeSH:** Aged;Aged, 80 and over;Alzheimer Disease -- complications (major);Alzheimer Disease -- diagnosis (major);Diagnosis, Computer-Assisted;Factor Analysis, Statistical;Female;Humans;Language Disorders -- etiology (major);Linguistics (major);Logistic Models;**Machine Learning**;Male;Mental Status Schedule;Middle Aged;Narration (major);Photic Stimulation;**Speech** -- physiology (major);Verbal Behavior

**Notes:** Publication model: Print;; Cited medium:Internet

**Publication date:** 2016

**Publication type:** Journal

**Publisher location:** NETHERLANDS

**Source attribution:** Medline, © Publisher specific

**Updates:** 2015-10-222015-12-082015-12-152016-03-162016-09-132016-11-24

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Document 311

## **Voice analysis as an objective state marker in bipolar disorder**

**Author:** Faurholt-Jepsen, M. 1 ; Busk, J. 2 ; Frost, M. 3 ; Vinberg, M. 1 ; Christensen, E.M. 1 ; Winther, O. 2 ; Bardram, J.E. 2 ; Kessing, L.V. 1

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**Publication info:** Translational Psychiatry 6.7 Springer Nature. (2016)

**Abstract (summary):** Changes in speech have been suggested as sensitive and valid measures of depression and mania in bipolar disorder. The present study aimed at investigating (1) voice features collected during phone calls as objective markers of affective states in bipolar disorder and (2) if combining voice features with automatically generated objective smartphone data on behavioral activities (for example, number of text messages and phone calls per day) and electronic self-monitored data (mood) on illness activity would increase the accuracy as a marker of affective states. Using smartphones, voice features, automatically generated objective smartphone data on behavioral activities and electronic self-monitored data were collected from 28 outpatients with bipolar disorder in naturalistic settings on a daily basis during a period of 12 weeks. Depressive and manic symptoms were assessed using the Hamilton Depression Rating Scale 17-item and the Young Mania Rating Scale, respectively, by a researcher blinded to smartphone data. Data were analyzed using random forest algorithms. Affective states were classified using voice features extracted during everyday life phone calls. Voice features were found to be more accurate, sensitive and specific in the classification of manic or mixed states with an area under the curve (AUC) = 0.89 compared with an AUC = 0.78 for the classification of depressive states. Combining voice features with automatically generated objective smartphone data on behavioral activities and electronic self-monitored data increased the accuracy, sensitivity and specificity of classification of affective states slightly. Voice features collected in naturalistic settings using smartphones may be used as objective state markers in patients with bipolar disorder.

**Accession number:** 2017720990

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**Correspondence author:** Faurholt-Jepsen, M. Psychiatric Center Copenhagen, Rigshospitalet, Blegdamsvej 9, Copenhagen, DK-2100, Denmark.

**Database:** Embase®; 1947 to date (1947 - current)

**Date created:** 2022-08-24

**Document status:** New

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**DOI:** <http://dx.doi.org/10.1038/TP.2016.123>

**Embase document status:** In Process; MEDLINE

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**Language:** English

**Language of abstract:** English

**Number of references:** 50

**Publication date:** 2016

**Publication type:** Journal

**Publisher:** Springer Nature

**Publisher location:** United Kingdom

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;MEDLINE;adult;area under the curve (major);article;bipolar disorder (major);clinical article;controlled study;depression (major);female;Hamilton Depression Rating Scale;human;male;mania;outpatient;random forest (major);sensitivity and specificity;smartphone;voice;voice analysis (major);Young Mania Rating Scale

**Updates:** 2022-08-24

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Document 312

**Answer ALS: Establishing a clinical and comprehensive multi-omics signature for ALS employing induced pluripotent stem cell derived motor neurons from 1000 sporadic and familial ALS patients nationwide**

**Author:** Rothstein, J. 1 ; Cudkowicz, M. 2 ; Svendsen, C. 3 ; Maragakis, N. 1 ; Berry, J. 2 ; Thompson, L. 4 ; Finkbeiner, S. 5 ; Van Eyke, J. 3 ; Fraenkel, E. 6 ; Mosmiller, E. 1 ; Vaughn, S. 2 ; Thompson, T. 4 ; Farr, M.S. 1 ; Baxi, E. 1

1 Johns Hopkins University, Baltimore, MD, United States jrothstein@jhmi.edu 2 Massachusetts General Hospital, Boston, MA, United States 3 Cedars-Sinai, Los Angeles, CA, United States 4 Univ California, Irvine, CA, United States 5 Gladstone Institute, San Francisco, CA, United States 6 MIT, Boston, MA, United States

**Publication info:** Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, suppl. Supplement 1 17 : 183. Taylor and Francis Ltd. (2016)

**Abstract (summary):** Background: ALS, like many other neurodegenerative diseases, likely represents a collection of different subtypes of patient populations and molecular etiologies. Over a dozen different genetic mutations cause familial ALS (fALS) and fALS is clinically indistinguishable from the far more common sporadic ALS. Disappointingly, no new drug treatments have been found to be reproducibly successful in large clinical trials since the first and only FDA approved drug, more than 20 years ago. Methods: Using approaches gleaned from personalized medicine approaches in cancer, Answer ALS was conceived and organized as a comprehensive multiomics approach to ALS to ascertain, at a population level, the various clinical molecular- biochemical subtypes of ALS. The overall organization was built on the collaborative NIH initiated NeuroLinc's consortium. Specifically, ALS patients nationwide are being enrolled at 6 University clinics distributed throughout the USA and longitudinally followed with deep clinical data collection. In addition, patients wear a personal health monitoring device with a linked Android/iOS app collecting 24/7 data on motor activity, sleep activity, heart rate, motor performance and learning "games", **voice** and pulmonary function. The iPS-derived neurons are centrally generated from a novel, rapid and highly reproducible specific differentiation protocol. Whole genome sequencing, transcriptomics, epigenomics, proteomics, metabolomics, lipomics, high content imaging and longitudinal high throughput single cell analysis are collected on the patients iPS motor neurons also employing standardized and parallel cultures. Results: Integrated clinical and biological signatures are being generated using bioinformatics, statistics and computational biology to establish patterns that may lead to a better understanding of the underlying mechanisms of disease. The data acquired in this consortium effort is open source and freely available online to academic and commercial researchers along with the library of patient derived iPS cells, all without IP restrictions. The data is being analyzed using deep **machine learning** algorithms performed in collaboration with partner organizations. Discussion: The overall goal of this comprehensive individualized clinical and biological national effort will be to identify biological subsets of ALS which will inform future clinical trials, help develop therapies targeting the proper molecular pathway for the right patient subgroup, provide a platform of human patient derived authentic neurons for use in patient subgroup drug discovery and appropriate **biomarker** and/or pharmacodynamic markers for use in clinical trials.

**Accession number:** 613441387

**Author e-mail address:** jrothstein@jhmi.edu

**Conference country:** Ireland

**Conference end date:** 2016-12-09

**Conference location:** Dublin

**Conference start date:** 2016-12-07

**Conference title:** 27th International Symposium on ALS/MND

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**Correspondence author:** Rothstein, J. Johns Hopkins University, Baltimore, MD, United States.

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**Document type:** Conference Abstract

**DOI:** <http://dx.doi.org/10.1080/21678421.2016.1232061/001>

**Embase document status:** Embase

**First available:** 2016-12-16

**Identifier (keyword):** Big data, Individualized medicine, Informatics, iPS cells

**Language:** English

**Language of abstract:** English

**Publication date:** 2016

**Publication type:** Journal

**Publisher:** Taylor and Francis Ltd

**Publisher location:** Netherlands

**Source attribution:** Embase, © Publisher specific

**Subject:** Embase;biological marker;bioinformatics (major);biology;cancer epidemiology;clinical trial;differentiation;epigenetics;genome;heart rate;human;imaging;induced pluripotent stem cell (major);lps;lung function;machine learning;metabolomics;motoneuron (major);motor activity;motor performance;nonhuman;organization;personalized medicine (major);postmarketing surveillance;proteomics;scientist;single cell analysis;sleep;statistics;transcriptomics;university;voice

**Updates:** 2016-12-16

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Document 313

## **A semi-supervised Support Vector Machine model for predicting the language outcomes following cochlear implantation based on pre-implant brain fMRI imaging**

**Author:** Tan, Lirong 1 ; Holland, Scott K. 2 ; Deshpande, Aniruddha K. 3 ; Chen, Ye 1 ; Choo, Daniel I. 4 ; Lu, Long J. 5

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**Publication info:** Brain and Behavior 5.12: 1-25. John Wiley and Sons Ltd. (Dec 1, 2015)

**Abstract (summary):** Introduction: We developed a **machine learning** model to predict whether or not a cochlear implant (CI) candidate will develop effective language skills within 2 years after the CI surgery by using the pre-implant brain fMRI data from the candidate. Methods: The language performance was measured 2 years after the CI surgery by the Clinical Evaluation of Language Fundamentals-Preschool, Second Edition (CELF-P2). Based on the CELF-P2 scores, the CI recipients were designated as either effective or ineffective CI users. For feature extraction from the fMRI data, we constructed contrast maps using the general linear model, and then utilized the Bag-of-Words (BoW) approach that we previously published to convert the contrast maps into feature vectors. We trained both supervised models and semi-supervised models to classify CI users as effective or ineffective. Results: Compared with the conventional feature extraction approach, which used each single voxel as a feature, our BoW approach gave rise to much better performance for the classification of effective versus ineffective CI users. The semi-supervised model with the feature set extracted by the BoW approach from the contrast of **speech** versus silence achieved a leave-one-out cross-validation AUC as high as 0.97. Recursive feature elimination unexpectedly revealed that two features were sufficient to provide highly accurate classification of effective versus ineffective CI users based on our current dataset. Conclusion: We have validated the hypothesis that pre-implant cortical activation patterns revealed by fMRI during infancy correlate with language performance 2 years after cochlear implantation. The two brain regions highlighted by our classifier are potential **biomarkers** for the prediction of CI outcomes. Our study also demonstrated the superiority of the semi-supervised model over the supervised model. It is always worthwhile to try a semi-supervised model when unlabeled data are available.

**Accession number:** 607203574

**Author e-mail address:** long.lu@cchmc.org

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**Correspondence author:** Lu, Long J. Division of Biomedical Informatics, MLC 7024, Cincinnati Children's Hospital Research Foundation, 3333 Burnet Avenue, Cincinnati, OH, 45229, United States.

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**DOI:** <http://dx.doi.org/10.1002/brb3.391>

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**Identifier (keyword):** Cochlear implantation, Language outcomes, Machine learning, Pre-implant fMRI, Semi-supervised SVM

**Language:** English

**Language of abstract:** English

**Number of references:** 112

**Publication date:** Dec 1, 2015

**Publication type:** Journal

**Publisher:** John Wiley and Sons Ltd

**Publisher location:** Southern Gate, PO19 8SQ, United Kingdom

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**Subject:** Embase;MEDLINE;brain (major);brain region;clinical evaluation of language fundamentals;cochlea prosthesis;cochlear implantation (major);extraction;functional magnetic resonance imaging (major);human;human experiment;implant (major);infancy;language (major);model (major);prediction;recipient;speech;statistical model;support vector machine (major);surgery;validation process;algorithm;Article;hearing test;language processing (major);measurement accuracy;priority journal;sensitivity and specificity

**Updates:** 2016-01-252017-05-12

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Document 314

## The unique heart sound signature of children with pulmonary artery hypertension

**Author:** Elgendi, Mohamed 1 ; Bobhate, Prashant 2 ; Jain, Shreepal 2 ; Guo, Long 2 ; Kumar, Shine 2 ; Rutledge, Jennifer 3 ; Coe, Yashu 3 ; Zemp, Roger 4 ; Schuurmans, Dale 5 ; Adatia, Ian 3

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**Publication info:** Pulmonary circulation 5.4: 631-9. (Dec 2015)

**Abstract (summary):** We hypothesized that vibrations created by the pulmonary circulation would create sound like the **vocal** cords during **speech** and that subjects with pulmonary artery hypertension (PAH) might have a unique sound **signature**. We recorded heart sounds at the cardiac apex and the second left intercostal space (2LICS), using a digital stethoscope, from 27 subjects (12 males) with a median age of 7 years (range: 3 months-19 years) undergoing simultaneous cardiac catheterization. Thirteen subjects had mean pulmonary artery pressure (mPAP) <25 mmHg (range: 8-24 mmHg). Fourteen subjects had mPAP ≥ 25 mmHg (range: 25-97 mmHg). We extracted the relative power of the frequency band, the entropy, and the energy of the sinusoid formants from the heart sounds. We applied linear discriminant analysis with leave-one-out cross validation to differentiate children with and without PAH. The significance of the results was determined with a t test and a rank-sum test. The entropy of the first sinusoid formant contained within an optimized window length of 2 seconds of the heart sounds recorded at the 2LICS was significantly lower in subjects with mPAP ≥ 25 mmHg relative to subjects with mPAP <25 mmHg, with a sensitivity of 93% and specificity of 92%. The reduced entropy of the first sinusoid formant of the heart sounds in children with PAH suggests the existence of an organized pattern. The analysis of this pattern revealed a unique sound **signature**, which could be applied to a noninvasive method to diagnose PAH.

**Accession number:** 26697170

**Correspondence author:** Elgendi, Mohamed Department of Computing Science, University of Alberta, Edmonton, Alberta, Canada ; Current address: Electrical and Computer Engineering in Medicine Group, University of British Columbia, and British Columbia Children's Hospital, Vancouver, British Columbia, Canada.

**Database:** MEDLINE®; 1946 to date (1946 - current)

**Date completed:** 2015-12-23

**Date created:** 2015-12-24

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**Document type:** Journal Article

**DOI:** <http://dx.doi.org/10.1086/683694>

**First available:** 2015-12-24

**Identifier (keyword):** auscultation, congenital heart disease, language recognition, machine learning, pulmonary hypertension

**Language:** English

**Language of abstract:** English

**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Print;; Cited medium:Print

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**Publication type:** Journal

**Publisher location:** UNITED STATES

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Document 315

### **Should we screen for cognitive decline and dementia?**

**Author:** Calzà, Laura 1 ; Beltrami, Daniela 2 ; Gagliardi, Gloria 2 ; Ghidoni, Enrico 3 ; Marcello, Norina 3 ; Rossini-Favretti, Rema 4 ; Tamburini, Fabio 4

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**Publication info:** Maturitas 82.1: 28-35. Elsevier Ireland Ltd. (Sep 1, 2015)

**Abstract (summary):** Due to increased life expectancy, the prevalence of cognitive decline related to neurodegenerative diseases and to non-neurological conditions is increasing in western countries. As with other diseases, the burden might be reduced through personalized interventions delivered at early stages of the disease. Thus, there is an increasing demand, from both social and healthcare systems, for instruments and strategies to recognize cognitive decline, and possibly distinguish the precursor of serious neurodegeneration from "benign senile forgetfulness" or the temporary consequences of illness or trauma. However, this goal faces both technical and ethical issues. In this

article we deal with the following: (i) re-definition of cognitive decline and its relationship with frailty definitions, starting from the recent work of international consensus groups for presymptomatic Alzheimer disease recognition; (ii) ethical problems concerning anonymous and personalized cognitive screening and the need for appropriate counselling; (iii) the need for more sensitive and specific tools to detect and distinguish pathological levels of cognitive decline and delineate the contribution of non-pathological decline to accumulated frailty impacts and (iv) the potential of the language domain and spontaneous **speech** analyses.

**Accession number:** 605087128

**Author e-mail address:** laura.calza@unibo.it

**Copyright:** Copyright 2015 Elsevier B.V., All rights reserved.

**Correspondence author:** Calzà, Laura Health Sciences and Technologies - Interdepartmental Center for Industrial Research (CIRI-SDV), University of Bologna, Via Tolara di Sopra 41/E, Ozzano Emilia, 40064, Italy.

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**Identifier (keyword):** Cognitive decline, Cognitive frailty, Older adults, Personalized diagnosis, Screening, Spontaneous **speech** analysis

**Language:** English

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**Subject:** Embase;MEDLINE;**biological marker** -- endogenous compound;adult (major);Alzheimer disease;consensus;counseling;degenerative disease;dementia (major);diagnosis (major);diseases;health care system;injury;language;life expectancy;nerve degeneration;precursor;prevalence;screening (major);**speech analysis**



(major);Article;autoanalysis;cognitive defect -- diagnosis (major);cognitive reserve;conceptual framework;dementia -- diagnosis (major);deterioration;early diagnosis;frailty +;human;immunohistology;machine learning;medical ethics;mild cognitive impairment;natural language processing;neuropsychological test;physical disease;practice guideline

**Updates:** 2015-08-282016-12-18

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Document 316

## **Digital biomarkers for mood disorders**

**Author:** Wicks, P. 1

1 PatientsLikeMe, Research and Development, Alrewas, United Kingdom

**Publication info:** European Neuropsychopharmacology, suppl. 2 25 : S112-S113. Elsevier. (Sep 2015)

**Abstract (summary):** Individuals with a variety of mental health conditions are increasingly using digital technology in their everyday lives from managing their finances to shopping and interacting with loved ones. A 2007 report suggested that 91% of mobile phone users have it within 3 feet of their body 24 hours a day, including when asleep. While traditional clinical biomarkers such as blood, neuroimaging, and cerebrospinal fluid are likely to have precedence in determining a biological marker of illness, digital channels are far more accessible for continually assessing phenotypic markers of illness, such as physical activity, sleep, voice, and valence of social interactions [e.g.1]. Digital systems also have the potential to reactively deploy appropriate interventions where patients are. For example a user in the United Kingdom who uses Google to search for “suicide methods” will be provided with the telephone line of the Samaritans hotline over other organic search results. In clinical settings, smartphone tools like Ginger.io have been used as a Behavioral Health Program to collect data in the background of patients with depression to identify patients in need of intervention from clinically trained professionals [2]. There are risks however and much of the digital space is developed by technology enthusiasts rather than clinically trained scientists, so while there is great potential a cautious and transparent scientific approach should be advocated, with patients themselves continually engaged in the design and evaluation process.

**Accession number:** 72129115

**Conference country:** Netherlands

**Conference end date:** 2015-09-01

**Conference location:** Amsterdam

**Conference start date:** 2015-08-29

**Conference title:** 28th European College of Neuropsychopharmacology, ECNP Congress

**Copyright:** Copyright 2015 Elsevier B.V., All rights reserved.

**Correspondence author:** Wicks, P. PatientsLikeMe, Research and Development, Alrewas, United Kingdom.

**Database:** Embase®; 1947 to date (1947 - current)

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**Subject:** Embase;biological marker (major);marker;mood disorder (major);European (major);college (major);psychopharmacology (major);human;patient;technology;diseases;finance;love;mental health;physical activity;mobile phone;cerebrospinal fluid;neuroimaging;shopping;sleep;voice;social interaction;blood;suicide;United Kingdom;telephone;health program;risk;scientist

**Updates:** 2016-02-10

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Document 317

### **Automated analysis of free speech predicts psychosis onset in high-risk youths**

**Author:** Bedi, Gillinder 1 ; Carrillo, Facundo 2 ; Cecchi, Guillermo A 3 ; Slezak, Diego Fernández 2 ; Sigman, Mariano 4 ; Mota, Natália B 5 ; Ribeiro, Sidarta 5 ; Javitt, Daniel C 6 ; Copelli, Mauro 7 ; Corcoran, Cheryl M 6

1 Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, NY, USA; Division on Substance Abuse, New York State Psychiatric Institute, New York, NY, USA, USA 2 Department of computer Science, School of Sciences, Universidad de Buenos Aires , Buenos Aires, Argentina, Argentina 3 Computational Biology Center-Neuroscience, IBM T.J. Watson

Research Center , Yorktown Heights, NY, USA, USA 4 Department of Physics, School of Sciences, Universidad de Buenos Aires , Buenos Aires, Argentina, Argentina 5 Brain Institute, Federal University of Rio Grande do Norte , Natal, Brazil, Brazil 6 Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, NY, USA; Division of Experimental Therapeutics, New York State Psychiatric Institute, New York, NY, USA, USA 7 Department of Physics, Federal University of Pernambuco , Recife, Brazil, Brazil

**Publication info:** NPJ schizophrenia 1 : 15030. (Aug 26, 2015)

## **Abstract (summary): BACKGROUND/OBJECTIVES**

Psychiatry lacks the objective clinical tests routinely used in other specializations. Novel computerized methods to characterize complex behaviors such as **speech** could be used to identify and predict psychiatric illness in individuals.

## **AIMS**

In this proof-of-principle study, our aim was to test automated **speech** analyses combined with **Machine Learning** to predict later psychosis onset in youths at clinical high-risk (CHR) for psychosis.

## **METHODS**

Thirty-four CHR youths (11 females) had baseline interviews and were assessed quarterly for up to 2.5 years; five transitioned to psychosis. Using automated analysis, transcripts of interviews were evaluated for semantic and syntactic features predicting later psychosis onset. **Speech** features were fed into a convex hull classification algorithm with leave-one-subject-out cross-validation to assess their predictive value for psychosis outcome. The canonical correlation between the **speech** features and prodromal symptom ratings was computed.

## **RESULTS**

Derived **speech** features included a Latent Semantic Analysis measure of semantic coherence and two syntactic **markers** of **speech** complexity: maximum phrase length and use of determiners (e.g., which). These **speech** features predicted later psychosis development with 100% accuracy, outperforming classification from clinical interviews. **Speech** features were significantly correlated with prodromal symptoms.

## **CONCLUSIONS**

Findings support the utility of automated **speech** analysis to measure subtle, clinically relevant mental state changes in emergent psychosis. Recent developments in computer science, including natural language processing, could provide the foundation for future development of objective clinical tests for psychiatry.

**Accession number:** 27336038

**Correspondence author:** Bedi, Gillinder Department of Psychiatry, College of Physicians and Surgeons of Columbia University, New York, NY, USA; Division on Substance Abuse, New York State Psychiatric Institute, New York, NY, USA.

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**Date completed:** 2016-06-23

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Document 318

## **Classification of laryngeal disorders based on shape and vascular defects of vocal folds**

**Author:** Irem Turkmen, H. 1 ; Elif Karşligil, M. 1 ; Kocak, Ismail 2

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**Publication info:** Computers in Biology and Medicine 62 : 76-85. Elsevier Ltd. (Jul 1, 2015)

**Abstract (summary):** Vocal fold disorders such as laryngitis, vocal nodules, and vocal polyps may cause hoarseness, breathing and swallowing difficulties due to vocal fold malfunction. Despite the fact that state of the art medical imaging techniques help physicians to obtain more detailed information, difficulty in differentiating minor anomalies of vocal folds encourages physicians to research new strategies and technologies to aid the diagnostic process. Recent studies on vocal fold disorders note the potential role of the vascular structure of vocal folds in differential diagnosis of anomalies. However, standards of clinical usage of the blood vessels have not been well established yet due to the lack of objective and comprehensive evaluation of the vascular structure. In this paper, we present a novel approach that categorizes vocal folds into healthy, nodule, polyp, sulcus vocalis, and laryngitis classes exploiting visible blood vessels on the superior surface of vocal folds and shapes of vocal fold edges by using image processing techniques and machine learning methods. We first detected the vocal folds on videolaryngostroboscopy images by using Histogram of Oriented Gradients (HOG) descriptors. Then we examined the shape of vocal fold edges in order to provide features such as size and splay portion of mass lesions. We developed a new vessel centerline extraction procedure that is specialized to the vascular structure of vocal folds. Extracted vessel centerlines were evaluated in order to get vascular features of vocal folds, such as the amount of vessels in the longitudinal and transverse form. During the last step, categorization of vocal folds was performed by a novel binary decision tree architecture, which evaluates features of the vocal fold edge shape and vascular structure. The performance of the proposed system was evaluated by using laryngeal images of 70 patients. Sensitivity of 86%, 94%, 80%, 73%, and 76% were obtained for healthy, polyp, nodule, laryngitis, and sulcus vocalis classes, respectively. These results indicate that visible vessels of vocal folds can act as a prognostic marker for vocal fold pathologies, as well as the vocal fold shape features, and may play a critical role in more effective diagnosis.

**Accession number:** 604003521

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**Copyright:** Copyright 2015 Elsevier B.V., All rights reserved.

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**First available:** 2015-05-25

**Identifier (keyword):** Classification of **vocal** fold disorders, Histogram of oriented gradients, Laryngeal image analysis, Measurement of **vocal** fold shape defects, Vascular vectors, Vessel centerline extraction

**Language:** English

**Language of abstract:** English

**Number of references:** 39

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**Subject:** Embase;MEDLINE;**marker**;architecture;blood vessel;breathing;classification (major);decision tree;diagnosis;diagnostic imaging;differential diagnosis;diseases (major);extraction (major);histogram (major);hoarseness;human;image analysis (major);image processing;laryngitis;larynx disorder (major);**machine learning**;pathology;patient;physician;polyp;procedures;swallowing;technology;**vocal cord** (major);Article;disease classification (major);histogram;laryngitis (major);laryngoscopy;priority journal;sulcus vocalis + (major);**vocal cord disorder** (major);vocal fold nodule + (major);vocal fold polyp + (major)

**Updates:** 2015-05-25

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Document 319

## **Automatic **speech** analysis for the assessment of patients with predementia and Alzheimer's disease**

**Author:** König, Alexandra 1 ; Satt, Aharon 2 ; Sorin, Alexander 2 ; Hoory, Ron 2 ; Toledo-Ronen, Orith 2 ; Derreumaux, Alexandre 3 ; Manera, Valeria 3 ; Verhey, Frans 4 ; Aalten, Pauline 4 ; Robert, Phillipe H 5 ; David, Renaud 5

1 Research Unit CoBTek - Cognition Behaviour Technology, Edmond & Lily Safra Research Center, University of Nice Sophia Antipolis, Nice, France; Alzheimer Centre Limburg, Maastricht University Medical Center, School for Mental Health and Neuroscience, Maastricht, The Netherlands, The Netherlands 2 Speech Technologies, IBM Research, Haifa, Israel, Israel 3 Research Unit CoBTek - Cognition Behaviour Technology, Edmond & Lily Safra Research Center, University of Nice Sophia

Antipolis, Nice, France, France 4 Alzheimer Centre Limburg, Maastricht University Medical Center, School for Mental Health and Neuroscience, Maastricht, The Netherlands, The Netherlands 5 Research Unit CoBTeK - Cognition Behaviour Technology, Edmond & Lily Safra Research Center, University of Nice Sophia Antipolis, Nice, France; Centre Mémoire de Ressources et de Recherche, CHU de Nice, Nice, France, France

**Publication info:** Alzheimer's & dementia (Amsterdam, Netherlands) 1.1: 112-24. (Mar 29, 2015)

## **Abstract (summary):** BACKGROUND

To evaluate the interest of using automatic **speech** analyses for the assessment of mild cognitive impairment (MCI) and early-stage Alzheimer's disease (AD).

## METHODS

Healthy elderly control (HC) subjects and patients with MCI or AD were recorded while performing several short cognitive **vocal** tasks. The **voice** recordings were processed, and the first **vocal markers** were extracted using **speech** signal processing techniques. Second, the **vocal markers** were tested to assess their "power" to distinguish among HC, MCI, and AD. The second step included training automatic classifiers for detecting MCI and AD, using **machine learning** methods and testing the detection accuracy.

## RESULTS

The classification accuracy of automatic audio analyses were as follows: between HCs and those with MCI, 79% ± 5%; between HCs and those with AD, 87% ± 3%; and between those with MCI and those with AD, 80% ± 5%, demonstrating its assessment utility.

## CONCLUSION

Automatic **speech** analyses could be an additional objective assessment tool for elderly with cognitive decline.

**Accession number:** 27239498

**Correspondence author:** König, Alexandra Research Unit CoBTeK - Cognition Behaviour Technology, Edmond & Lily Safra Research Center, University of Nice Sophia Antipolis, Nice, France; Alzheimer Centre Limburg, Maastricht University Medical Center, School for Mental Health and Neuroscience, Maastricht, The Netherlands.

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**Identifier (keyword):** Alzheimer's, Assessment, Audio, Dementia, Information and communication technology (ICT), Mild cognitive impairment, **Speech** analyses, **Vocal** task

**Language:** English

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Document 320

## **Automatic **speech** analysis for the assessment of pre-demented and alzheimer patients**

**Author:** König, A. 1 ; Satt, A. 2 ; Sorin, A. 2 ; Derreumaux, A. 1 ; David, R. 3 ; Verhey, F. 4 ; Aalten, P. 4 ; Robert, P. 1

1 CobteK, Institut Claude Pompidou, Nice, France 2 Speech Lab, IBM Research, Haifa, Israel 3 CHU De Nice, Centre Mémoire De Ressources Et De Recherche, Nice, France 4 School for Mental Health and Neuroscience, Alzheimer Center, Limburg Maastricht University, Maastricht, Netherlands

**Publication info:** Neurodegenerative Diseases, suppl. 1 15 : 1090. S. Karger AG. (Mar 2015)

**Abstract (summary):** Background: Various types of dementia and MCI are manifested as irregularities in human **speech** and language, which have proven to be strong predictors for the disease presence and progression. Therefore, automatic **speech** analysis is expected to be an useful tool in providing indicators for assessment and detection of early stage Alzheimer's disease (AD) and MCI. Method: 15 Healthy elderly subjects (HC), 23 MCI patients and 26 AD patients were recorded while performing several short **vocal** cognitive tasks, including verbal fluency, picture description and counting down, during a regular consultation. **Voice** recordings were processed in two steps: first **vocal markers** were extracted using **speech** signal processing techniques; second, **vocal markers**



were tested to assess their 'power' to distinguish between HC, MCI and AD. The second step included training automatic classifiers for detecting MCI and AD, based on **machine learning** methods, and testing the detection accuracy. Results: classification accuracy of automatic audio analyses were as follows: between HC and MCI:  $79 \pm 5\%$ , between HC and AD:  $87 \pm 3\%$ , and between MCI and AD:  $80 \pm 5\%$ . Conclusions: Decline in cognitive functioning affects **speech** production in different ways. Preliminary analysis indicates the potential value of **vocal** cognitive tasks for accurate automatic differentiation between HC, MCI and AD. This can provide the clinician with meaningful information for assessment and early diagnosis purposes, based on non-invasive, simple and low-cost method. Investigations of new and improved **vocal** tasks, signal processing tools and pattern recognition tools, are planned.

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**Conference country:** France

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**Conference start date:** 2015-03-18

**Conference title:** 12th International Conference Alzheimer's and Parkinson's Diseases, AD/PD 2015

**Copyright:** Copyright 2015 Elsevier B.V., All rights reserved.

**Correspondence author:** König, A. CobteK, Institut Claude Pompidou, Nice, France.

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**Subject:** Embase;**marker**;patient (major);**speech analysis** (major);human (major);Parkinson disease (major);**speech**;cognition;signal processing;consultation;**machine learning**;tracheobronchial

stent;classifier;aged;dementia;voice;pattern recognition;classification;sound analysis;early diagnosis;speech and language;recording;Alzheimer disease

**Updates:** 2015-04-25

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Document 321

## **Social biomarkers for early signs of dementia: Increased spoken word counts among older adults with mild cognitive impairment (MCI)**

**Author:** Kaye, Jeffrey 1 ; Gregor, Mattie 1 ; Matteck, Nora 1 ; Asgari, Meysam 1 ; Bowman, Molly 1 ; Ybarra, Oscar 2 ; Dodge, Hiroko 3

1 Oregon Health and Science University, Portland, OR, United States kaye@ohsu.edu 2 University of Michigan, Ann Arbor, MI, United States 3 Oregon Health and Science University, University of Michigan Health System, Portland, OR, United States

**Publication info:** Alzheimer's and Dementia, suppl. 4 10 : P915-P916. Elsevier Inc. (Jul 2014)

**Abstract (summary):** Background: It is of significant importance to detect early signs indicating the transition from normal cognitive aging to MCI. Although biomarkers have been extensively examined as early indicators of the pathological process for AD, assessing these biomarkers is expensive and challenging. Behavioral activity markers offer an alternative tool for detection of those in transition. We hypothesized that MCI subjects talk more than age/gender- matched normal peers in freely-enacted conversations, possibly due to their impaired ability in identifying social cues required for smooth interactions or in self-monitoring, organizing and conveying thoughts. This hypothesis was examined in a sub-study within a randomized controlled clinical trial (RCT) that assessed whether daily 30 minute face-to-face semi-structured conversations with trained interviewers via webcam and Internet-enabled personal computers improves cognitive function among those with either normal cognition or MCI (ClinicalTrials.gov: NCT01571427). Methods: Proportions of total words spoken by participants (vs. by interviewers) during recorded conversational sessions in the RCT were compared between those with MCI and normal cognition (project A). Recorded conversations were transcribed by a single transcriber. As an exploratory study (project B), average total talk time per day spoken by each participant in daily life collected through a small wearable digital recording device was also examined by state-of-the-art speech detection algorithms. 41 subjects in the conversational experimental group with valid recorded sessions (project A) and 45 subjects who consented to record their daily conversation (project B) were used in this study. Interviewers were blind to cognitive status of the subject. Results: The mean (SD) % of words spoken by participants was higher ( $p < 0.01$ ) among MCI (69.5% (9.7)) than normal (60.3% (11.4)) subjects in linear regression models adjusting for age and gender. MCI participants spoke longer ( $p = 0.037$ ) by 105 minutes on average per day during daily life than normal subjects in GEE models controlling for age, education, gender and living arrangement. Conclusions: MCI subjects may exhibit subtle language processing deficits that affect social cognitive abilities required for smooth social interactions, leading to more words spoken during conversations or

longer daily talking time. The assessment approach used here may provide an ecologically valid behavioral marker sensitive to transitions to MCI.

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**Author e-mail address:** kaye@ohsu.edu

**Conference country:** Denmark

**Conference end date:** 2014-07-17

**Conference location:** Copenhagen

**Conference start date:** 2014-07-12

**Conference title:** Alzheimer's Association International Conference 2014

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**Correspondence author:** Kaye, J. Oregon Health and Science University, Portland, OR, United States.

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**Subject:** Embase; biological marker (major); marker; dementia (major); adult (major); mild cognitive impairment (major); human; conversation; cognition; model; gender; microcomputer; Internet; aging; controlled clinical trial; hypothesis; linear regression analysis; self monitoring; normal human; language processing; social interaction; speech; algorithm; devices; recording; education; behavior

**Updates:** 2014-09-30

## **The dem@care project **speech** recording and automatic analysis for the assessment of Alzheimer disease and related disorders**

**Author:** Satt, Aharon 1 ; König, Alexandra 2 ; Sorin, Alexander 1 ; Toledo-Ronen, Orith 3 ; Hoory, Ron 3 ; David, Renaud 4 ; Verhey, Frans R.J. 5 ; Aalten, Pauline 6 ; Robert, Philippe H. 7

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**Publication info:** Alzheimer's and Dementia, suppl. 4 10 : P685. Elsevier Inc. (Jul 2014)

**Abstract (summary):** Background: Assessment of early stage Alzheimer's disease (E-AD) and other dementia types, as well as Mild Cognitive Impairment (MCI) is complex; a broad range of heterogeneous assessment methods exist. Various types of dementia and MCI are manifested as irregularities in human **speech** and language, which have proven to be strong predictors for the disease presence and progression. Therefore, automatic **speech** analysis is expected to be a useful tool in providing indicators for assessment and detection of early stage dementia and MCI. Methods: 13 Healthy elderly subjects (HC), 22 MCI patients and 23 E-AD patients were recorded while performing several short **vocal** cognitive tasks during a regular consultation. These tasks included verbal fluency, picture description and counting down. The **voice** recordings were processed in two steps: in the first step, **vocal markers** were extracted using **speech** signal processing techniques; in the second, the **vocal markers** were tested to assess their 'power' to distinguish between HC, MCI and E-AD. The second step included training automatic classifiers for detecting MCI and E-AD, based on **machine learning** methods, and testing the detection accuracy. Results: Preliminary results show the value of certain **vocal** tasks for distinguishing between HC, MCI and E-AD. Using the above data, we demonstrated classification accuracy as follows: between HC and MCI: 82±8%, between HC and E-AD: 87±5%, and between MCI and E-AD: 81 ± 7%. Detailed description will be presented at the AAIC meeting. Conclusions: Decline in cognitive functioning affects **speech** production in different ways. Preliminary analysis indicates the potential value of **vocal** cognitive tasks for accurate automatic differentiation between HC, MCI and E-AD. This can provide the clinician with meaningful information for assessment and early diagnosis purposes, based on non-invasive, simple and low-cost method. Investigations of new and improved **vocal** tasks, signal processing tools and pattern recognition tools, are planned. (Figure Presented).

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**Author e-mail address:** a.konig@maastrichtuniversity.nl

**Conference country:** Denmark

**Conference end date:** 2014-07-17

**Conference location:** Copenhagen

**Conference start date:** 2014-07-12

**Conference title:** Alzheimer's Association International Conference 2014

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**Correspondence author:** König, A. School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands.

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**Subject:** Embase;marker;speech (major);recording (major);autoanalysis (major);diseases (major);human;dementia;cognition;patient;signal processing;classifier;voice;mild cognitive impairment;tracheobronchial stent;consultation;aged;speech analysis;early diagnosis;speech and language;classification;machine learning;pattern recognition;Alzheimer disease

**Updates:** 2014-09-30

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Document 323

### **On the selection of non-invasive methods based on speech analysis oriented to automatic Alzheimer disease diagnosis**

**Author:** López-de-Ipiña, Karmele 1 ; Alonso, Jesus-Bernardino; Travieso, Carlos Manuel; Solé-Casals, Jordi; Egiraun, Harkaitz; Faundez-Zanuy, Marcos; Ezeiza, Aitzol; Barroso, Nora; Ecay-Torres, Miriam; Martinez-Lage, Pablo; Martinez de Lizardui, Unai

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**Publication info:** Sensors (Basel, Switzerland) 13.5: 6730-45. (May 21, 2013)

**Abstract (summary):** The work presented here is part of a larger study to identify novel technologies and **biomarkers** for early Alzheimer disease (AD) detection and it focuses on evaluating the suitability of a new approach for early AD diagnosis by non-invasive methods. The purpose is to examine in a pilot study the potential of applying intelligent algorithms to **speech** features obtained from suspected patients in order to contribute to the improvement of diagnosis of AD and its degree of severity. In this sense, **Artificial Neural Networks (ANN)** have been used for the automatic classification of the two classes (AD and control subjects). Two human issues have been analyzed for feature selection: Spontaneous **Speech** and Emotional Response. Not only linear features but also non-linear ones, such as Fractal Dimension, have been explored. The approach is non invasive, low cost and without any side effects. Obtained experimental results were very satisfactory and promising for early diagnosis and classification of AD patients.

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**Author e-mail address:** karmele.ipina@ehu.es

**Correspondence author:** López-de-Ipiña, Karmele Systems Engineering and Automation Department, University of the Basque Country UPV/EHU, Donostia 20018, Spain.

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**MeSH:** Adult;Aged;Aged, 80 and over;Alzheimer Disease -- diagnosis (major);Alzheimer Disease -- physiopathology;Automation;Diagnostic Techniques and Procedures (major);Emotions;Female;Fractals;Humans;Male;Middle Aged;Pilot Projects;Signal Processing, Computer-Assisted;**Speech** -- physiology (major);Temperature;Young Adult

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Document 324

## **Evaluation of **speech** impairment in early stages of Parkinson's disease: A prospective study with the role of pharmacotherapy**

**Author:** Rusz, Jan 1 ; Čmejla, Roman 2 ; Růžičková, Hana 3 ; Klempíř, Jiří 3 ; Majerová, Veronika 3 ; Picmausová, Jana 3 ; Roth, Jan 3 ; Růžička, Evžen 3

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**Publication info:** Journal of Neural Transmission 120.2: 319-329. Springer Wien. (Feb 2013)

**Abstract (summary):** Despite the initial reports showing beneficial effects of dopaminergic treatment on **speech** in Parkinson's disease (PD), more recent studies based upon valid measurements have not approved any improvement of **speech** performance under pharmacotherapy. The aim of this study was to analyze the effect of treatment initiation on the progression of **speech** impairment in PD, using novel evaluation criteria. Nineteen de novo patients with PD were tested and retested within 2 years after the introduction of antiparkinsonian therapy. As controls, 19 age-matched individuals were recorded. **Speech** examination included sustained **phonation**, fast syllable repetition, reading text, and monolog. Quantitative acoustic analyses of the key aspects of **speech** based on Gaussian kernel distribution, statistical decision-making theory, and healthy **speech** observation were used to assess the improvement or deterioration of **speech**. A trend for **speech** performances to improve was demonstrated after treatment mainly in quality of **voice**, intensity variability, pitch variability, and articulation. The treatment-related improvement differed in various aspects of **speech** for individual PD patients. Improvements in vowel articulation and pitch variability correlated with treatment-related changes in bradykinesia and rigidity, whereas **voice** quality and loudness variability improved independently. Using a novel approach of acoustic analysis and advanced statistics, improvements in **speech** performance can be demonstrated in PD patients after the introduction of antiparkinsonian

therapy. Moreover, changes in **speech** articulation and pitch variability appear to be related with dopaminergic responsiveness of bradykinesia and rigidity. Therefore, **speech** may be a valuable **marker** of disease progression and treatment efficacy in PD. © 2012 Springer-Verlag.

**Accession number:** 52102538

**Author e-mail address:** eruzi@lf1.cuni.cz

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**Correspondence author:** Růžička, E. Department of Neurology, Centre of Clinical Neuroscience, Charles University in Prague, Kateřinská 30, 120 00 Prague 2, Czech Republic.

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**Identifier (keyword):** Acoustic analysis, **Dysarthria**, Levodopa, Parkinson's disease, **Speech** disorders

**Language:** English

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**Number of references:** 61

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**Publisher location:** Sachsenplatz 4-6, P.O. Box 89, A-1201, Austria

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**Subject:** Embase;MEDLINE;antiparkinson agent;levodopa (major);**marker**;acoustic analysis (major);bradykinesia;decision making;deterioration;disease course;drug therapy (major);**dysarthria** (major);examination;human (major);**kernel method**;**loudness**;Parkinson disease (major);patient;**phonation**;prospective study (major);reading;rigidity;**speech**;**speech articulation**;**speech disorder** (major);statistical distribution;statistics;therapy;**voice**;vowel;adult;aged;article;clinical article;controlled study;female;gait disorder;human;male;priority journal;prospective study;**speech analysis**

**Updates:** 2013-06-12



## Selecting Disorder-Specific Features for Speech Pathology Fingerprinting

**Author:** Berisha, Visar 1 ; Sandoval, Steven 2 ; Utianski, Rene 1 ; Liss, Julie 1 ; Spanias, Andreas 2

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**Publication info:** Proceedings of the ... IEEE International Conference on Acoustics, Speech, and Signal Processing. ICASSP (Conference) : 7562-7566. (2013)

**Abstract (summary):** The general aim of this work is to learn a unique statistical signature for the state of a particular speech pathology. We pose this as a speaker identification problem for dysarthric individuals. To that end, we propose a novel algorithm for feature selection that aims to minimize the effects of speaker-specific features (e.g., fundamental frequency) and maximize the effects of pathology-specific features (e.g., vocal tract distortions and speech rhythm). We derive a cost function for optimizing feature selection that simultaneously trades off between these two competing criteria. Furthermore, we develop an efficient algorithm that optimizes this cost function and test the algorithm on a set of 34 dysarthric and 13 healthy speakers. Results show that the proposed method yields a set of features related to the speech disorder and not an individual's speaking style. When compared to other feature-selection algorithms, the proposed approach results in an improvement in a disorder fingerprinting task by selecting features that are specific to the disorder.

**Accession number:** 25005047

**Correspondence author:** Berisha, Visar Department of Speech and Hearing Science, Arizona State University, Tempe, AZ 85287.

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**Identifier (keyword):** dysarthria, feature selection, machine learning, speech pathology

**Language:** English

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**Medline document status:** PubMed-not-MEDLINE

**Notes:** Publication model: Print;; Cited medium:Print

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**Updates:** 2014-07-122016-10-222016-10-262020-09-292021-10-192021-10-22

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Document 326

## **Combining computational neuroscience and body sensor networks to investigate Alzheimer's disease**

**Author:** Bergmann, Jeroen 1 ; Howard, Newton 2

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**Publication info:** BMC Neuroscience, suppl. 1 13 BioMed Central Ltd. (Jul 16, 2012)

**Abstract (summary):** Alzheimer's disease is a syndrome of acquired cognitive defects that interferes with normal brain function. While its biochemical effects are well documented, the cause of Alzheimer's disease is still not known and the best available interventions remain merely symptomatic. Different treatment modalities have been explored over the last few decades. Pharmaceutical interventions currently consist of medicines that focus on the neuropsychiatric symptoms and disease-modifying treatments. The importance of early intervention to the efficacy of treatments has led to an emphasis on detection and diagnosis in clinical research, and techniques using imaging, biomarkers and genetic information as tools for early detection have become prevalent. However, multifaceted noninvasive screening tools that incorporate computational algorithms and do not rely on imaging are not being widely developed. This paper argues that a computation method originally developed to explain mental processes can be adapted to assist in the early detection of Alzheimer's disease. Temporal changes in behaviour and speech are occurring in the early stages of the disease. A Body Sensor Network (BSN) can be utilized to collect temporal information during everyday living which can be further processed with an algorithm that allows for natural randomness. This method shows that novel non-invasive screening tools for Alzheimer's

disease can be devised based on measuring real-life behaviour. Conclusions: It has been shown that BSNs can be utilized to measure a range of activities. A MSI classification algorithm can subsequently categorize the temporal changes during ADL activities, while allowing for natural occurring randomness [1]. The BSN can be unobtrusive to allow for monitoring over longer periods of time [2]. The technique outlined here can be used for diagnostic purposes, but it can also be implemented to screen for treatment effects of new and existing interventions.

**Accession number:** 71044071

**Author e-mail address:** nhmit@mit.edu

**Conference country:** United States

**Conference end date:** 2012-07-26

**Conference location:** Decatur, GA

**Conference start date:** 2012-07-21

**Conference title:** 21st Annual Computational Neuroscience Meeting, CNS 2012

**Copyright:** Copyright 2013 Elsevier B.V., All rights reserved.

**Correspondence author:** Bergmann, J. Medical Engineering Solutions in Osteoarthritis Centre of Excellence, Imperial College, London, W68RF, United Kingdom.

**Database:** Embase®; 1947 to date (1947 - current)

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**Subject:** Embase;sensor (major);Alzheimer disease (major);central nervous system (major);diagnosis;screening;algorithm;imaging;speech;cognitive defect;clinical research;monitoring;mental function;classification algorithm;early intervention;brain function

**Updates:** 2013-04-30

## Acoustic analysis of speech progression in Parkinson's disease

**Author:** Rusz, J. 1 ; Cmejla, R. 1 ; Ruzickova, H. 1 ; Klempir, J. 1 ; Majerova, V. 1 ; Picmausova, J. 1 ; Roth, J. 1 ; Ruzicka, E. 1

1 Czech Technical University in Prague (Prague, CZ); Charles University in Prague (Prague, CZ)

**Publication info:** Journal of Neurology, suppl. 1 259.1: S4. D. Steinkopff-Verlag. (Jun 2012)

**Abstract (summary):** Background: Hypokinetic dysarthria in Parkinson's disease (PD) is a multidimensional impairment of phonation, respiration, articulation, and prosody. While the beneficial effect of dopaminergic therapy on the principal motor symptoms in PD has been well-documented over decades, its effect on speech remains unclear. The aim of this study was to investigate the feasibility of acoustic measures in analyzing the effect of treatment initiation on the progression of speech impairment in PD. Methods: 19 de novo patients with PD were tested and re-tested after 13-24 months after the introduction of antiparkinsonian therapy. As a control group, 19 age-matched healthy persons were recorded. Speech data included sustained phonation, fast syllable repetition, reading text, and monologue. Unified PD Rating Scale motor subscore (UPDRS III) was rated in both evaluations. Voice parameters were obtained using quantitative acoustic analyses of the key aspects of speech. Subsequently, the evaluation criteria based upon Gaussian kernel distributions, statistical decision-making theory, and minimal detectable change of healthy speech was designed to assess individual changes of parkinsonian speech in the course of treatment. Results: A trend for speech performances to improve was demonstrated after treatment mainly in quality of voice, loudness and pitch variability, and articulation. The treatment-related changes differed individually across various aspects of speech. Improvements in vowel articulation correlated with treatment-related changes in bradykinesia ( $r = 0.45$ ,  $p < 0.05$ ) and rigidity ( $r = 0.52$ ,  $p < 0.05$ ). In addition, there was a significant correlation between changes in rigidity and pitch variability ( $r = 0.45$ ,  $p < 0.05$ ). Voice quality and loudness variability were improved with dopaminergic medication independently of changes in motor performances. Conclusions: Acoustic analysis and advanced statistics revealed improvements in speech parameters after the introduction of antiparkinsonian therapy in PD patients. Moreover, changes in vowel articulation and pitch variability appear to be related with dopaminergic responsiveness of bradykinesia and rigidity. Therefore, speech can be considered as a marker of disease progression. Acoustic analysis appears as a helpful tool for monitoring the severity of speech impairment and the effects of therapy in PD.

**Accession number:** 71229678

**Conference country:** Czech Republic

**Conference end date:** 2012-06-12

**Conference location:** Prague

**Conference start date:** 2012-06-09

**Conference title:** 22nd Meeting of the European Neurological Society

**Copyright:** Copyright 2013 Elsevier B.V., All rights reserved.

**Correspondence author:** Ruzs, J.

**Database:** Embase®; 1947 to date (1947 - current)

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**DOI:** <http://dx.doi.org/10.1007/s00415-012-6524-4>

**Embase document status:** Embase

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**Publication date:** Jun 2012

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**Subject:** Embase;antiparkinson agent;marker;speech (major);acoustic analysis (major);society (major);Parkinson disease (major);therapy;human;rigidity;voice parameter;phonation;vowel;bradykinesia;patient;loudness;voice;speech disorder;kernel method;Unified Parkinson Disease Rating Scale;reading;monitoring;normal human;statistics;motor performance;disease course;drug therapy;decision making;control group;dysarthria

**Updates:** 2013-11-27

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Document 328

## **The omega point and beyond: The singularity event**

**Author:** Castillo, M.

**Publication info:** American Journal of Neuroradiology 33.3: 393-395. American Society of Neuroradiology. (Mar 2012)

**Accession number:** 364478115

**Copyright:** Copyright 2012 Elsevier B.V., All rights reserved.

**Correspondence author:** Castillo, M.

**Database:** Embase®; 1947 to date (1947 - current)

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**Language:** English

**Number of references:** 13

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**Publication type:** Journal

**Publisher:** American Society of Neuroradiology

**Publisher location:** 800 Enterprise Drive, IL 60521, United States

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**Subject:** Embase;MEDLINE;biological marker;aging;artificial intelligence (major);astronomy;automatic speech recognition;biomanipulation;computer;cosmos;destruction;DNA modification;editorial;evolution;food and drug administration;functional neuroimaging;genetic manipulation;genome;human;human genome;humanism;information technology;music;nanomedicine;nerve cell;public hospital;synaptic transmission

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Document 329

### **Pattern of neural responses to verbal fluency shows diagnostic specificity for schizophrenia and bipolar disorder**

**Author:** Costafreda, Sergi G 1 ; Fu, Cynthia H Y; Picchioni, Marco; Touloupoulou, Timothea; McDonald, Colm; Kravariti, Eugenia; Walshe, Muriel; Prata, Diana; Murray, Robin M; McGuire, Philip K

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**Publication info:** BMC psychiatry 11 : 18. (Jan 28, 2011)

## **Abstract (summary): BACKGROUND**

Impairments in executive function and language processing are characteristic of both schizophrenia and bipolar disorder. Their functional neuroanatomy demonstrate features that are shared as well as specific to each disorder. Determining the distinct pattern of neural responses in schizophrenia and bipolar disorder may provide **biomarkers** for their diagnoses.

## **METHODS**

104 participants underwent functional magnetic resonance imaging (fMRI) scans while performing a phonological verbal fluency task. Subjects were 32 patients with schizophrenia in remission, 32 patients with bipolar disorder in an euthymic state, and 40 healthy volunteers. Neural responses to verbal fluency were examined in each group, and the diagnostic potential of the pattern of the neural responses was assessed with **machine learning** analysis.

## **RESULTS**

During the verbal fluency task, both patient groups showed increased activation in the anterior cingulate, left dorsolateral prefrontal cortex and right putamen as compared to healthy controls, as well as reduced deactivation of precuneus and posterior cingulate. The magnitude of activation was greatest in patients with schizophrenia, followed by patients with bipolar disorder and then healthy individuals. Additional recruitment in the right inferior frontal and right dorsolateral prefrontal cortices was observed in schizophrenia relative to both bipolar disorder and healthy subjects. The pattern of neural responses correctly identified individual patients with schizophrenia with an accuracy of 92%, and those with bipolar disorder with an accuracy of 79% in which mis-classification was typically of bipolar subjects as healthy controls.

## **CONCLUSIONS**

In summary, both schizophrenia and bipolar disorder are associated with altered function in prefrontal, striatal and default mode networks, but the magnitude of this dysfunction is particularly marked in schizophrenia. The pattern of response to verbal fluency is highly diagnostic for schizophrenia and distinct from bipolar disorder. Pattern classification of functional MRI measurements of language processing is a potential diagnostic marker of schizophrenia.

**Accession number:** 21276242

**Author e-mail address:** sergi.1.costafreda@kcl.ac.uk

**Correspondence author:** Costafreda, Sergi G Institute of Psychiatry, King's College London, De Crespigny Park, London UK.

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**MeSH:** Adult;Bipolar Disorder -- diagnosis (major);Bipolar Disorder -- physiopathology;Bipolar Disorder -- psychology;Brain -- physiopathology (major);Brain Mapping;Cerebral Cortex -- physiopathology;Cognition Disorders -- diagnosis (major);Cognition Disorders -- physiopathology;Female;Humans;Magnetic Resonance Imaging;Male;Neuropsychological Tests -- statistics & numerical data (major);Prefrontal Cortex -- physiopathology;Schizophrenia -- diagnosis (major);Schizophrenia -- physiopathology;Schizophrenic Psychology;Sensitivity and Specificity;Speech Disorders -- diagnosis;Speech Disorders -- physiopathology;Speech Disorders -- psychology;Young Adult

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Document 330

## **Acoustic and temporal analysis of speech: A potential biomarker for schizophrenia**

**Author:** Rapcan, Viliam 1 ; D'Arcy, Shona 1 ; Yeap, Sherlyn 2 ; Afzal, Natasha 3 ; Thakore, Jogin 4 ; Reilly, Richard B. 5



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**Publication info:** Medical Engineering and Physics 32.9: 1074-1079. Elsevier Ltd. (Nov 2010)

**Abstract (summary):** Currently, there are no established objective **biomarkers** for the diagnosis or monitoring of schizophrenia. It has been previously reported that there are notable qualitative differences in the **speech** of schizophrenics. The objective of this study was to determine whether a quantitative acoustic and temporal analysis of **speech** may be a potential **biomarker** for schizophrenia. In this study, 39 schizophrenic patients and 18 controls were digitally recorded reading aloud an emotionally neutral text passage from a children's story. Temporal, energy and **vocal** pitch features were automatically extracted from the recordings. A classifier based on linear discriminant analysis was employed to differentiate between controls and schizophrenic subjects. Processing the recordings with the algorithm developed demonstrated that it is possible to differentiate schizophrenic patients and controls with a classification accuracy of 79.4% (specificity. =83.6%, sensitivity. =75.2%) based on **speech** pause related parameters extracted from recordings carried out in standard office (non-studio) environments. Acoustic and temporal analysis of **speech** may represent a potential tool for the objective analysis in schizophrenia. © 2010 IPEM.

**Accession number:** 51024407

**Author e-mail address:** rapcanv@tcd.ie

**Copyright:** Copyright 2012 Elsevier B.V., All rights reserved.

**Correspondence author:** Rapcan, V. Trinity Centre for Bioengineering, Trinity College Dublin, Dublin 2, Ireland.

**Database:** Embase®; 1947 to date (1947 - current)

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**Document type:** Article

**DOI:** <http://dx.doi.org/10.1016/j.medengphy.2010.07.013>

**Embase document status:** Embase; MEDLINE

**First available:** 2010-11-08

**Identifier (keyword):** Acoustic and temporal analysis, **Biomarker**, Energy, Pause, Schizophrenia, **Speech**, Utterance, **Vocal** pitch

**Language:** English

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**Publisher location:** Langford Lane, Kidlington, OX5 1GB, United Kingdom

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**Subject:** Embase;MEDLINE;biological marker (major);biological marker;algorithm;child;classification;classifier;diagnosis;discriminant analysis;monitoring;patient;reading;recording;schizophrenia (major);speech (major);adult;article;audio recording;clinical article;controlled study;diagnostic accuracy;female;human;male;pitch;priority journal;quantitative analysis;schizophrenia -- diagnosis (major);sensitivity and specificity;sex difference;signal detection;sound transmission;speech analysis (major)

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Document 331

### **Diagnostic assessment of childhood apraxia of speech using automatic speech recognition (ASR) methods**

**Author:** Hosom, John-Paul 1 ; Shriberg, Lawrence 2 ; Green, Jordan R. 3

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**Publication info:** Journal of Medical Speech-Language Pathology 12.4: 167-171. Delmar Learning. (Dec 2004)

**Abstract (summary):** We report findings from two feasibility studies using automatic speech recognition (ASR) methods in childhood speech sound disorders. The studies evaluated and implemented the automation of two recently proposed diagnostic markers for suspected apraxia of speech (AOS) termed the Lexical Stress Ratio (LSR) and the Coefficient of Variation Ratio (CVR). The LSR is a weighted composite of amplitude area, frequency area, and duration in the stressed compared to the unstressed vowel as obtained from a speaker's productions of eight trochaic word forms. Composite weightings for the three stress parameters were determined from a principal components analysis. The CVR expresses the average normalized variability of durations of pause

and **speech** events obtained from a conversational **speech** sample. We describe the automation procedures used to obtain LSR and CVR scores for four children with suspected AOS and report comparative findings. The LSR values obtained with ASR were within 1.2 to 6.7% of the LSR values obtained manually using Computerized **Speech** Lab (CSL). The CVR values obtained with ASR were within 0.7 to 2.7% of the CVR values obtained manually using Matlab. These results indicate the potential of ASR-based techniques to process these and other diagnostic **markers** of childhood **speech** sound disorders.

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**Author e-mail address:** hosom@cslu.ogi.edu

**Copyright:** Copyright 2012 Elsevier B.V., All rights reserved.

**Correspondence author:** Hosom, J.-P. Ctr. for Spoken Lang. Understanding, Oregon Health and Science University, 20000 N.W. Walker Road, Beaverton, OR 97006, United States.

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**Number of references:** 12

**Publication date:** Dec 2004

**Publication type:** Journal

**Publisher:** Delmar Learning

**Publisher location:** 5 Maxwell Drive, P.O. Box 8007, NY 12065-8007, United States

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**Subject:** Embase;**marker**;amplitude modulation;apraxia (major);automation;child;childhood (major);conference paper;diagnosis (major);feasibility study;frequency modulation;human;priority journal;**speech** (major);**speech analysis**;**speech discrimination** (major);**speech disorder**;vowel;apraxia - - diagnosis (major);**speech**;**speech discrimination**;**speech disorder** -- diagnosis (major)

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Document 332

## Abnormal **speech** perception in schizophrenia with auditory hallucinations

**Author:** Lee, Seung-Hwan 1 ; Chung, Young-Cho 2 ; Yang, Jong-Chul 2 ; Kim, Yong-Ku 3 ; Suh, Kwang-Yoon 3

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**Publication info:** Acta neuropsychiatrica 16.3: 154-9. (Jun 2004)

### **Abstract (summary):** BACKGROUND

The neurobiological mechanism of auditory hallucination (AH) in schizophrenia remains elusive, but AH can be caused by the abnormality in the **speech** perception system based on the **speech** perception **neural network model**.

### OBJECTIVES

The purpose of this study was to investigate whether schizophrenic patients with AH have the **speech** processing impairment as compared with schizophrenic patients without AH, and whether the **speech** perception ability could be improved after AH had subsided.

### METHODS

Twenty-four schizophrenic patients with AH were compared with 25 schizophrenic patients without AH. Narrative **speech** perception was assessed using a masked **speech** tracking (MST) task with three levels of superimposed **phonetic** noise. Sentence repetition task (SRT) and auditory continuous performance task (CPT) were used to assess grammar-dependent verbal working memory and non-language attention, respectively. These tests were measured before and after treatment in both groups.

### RESULTS

Before treatment, schizophrenic patients with AH showed significant impairments in MST compared with those without AH. There were no significant differences in SRT and CPT correct (CPT-C) rates between both groups, but CPT incorrect (CPT-I) rate showed a significant difference. The low-score CPI-I group showed a significant difference in MST performance between the two groups, while the high-score CPI-I group did not. After treatment (after AH subsided), the hallucinating schizophrenic patients still had significant impairment in MST performance compared with non-hallucinating schizophrenic patients.

### CONCLUSIONS

Our results support the claim that schizophrenic patients with AH are likely to have a disturbance of the **speech** perception system. Moreover, our data suggest that non-language attention might be a key factor influencing **speech** perception ability and that **speech** perception dysfunction might be a trait **marker** in schizophrenia with AH.

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**Correspondence author:** Lee, Seung-Hwan 1Department of Psychiatry, College of Medicine, Inje University.

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