UDSv4 Digital Voice Workshop

Wednesday, June 26

NACC

UNIVERSITY *of* WASHINGTON

Welcome!

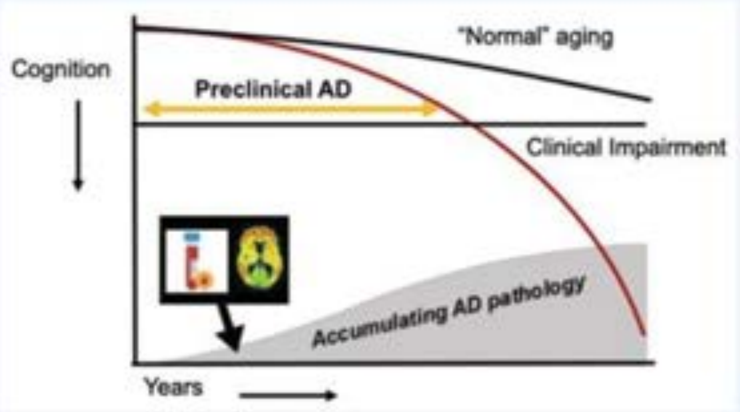
Workshop Agenda

- **Welcome –** Sarah Biber, PhD (NACC)
- **History of Digital Voice –** Rhoda Au, PhD, MBA (Boston University)
- **The Importance of Digital Voice –** Brad Dickerson, MD (MGB ADRC)
- **Consent and IRB –** Sudeshna Das, PhD (MGB ADRC)
- **Digital Voice Data Collection –** Cody Karjadi, MS (Boston University)
- **Flexibility in Data Protocol Adherence –** Jeff Kaye, MD (OHSU)
- **FAQs –** Melissa Lamar, PhD (Rush ADRC)
- **Closing Remarks –** Nina Silverberg, PhD (NIA)

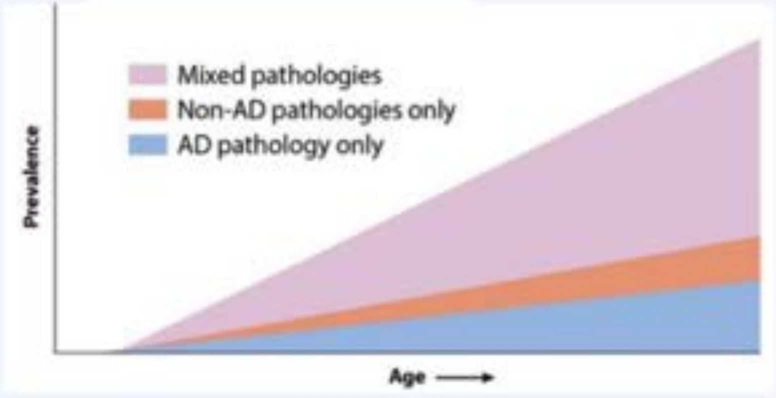
NACC is committed to collaborating with the ADRCs to advance digital data collection

Key ADRD Challenges and Opportunities

Advance Early Detection

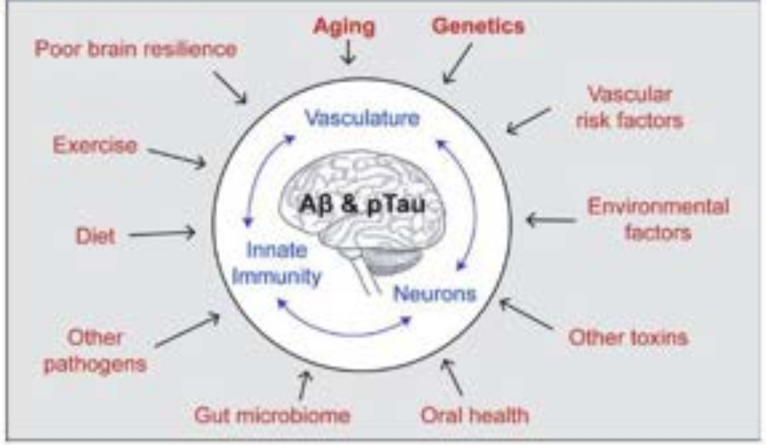


Disentangle Heterogeneity

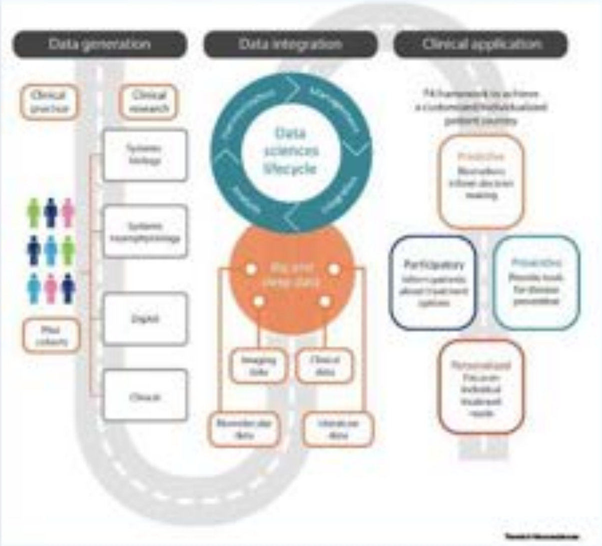


Validate Blood Biomarkers

Identify and Stratify Risk Factors and Protective Mechanisms



Precision Medicine

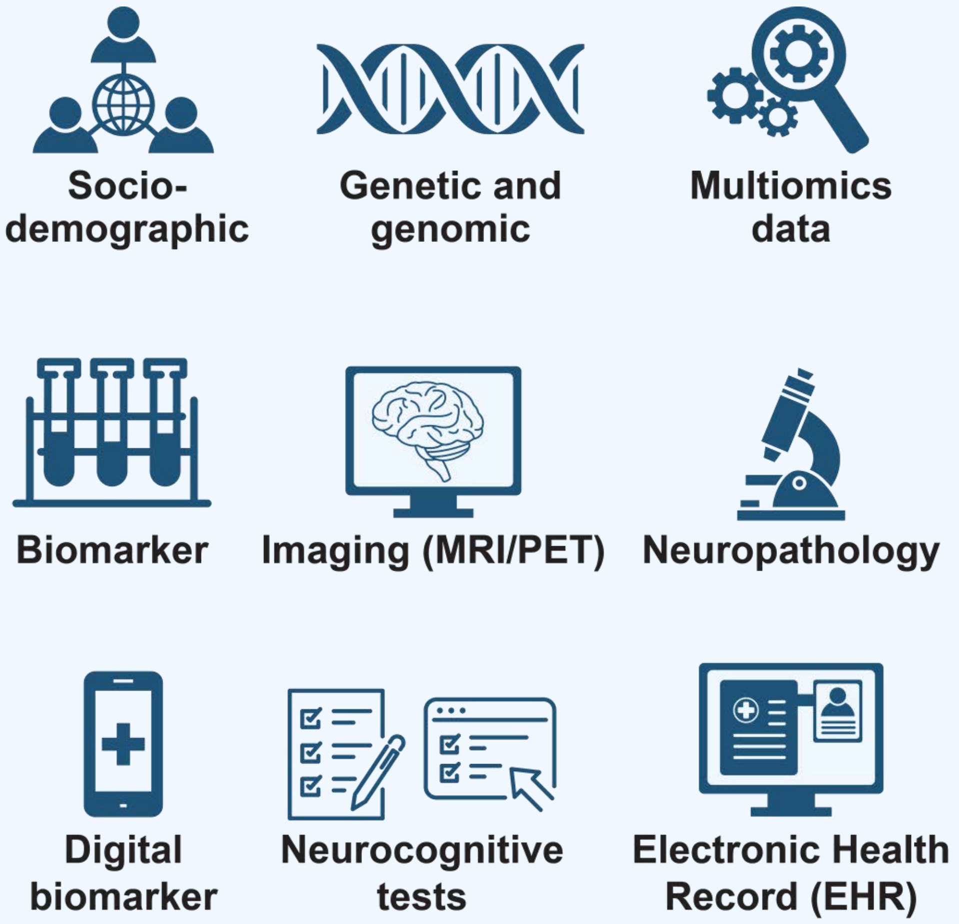


Improve Generalizability

Tackling Complex ADRD Challenges

Requires Multimodal Data!

Researchers need to be able to readily access increasing amounts of multimodal data that are high-quality, harmonized, and integrated to advance the field



Tackling Complex ADRD Challenges

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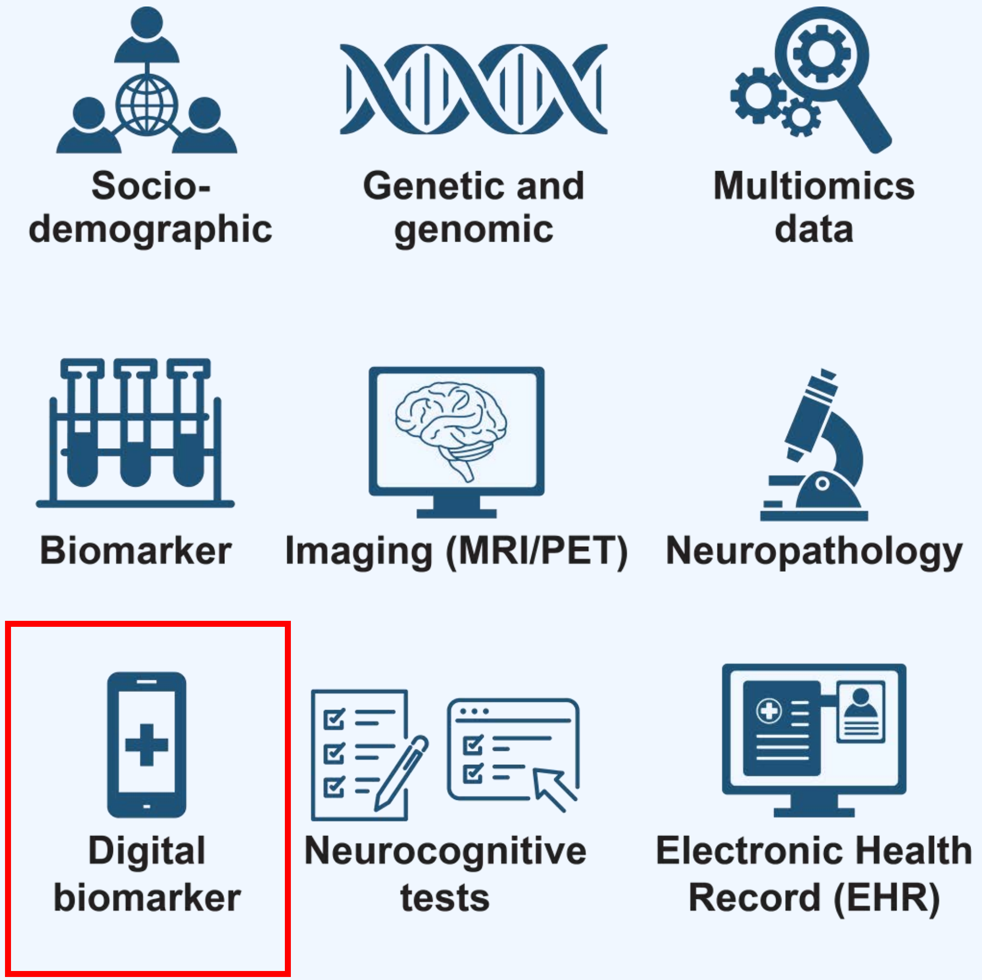
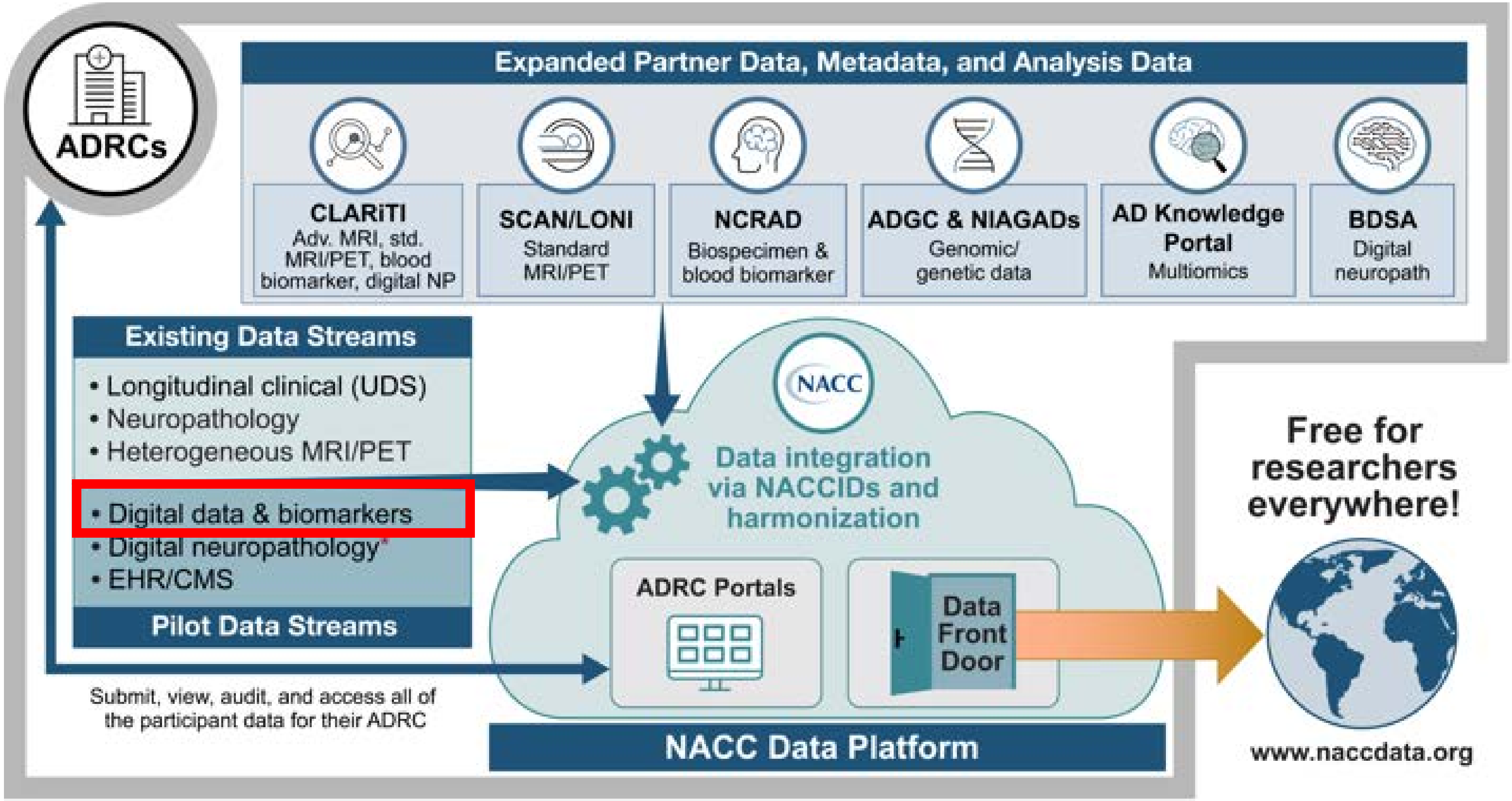


New NACC Data Platform: A Modern Cloud-based Multimodal Data Integration, Harmonization, and Sharing Platform



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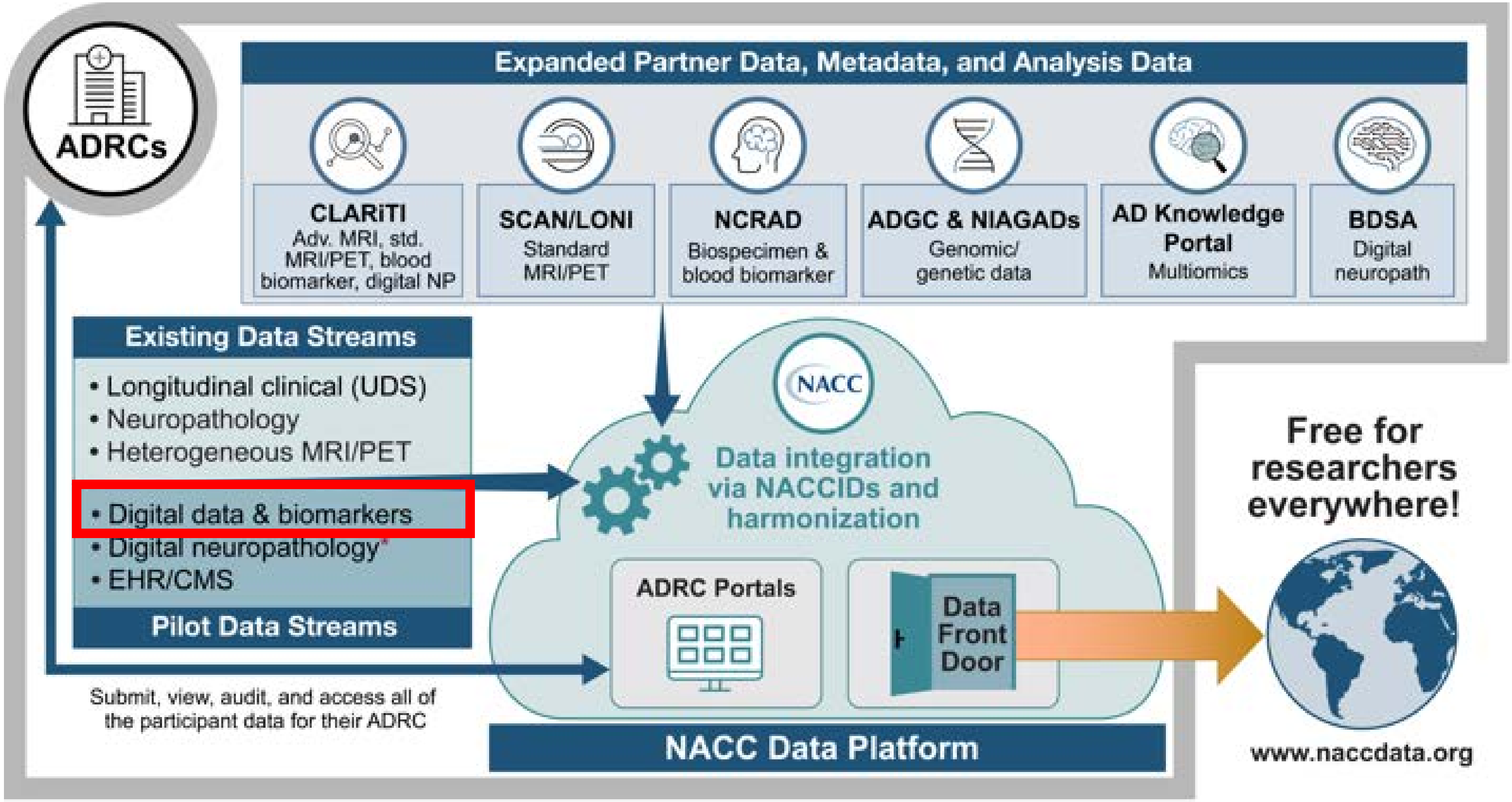

NACC

NACC's new IRB allows for digital data collection, storage, and sharing

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Overview

Digital data collection covers a lot of concepts and is very heterogenous

Many are collecting data and there are few, if any, standards or standardization

THE DIGITAL WILD WEST

CTF Technology Workgroup

Establishing standards for digital data collection across the ADRC Program

CTF Tech WG Parent: Sets governance for workgroup and teams, approves charters, provides guidelines

Leads:
- **ADRC Co-Lead:** Rhoda Au
- **NACC Co-Lead:** Sarah Biber

Other Members:
- Team co-leads, Nina Silverberg, Bud Kukull, Alan Lerner, Erin Abner, Greg Jicha, and Allan Levey

Teams

In-Clinic UDS Digital Instruments

- **Co-leads:** Kate Possin, Teresa Gomez-Isla, Hiroko Dodge, NACC co-lead TBA
- **Overview:** Cognitive and non-cognitive; TabCAT; and other UDS digital instruments used in the clinic

TabCAT

Virtual Standard UDS Digital Instruments

- **Co-leads:** Sudeshna Das, Zach Beattie, Melissa Lamar, NACC co-lead TBA
- **Overview:** Cognitive and non-cognitive; Virtual version of standard

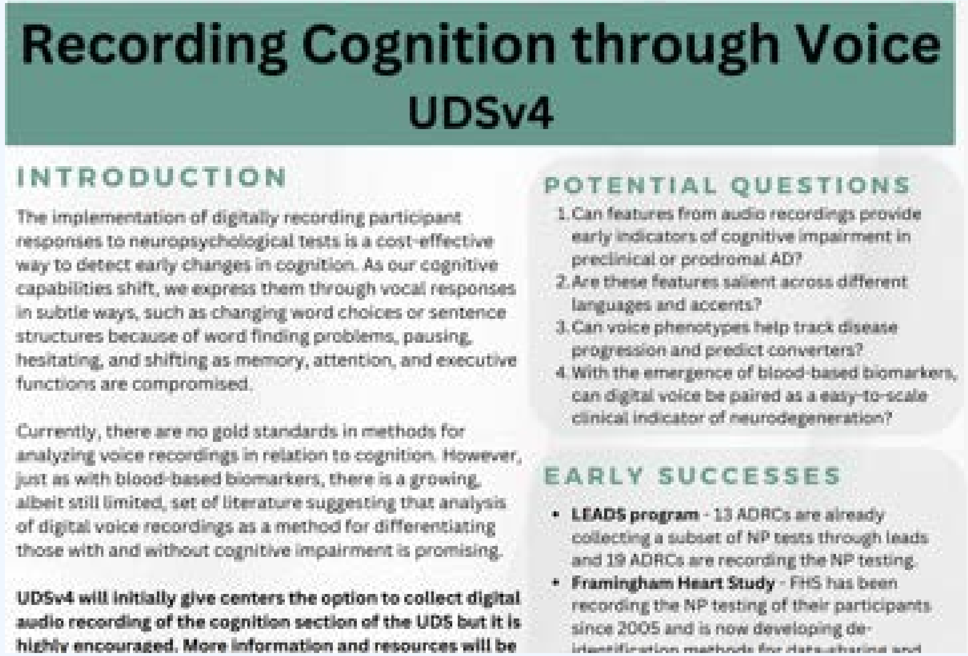
New Non-UDS Digital Instruments

- **Co-leads:** Jeff Kaye, Jason Hassenstab, Kate Papp, NACC co-lead TBA
- **Overview:** Cognitive and non-cognitive; new digital instruments not currently included in UDS; in-clinic or out of clinic; including surveys

CTF Technology Workgroup

Establishing standards for digital data collection across the ADRC Program

Digital voice recordings of the UDSv4 neuropsychological exam


Recording Cognition through Voice
UDSv4

INTRODUCTION

The implementation of digitally recording participant responses to neuropsychological tests is a cost-effective way to detect early changes in cognition. As our cognitive capabilities shift, we express them through vocal responses in subtle ways, such as changing word choices or sentence structures because of word finding problems, pausing, hesitating, and shifting as memory, attention, and executive functions are compromised.

Currently, there are no gold standards in methods for analyzing voice recordings in relation to cognition. However, just as with blood-based biomarkers, there is a growing, albeit still limited, set of literature suggesting that analysis of digital voice recordings as a method for differentiating those with and without cognitive impairment is promising.

UDSv4 will initially give centers the option to collect digital audio recording of the cognition section of the UDS but it is highly encouraged. More information and resources will be

POTENTIAL QUESTIONS

1. Can features from audio recordings provide early indicators of cognitive impairment in preclinical or prodromal AD?
2. Are these features salient across different languages and accents?
3. Can voice phenotypes help track disease progression and predict converters?
4. With the emergence of blood-based biomarkers, can digital voice be paired as a easy-to-scale clinical indicator of neurodegeneration?

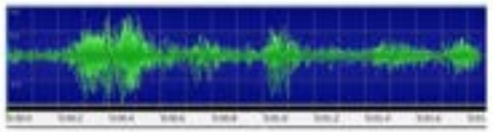
EARLY SUCCESSES

- **LEADS program** - 13 ADRCs are already collecting a subset of NP tests through leads and 19 ADRCs are recording the NP testing.
- **Framingham Heart Study** - FHS has been recording the NP testing of their participants since 2005 and is now developing de-identification methods for data-sharing and

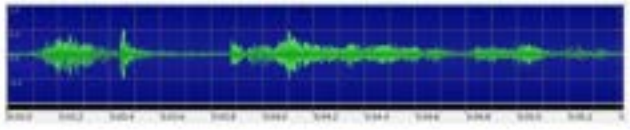
Dr. Rhoda Au

Boston University ADRC

No impairment (2009)



Mild cognitive impairment (2015)



Piloting Digital Data Collection, Analysis, Integration, and Sharing

Tests

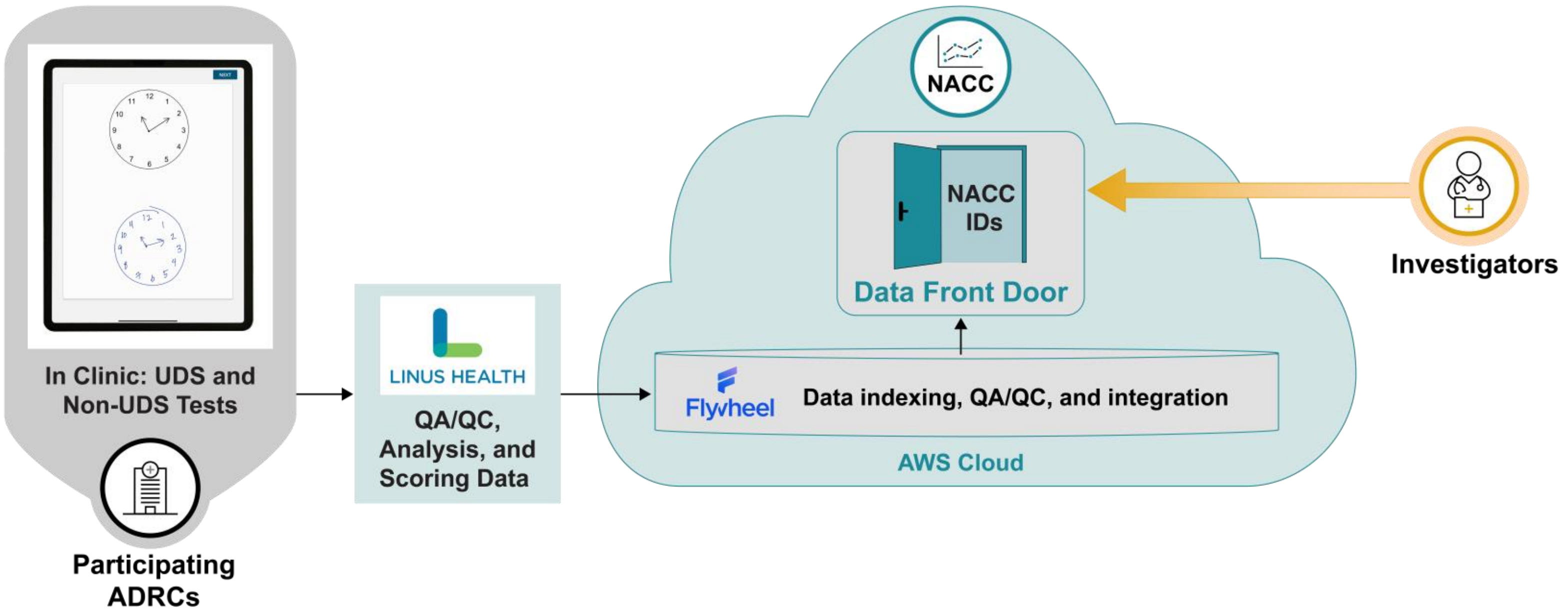
UDS:

- **Digital clock drawing test**
- **Category naming tests**

Non-UDS:

- **Candy theft picture description**
- **VisMET**

Pipeline Development



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NACC/Gates Digital Pilot Program

- **Goals:**
  - Accelerate innovative digital biomarker collection and sharing across the ADRC Program to advance AD/ADRD research and discovery
  - Leverage technology to capture more data with less burden for participants and ADRCs
- **Budget:** 1-3 pilots ranging from $250K to $1M (direct costs)
- **Pilot length:** 1-2 years
- **Eligibility:** Open to any ADRC or non-ADRC groups or companies. They must have multiple ADRC collaborators.
- **Funding will be provided through NACC and will support:**
  - **Partners:** Provide digital instruments*
  - **ADRCs:** Data collection with innovative digital instruments
  - **NACC:** Integrating this data into the NACC Data Platform and sharing it with the AD/ADRD researchers through the Data Front Door

  **Instruments can be from a variety of sources and offered in kind*
- **Selection Committee:** Digital data experts from across industry, academia, and government

NACC/Gates Digital Pilot Program

NACC | Gates Ventures

Pilot Requirements
- Adds research value and enhances metrics
- Reduces burden
- Expands and addresses diversity
- Involves multiple ADRCs
- Demonstrates scalability (including to other ADRCs)
- Amenable to a data challenge down the line
- Partnering companies must provide the raw digital files to NACC

Example Modalities: Sleep, movement, gait (phone gyroscope measures), fall detection, voice, video, language, eye tracking, digitized UDS, non-UDS, mood, diet, biological measures, driving, keystrokes

Example Tools: Wearables, sensors, multi-sensor, smart phone apps, algorithms

Proposed Timeline for Pilot Launch

- **May 2nd, 2023:** Announce at the ADRC meeting
- **Fall 2023:** Release the RFA and select winners
- **Winter 2023:** Launch pilots

Potential Follow-Up Support

- Funded Data Challenge using data collected from the pilot
- Promising digital pilots may be scaled to the full ADRC Program via NACC's U24 renewal
- SBIR/STTR

NIA Small Business Programs (SBIR & STTR)

Non-dilutive Funding for Healthy Aging Innovations

https://www.nia.nih.gov/research/sbir

AD/ADRD DIGITAL PILOT PROGRAM

Winners to be announced next week...

PI: Jeffrey Kaye, PhD
EFFECT-AD: Everyday Frequent Functional Evaluation with Crosscutting Technology for AD

OHSU · UCSF University of California San Francisco · South Texas Aging & Disability Resource Center · Panoramic Digital Health

PI: Joseph Winer, PhD
Characterizing sleep-wake activity patterns across the spectrum of AD/ADRD

Stanford University · Vanderbilt University

PI: Raeanne Moore, PhD
CLARIFY- speeCh anaLysis And keystRoke trackIng For earlY AD detection

UC San Diego School of Medicine · KeyWise · South Texas Aging & Disability Resource Center · ki elements

PI: Ehsan Adeli, PhD
Scalable Next-Generation Smartphone Gait Assessment for Early Detection of AD/ADRD

Stanford University · Boston University · UCSF University of California San Francisco

PI: Kayci Vickers, PhD
Pilot Study to Evaluate VisMET on the Linus Health Platform at Multiple ADRCs

Emory University · UC San Diego School of Medicine · Boston University · Linus Health

PI: Emma Rhodes, PhD
Remote Digital Monitoring to Detect Behavioral & Neuropsychiatric Symptoms in ADRD

Perelman School of Medicine University of Pennsylvania · UCSF University of California San Francisco · ŌURA

NACC · Gates Ventures

Open Science on Digital Data

Data Science ‘Community Challenges’ are a popular way to do science.

- They pose questions that data scientists can answer, and the answers are only known by the organizers
- These challenges have facilitated unbiased improvement in machine learning in many fields
- Mooney has been leading, participating, and advising these challenges for decades

Thank you!

Connect with NACC

Sarah Biber, PhD – Executive Director

biber@uw.edu

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Painting of the original MGH Bulfinch building by Kemon Sermos who was living with a diagnosis of FTD

The importance of digital voice in neurodegenerative diseases

NACC UDS 4.0 Digital Voice Workshop

Brad Dickerson, MD

Director, MGH FTD Unit & Imaging Core Leader, Mass Alz Dis Research Center

What’s in a voice?

In some cases, the earliest indicator of a neurodegenerative disease

The New York Times

Account

Linda Ronstadt, Retired From Singing, Is Still a Glorious Voice

The 73-year-old is the subject of a new documentary and a Kennedy Center honoree. She’s also as self-effacing and gutsy as ever.

The first symptom of her eventual diagnosis of Progressive Supranuclear Palsy was the loss of her ability to sing

What’s in a voice?

In some cases, the earliest indicator of a neurodegenerative disease

SPORTS MEDIA

NESN’s Jack Edwards opens up about his speech issues: ‘I’m slowing down all the time’

By Chad Finn Globe Staff, Updated February 22, 2024, 5:00 a.m. 196

Jack Edwards has been calling Bruins games on NESN since the 2005-06 season. JIM DAVIS/GLOBE STAFF

The irony of his circumstances has not eluded Jack Edwards.

Primary Progressive Apraxia of Speech—working with us, gave permission to analyze his “Voice of the Bruins” game recordings going back decades

Digital voice analytics as a biomarker of clinical syndromes or etiologic diagnoses

- Motor speech
  - Primary progressive apraxia of speech
  - Progressive dysarthria
    - PSP, CBD, ALS, PD, etc. (may present as a primary motor speech disorder)
- Cognitive functions
  - Primary progressive aphasia
  - Amnestic MCI/dementia
  - Posterior cortical atrophy syndrome
  - Psychosis & other thought disorders
- Affective functions
  - Depression/anxiety
  - Disinhibition
  - Mania

Popp Z, Au R et al., J Am Heart Assoc, 2024
Rezaii N et al., Br J Psych, 2022

MGH FTD Unit experience with digital voice

- We have been recording digital audio samples of cognitive assessments in cognitively unimpaired older adults and in patients with neurodegenerative disorders in the MGH FTD Unit since 2008.

- Digital audio recorders were used from 2008 to 2018 and since then secure online platforms and phones have been used to capture audio data.

- Participants are consented for recording and sharing of digital audio (>99% opt in).

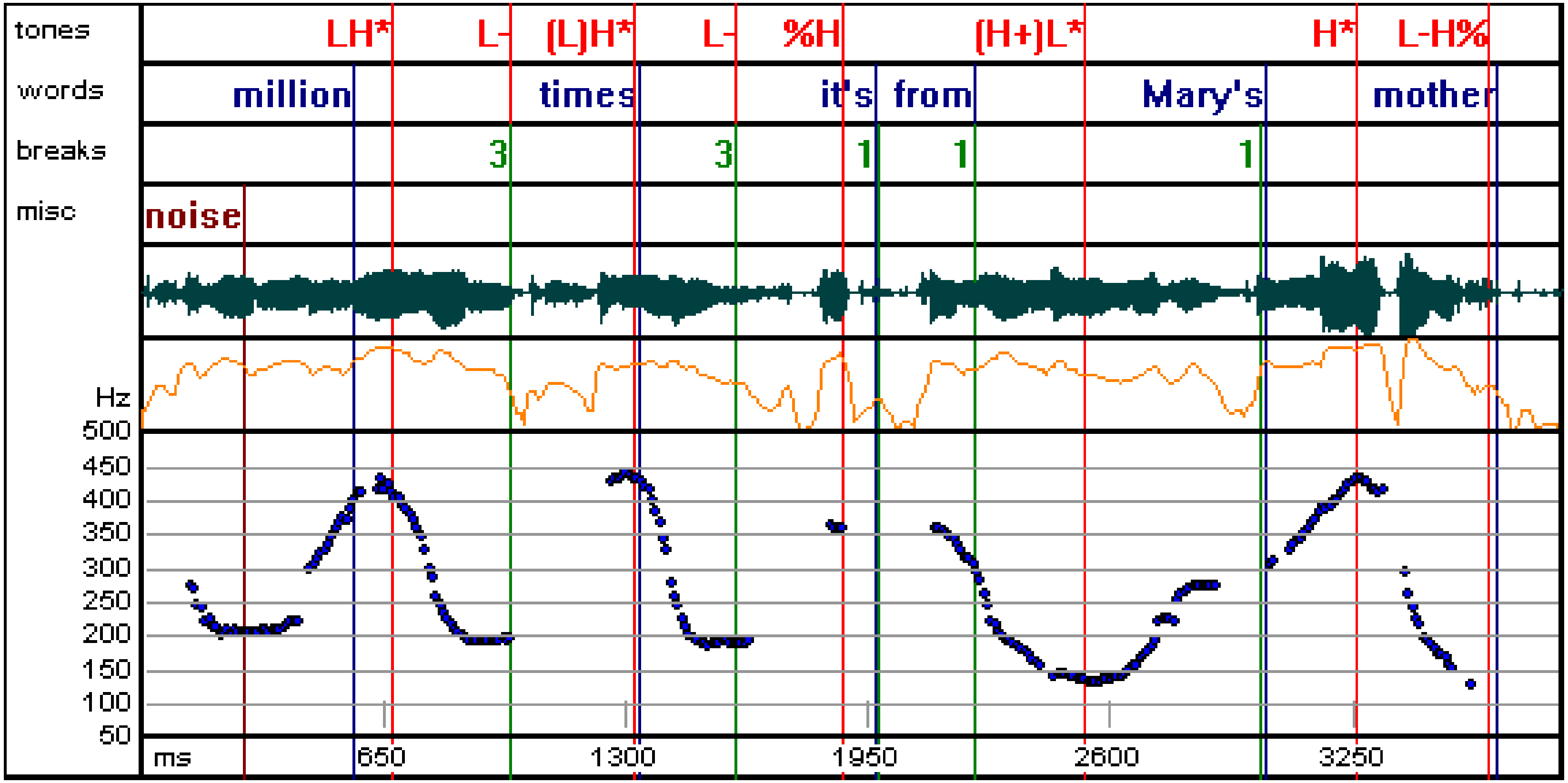
- Digital audio files are stripped of any PHI/PII.

- Files are stored locally and in secure online storage space.

Apraxia of speech
(often occurs with dysarthria)

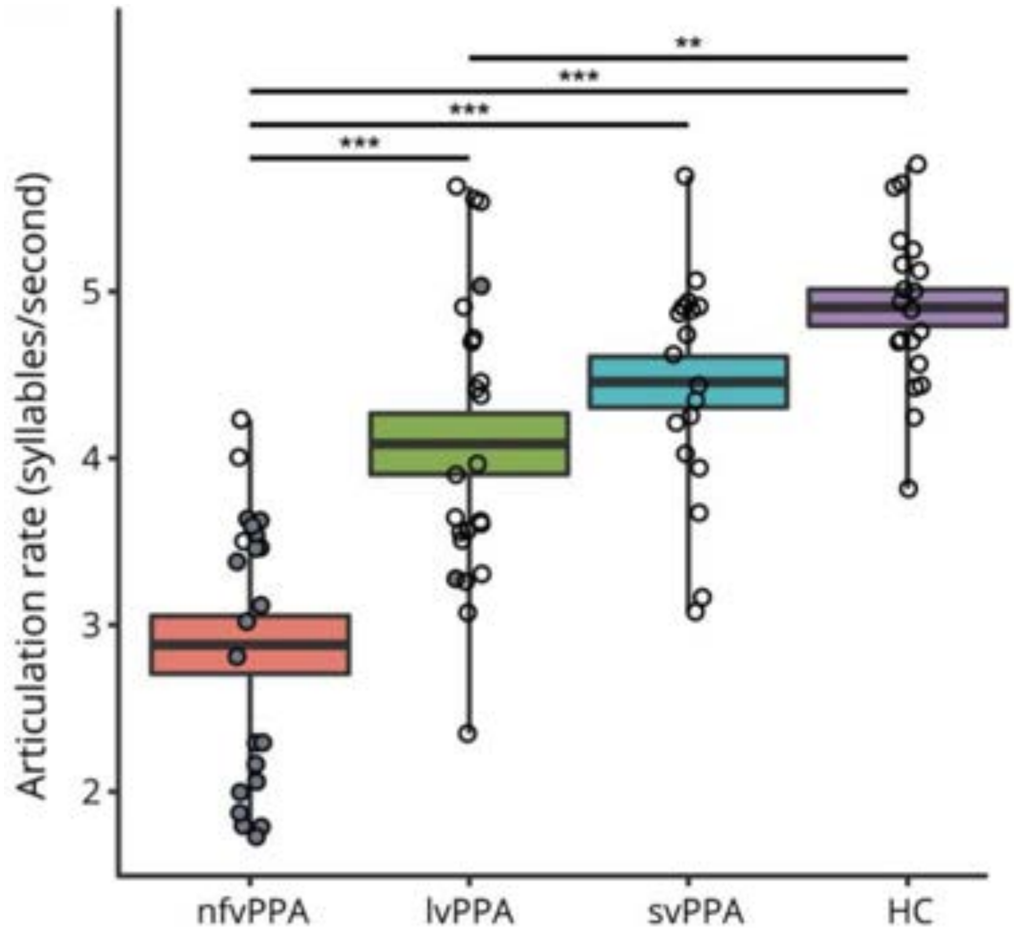
Quantification of slowing of articulation rate in PPA

Traditionally done with ordinal rating scales by trained clinicians



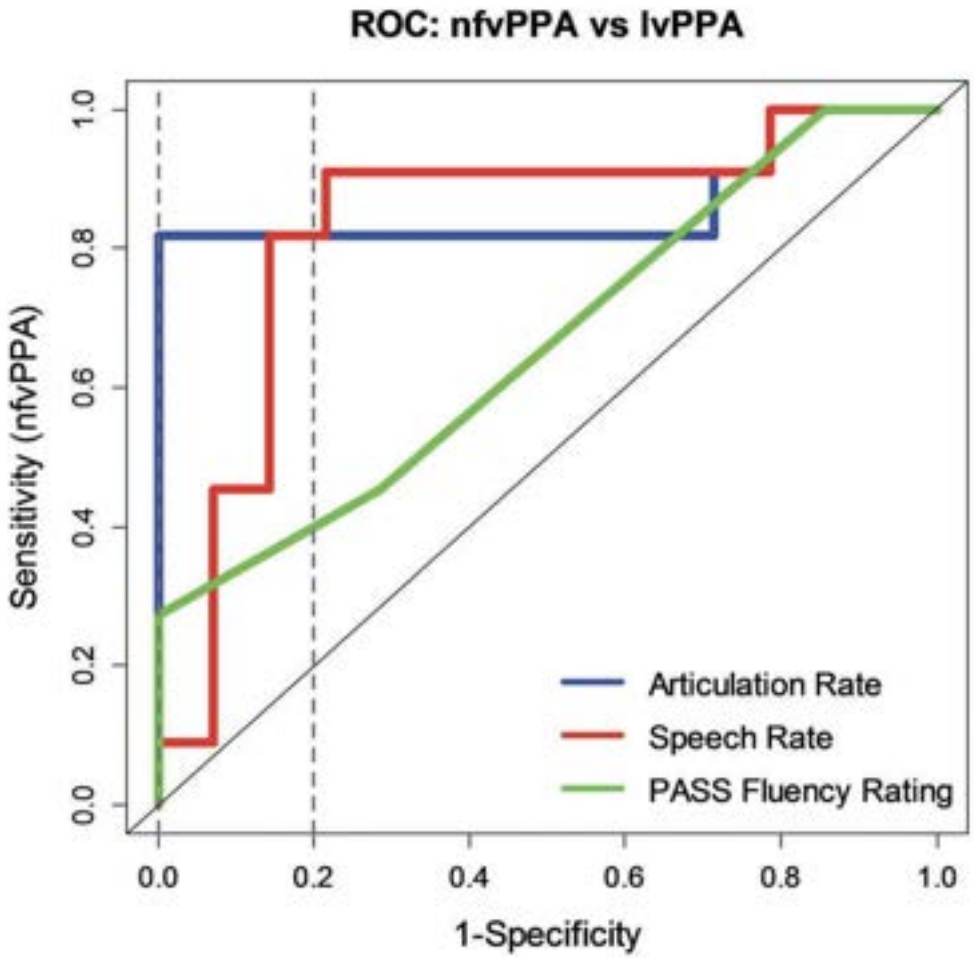
Cordella, Green et al., Neurology, 2019

Nonfluent/agrammatic variant PPA patients have slowed articulation rate



Cordella, Green et al., Neurology, 2019

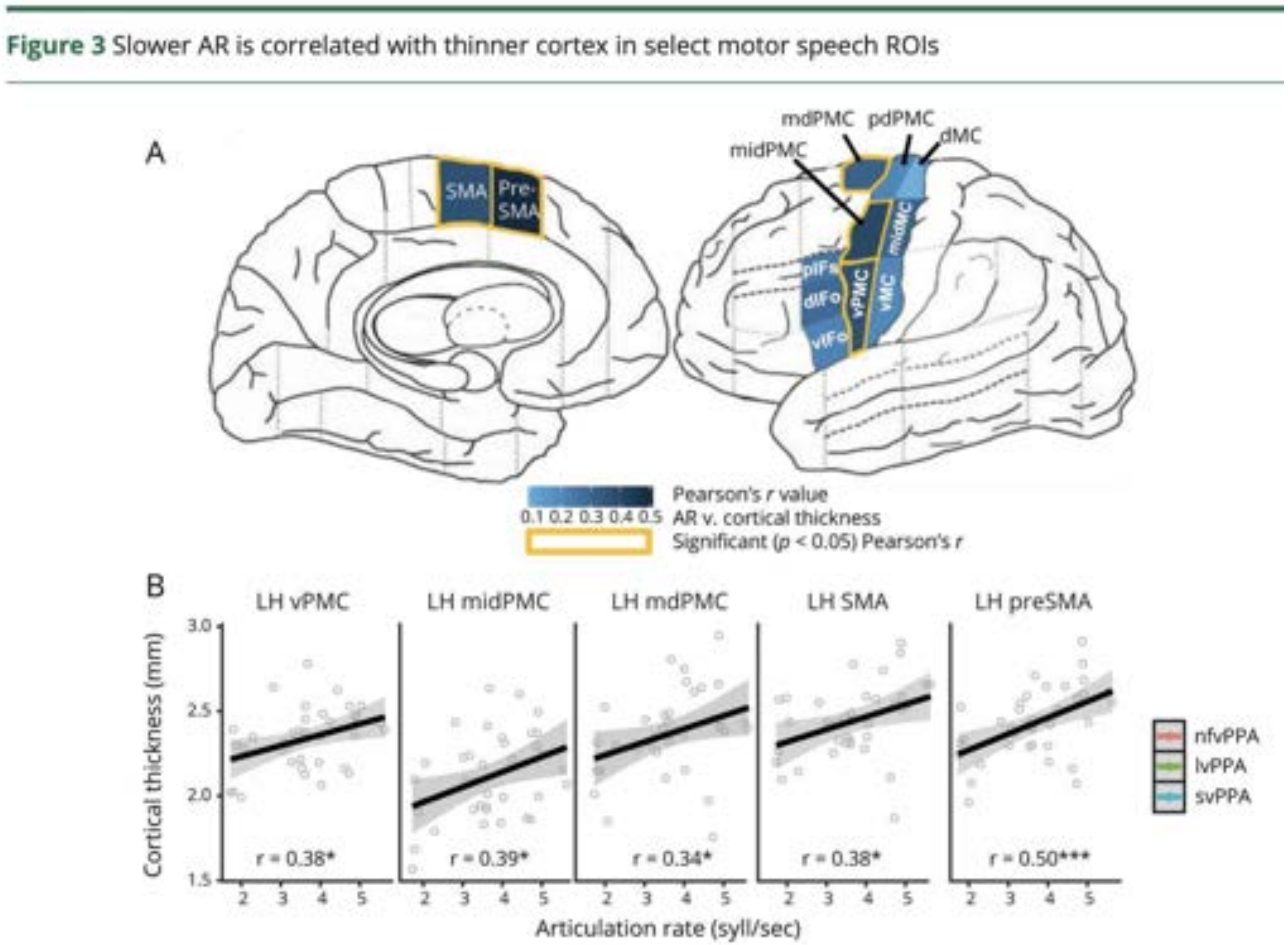
Quantitative measures of speech/articulation rate better identify nonfluent PPA patients than clinician ratings



(quantitative acoustic: 0.86)
(quantitative acoustic: 0.83)
(clinician rating): 0.66

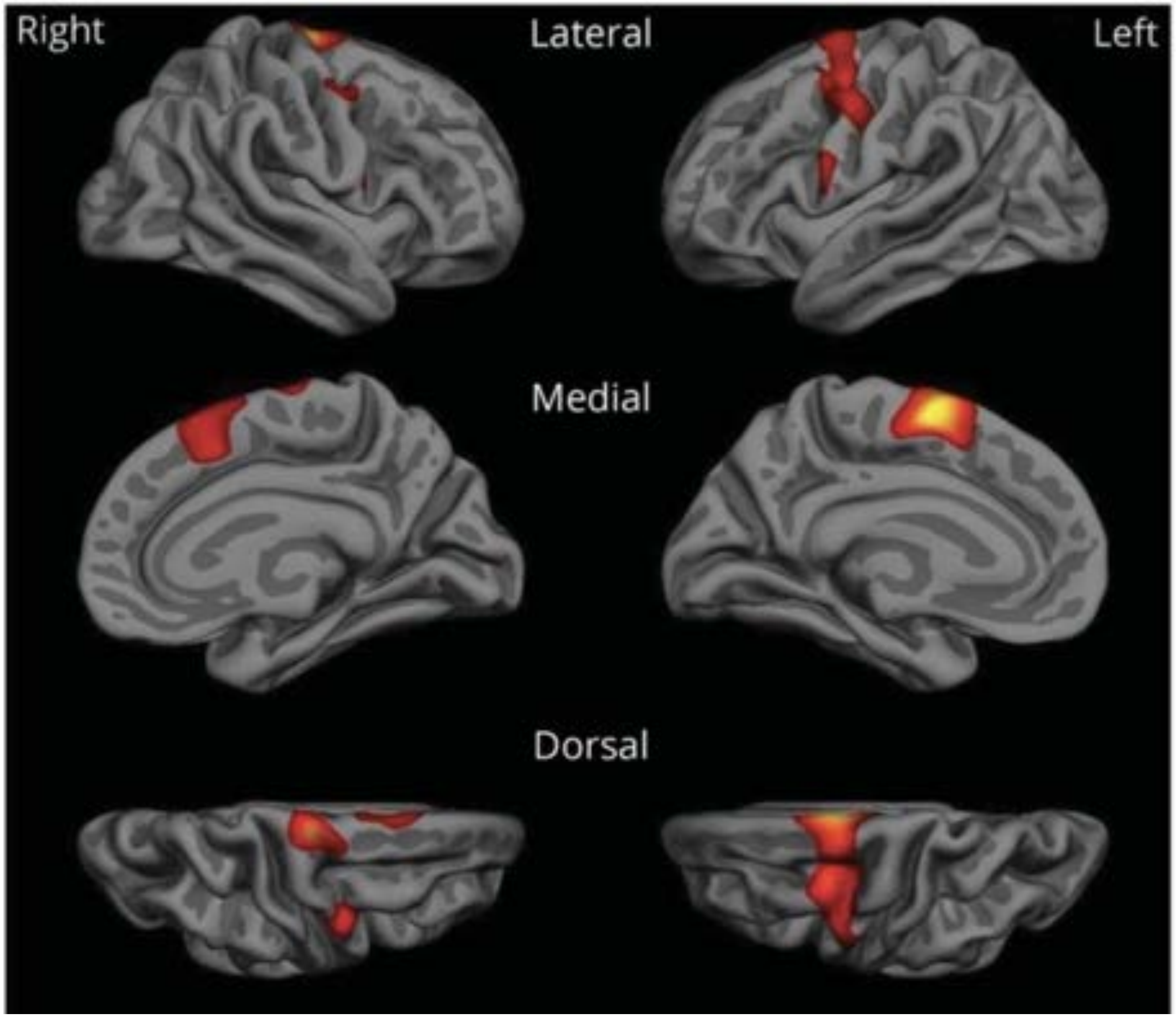
Cordella, et al., Aphasiology, 2016

Slowing of articulation rate correlates with atrophy in motor speech cortical areas from Dr. Frank Guenther's (BU) DIVA model of speech production



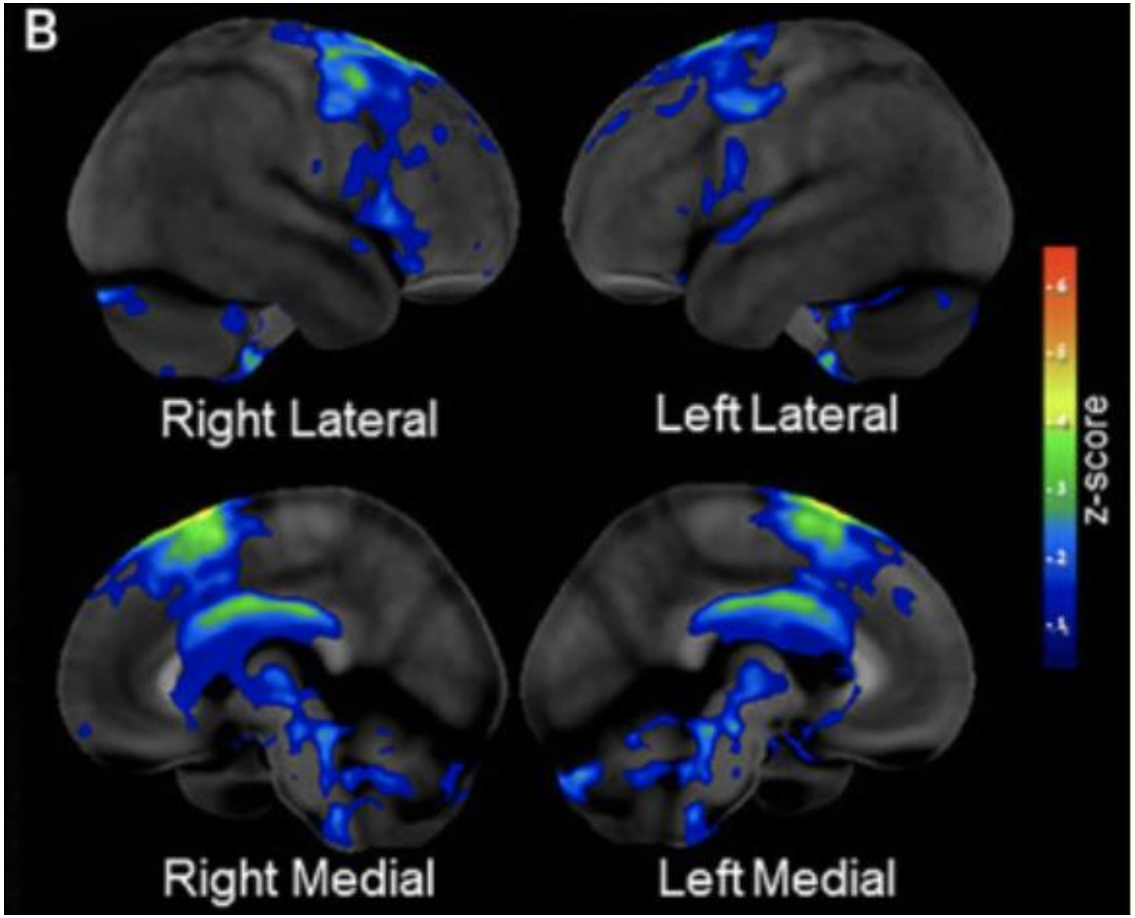
Cordella et al., Neurology, 2019

Across the entire cortex, this effect is specific to motor speech cortical areas from the DIVA model of speech



Cordella et al., Neurology, 2019

In single cases of apraxia of speech, atrophy and hypometabolism are localized as predicted based on brain systems subserving motor control of speech



Botha & Josephs, 2019

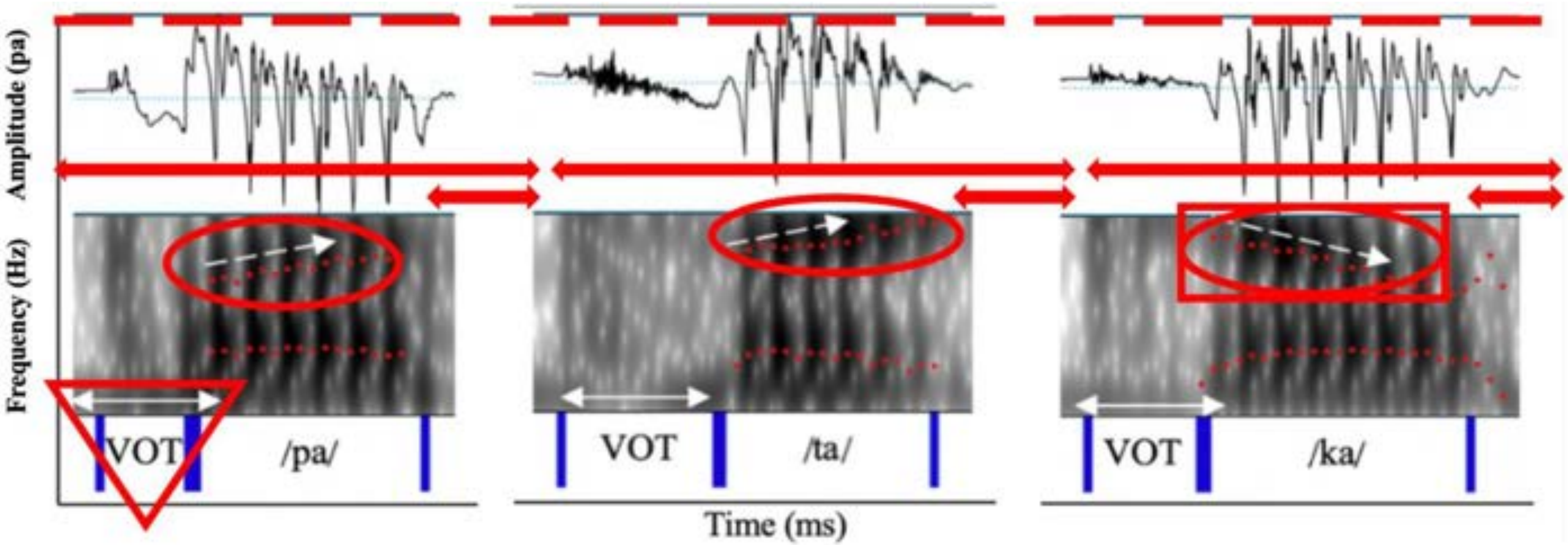
Four neurological disorders affecting motor speech: ALS, progressive ataxia, Parkinson's disease, nonfluent PPA/apraxia of speech

Diagnosis	Speech Motor Subtype	Neurological Deficit	Pathophysiological Impairment	Example Articulatory Patterns	
ALS	spastic, flaccid, or mixed spastic-flaccid dysarthria	upper and/or lower motor neurons	strength and/or tone	reduced speed; distorted vowels	N=46
PA	ataxic dysarthria	cerebellum	timing	uncoordinated syllable sequences; irregular breakdowns	N= 52
PD	hypokinetic dysarthria	basal ganglia	scale and speed	short rushes of speech; repeated phonemes	N= 60
nfPPA+PAOS	apraxia	left frontal lobe	planning	slow rate; segmented syllables	N= 20

Fig. 1 Clinical groups selected for current study along with their associated speech motor subtype, presumed neurological deficit and pathophysiological mechanism, and example articulatory pat- ... amyotrophic lateral sclerosis, *PA* progressive ataxia, *PD* Parkinson's disease, *nfPPA + PAOS* the nonfluent variant of primary progressive aphasia and progressive apraxia of speech)

Rowe H et al., J Neural Transm, 2022

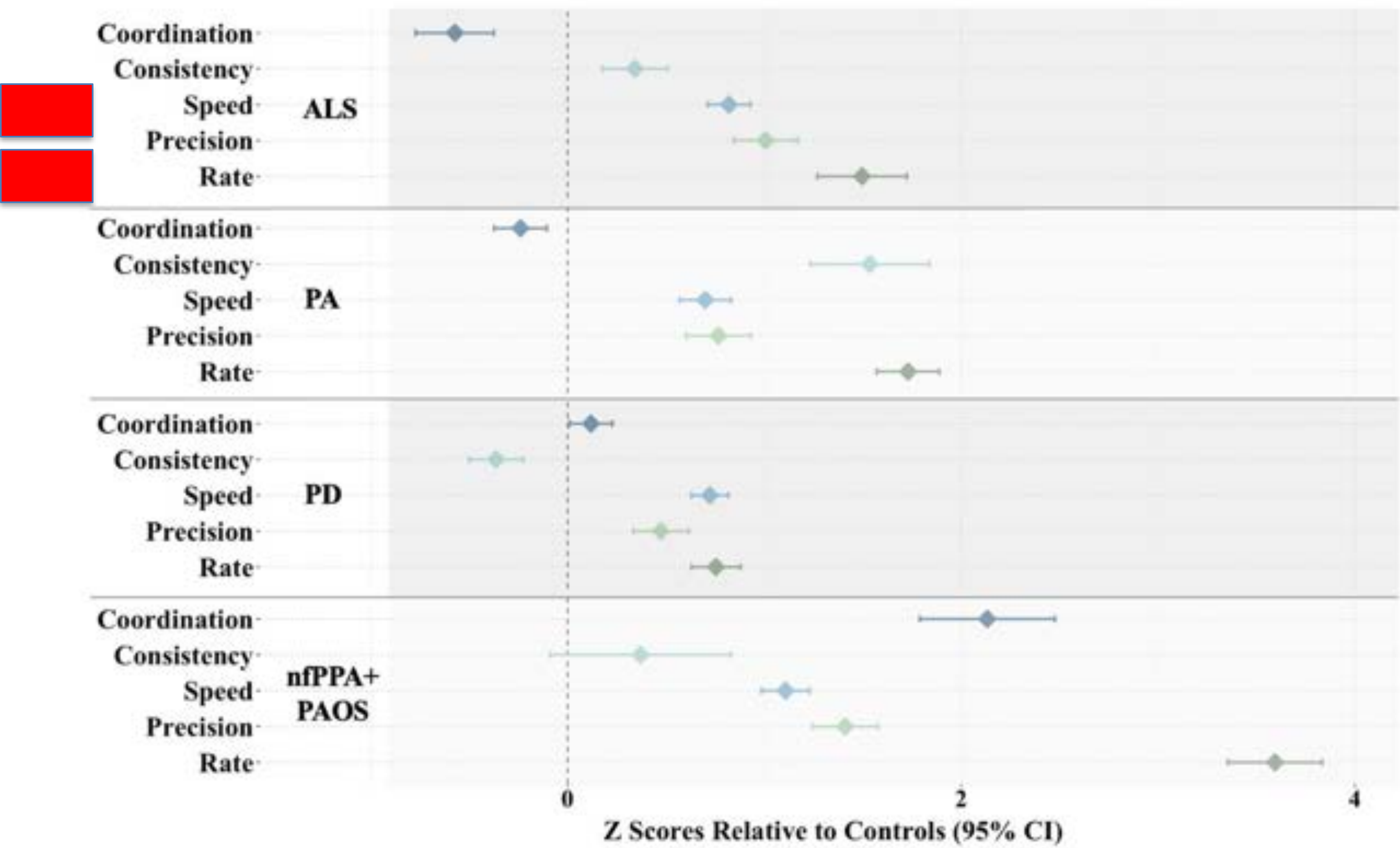
5 acoustic features of motor speech



- (1) Red arrows=**Coordination** (proportion of stop gap [i.e., short red arrow] to total syllable length [i.e., long red arrow]); (2) Red triangle = **Consistency** (standard deviation of voice onset times [VOTs] for each consonant across three repetitions); (3) Red circles=**Precision** (standard deviation of three formant slopes for /pa/, /ta/, and /ka/ within each repetition); (4) Red square=**Speed** (mean of formant slope for /ka/ across three repetitions); and (5) Red dashed line = **Rate** (syllables produced per second)

Rowe H et al., J Neural Transm, 2022

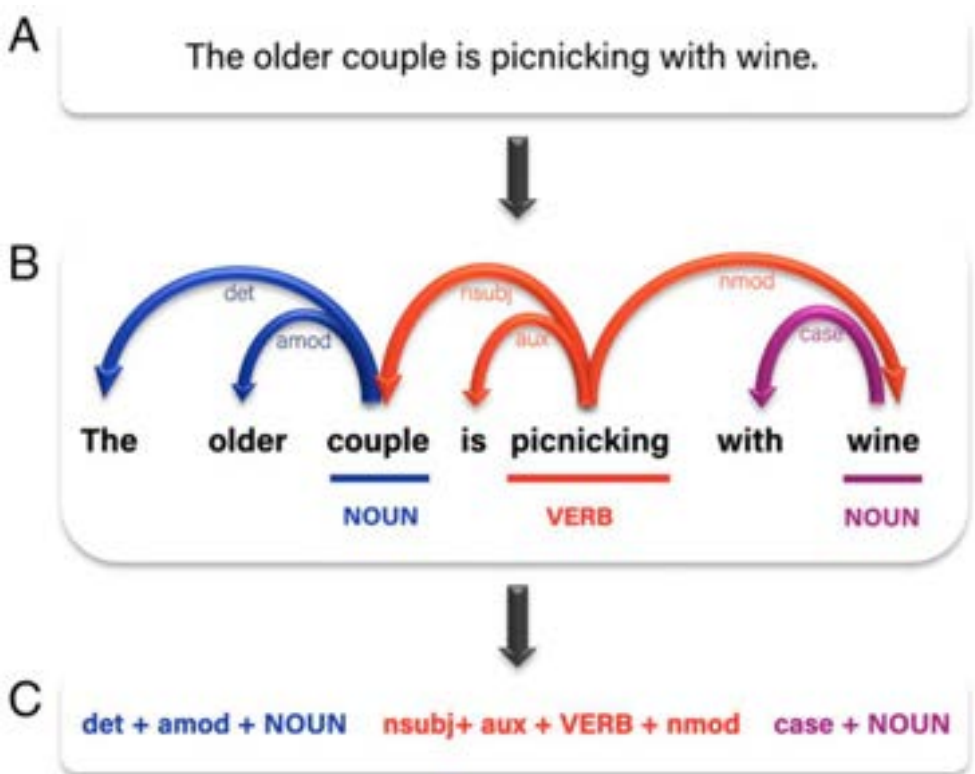
Each diagnosis has characteristic acoustic features of speech that differentiate it from others



Rowe H et al., J Neural Transm, 2022

Syntax-lexicon tradeoff in language

- Word frequency is a widely used measure in studies of linguistics.
- The frequency of syntactic sentence structures has not previously been measured.
- We developed a novel metric of syntactic complexity and examined both word (lexical) and syntactic frequencies in PPA.

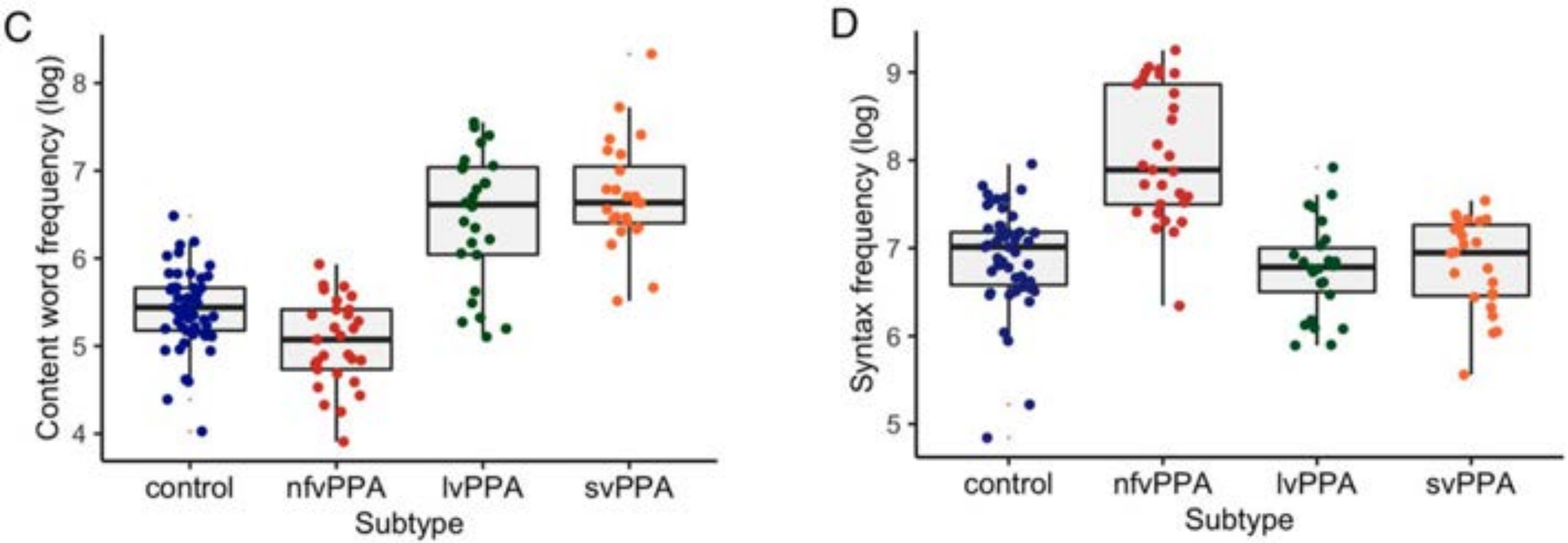


Rezaii N, et al., Dickerson, B, Gibson E, PNAS, 2022

Syntax-lexicon tradeoff in language

Logopenic and semantic PPA patients use higher frequency words as expected based on prior work.

Non-fluent/agrammatic PPA patients use higher frequency syntax, as predicted.

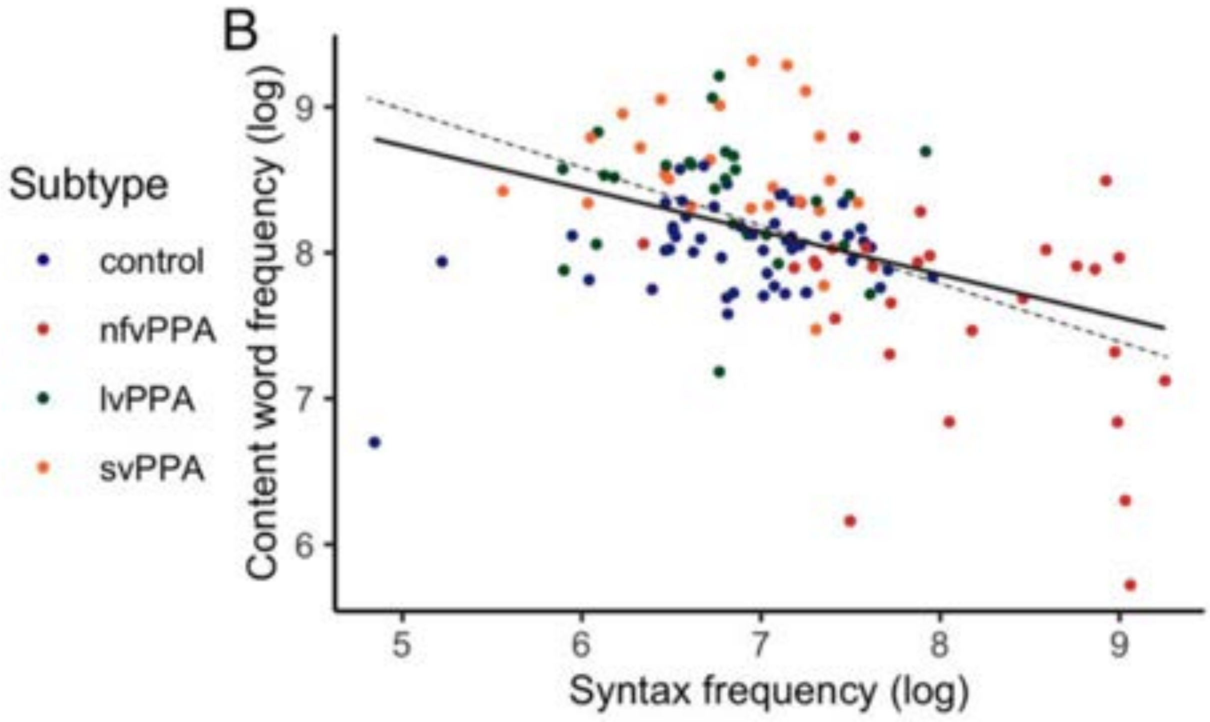


Non-fluent/agrammatic PPA patients use lower frequency words, possibly as a way to convey meaning efficiently.

Rezaii N, et al., Dickerson, B, Gibson E, PNAS, 2022

Syntax-lexicon tradeoff in language

- In the entire PPA patient group, lexical and syntactic complexity—as measured by their frequencies—are inversely correlated.
- This syntax-lexicon trade-off is also present in the utterances of healthy speakers, suggesting that it may be a general property of the process by which humans turn thoughts into speech.



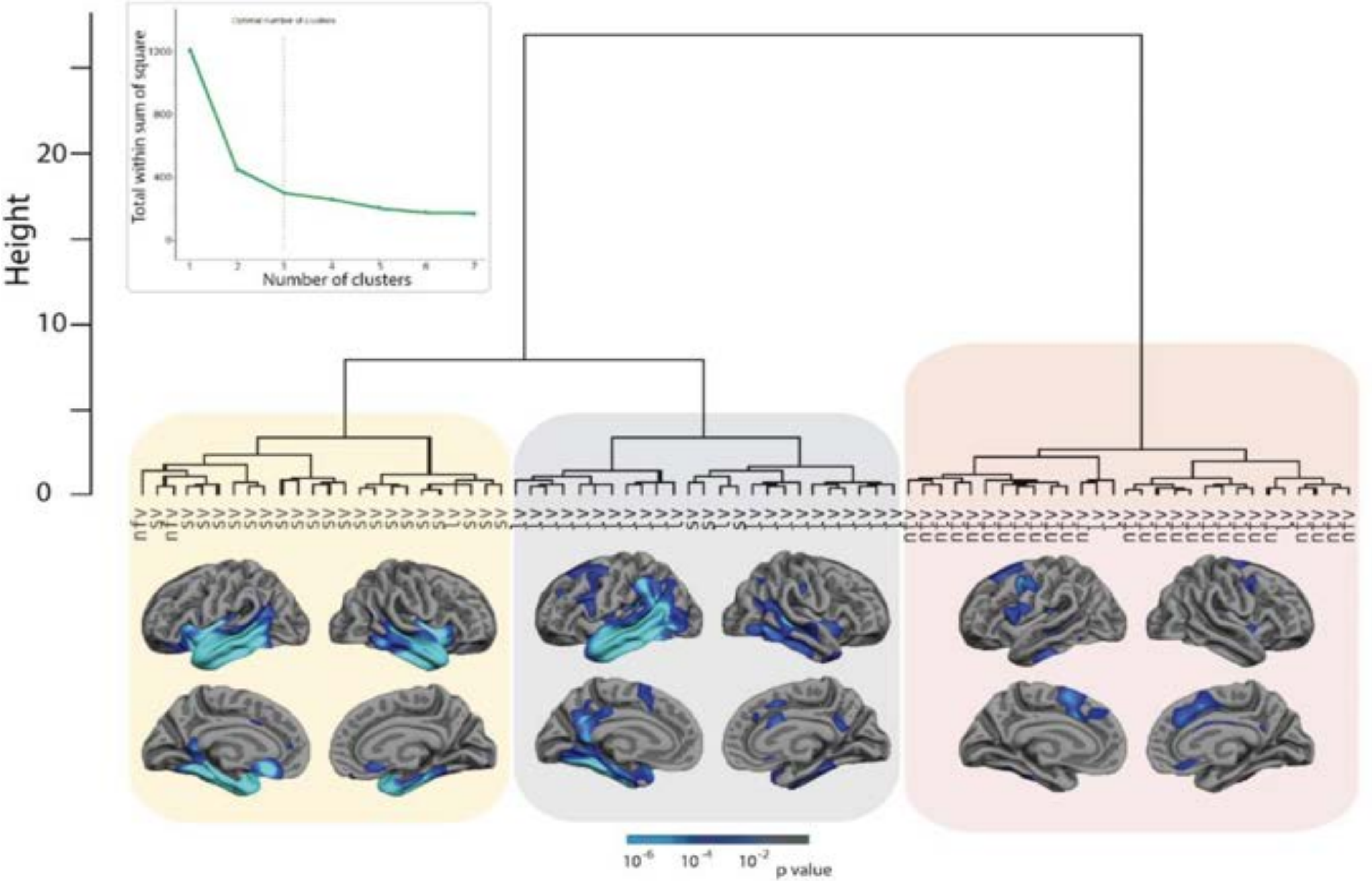
Rezaii N, et al., Dickerson, B, Gibson E, PNAS, 2022

Using Generative Artificial Intelligence to Classify Primary Progressive Aphasia from Connected Speech

- Debate continues about whether PPA is best subdivided into three variants and also regarding the most distinctive linguistic features for classifying PPA variants.
- We harnessed the capabilities of artificial intelligence (AI) and natural language processing (NLP) to perform **unsupervised** classification of concise, connected speech samples from 78 PPA patients.
- Large Language Models discerned 3 distinct PPA clusters, with 88.5% agreement with independent clinical diagnoses.
- Patterns of cortical atrophy of 3 data-driven clusters corresponded to the localization in the clinical diagnostic criteria.

Rezaii N, et al., Dickerson, B, Wolff P, in revision

Unsupervised generative AI identifies 3 clusters of PPA patients with language similar to each other



Rezaii N, et al., Dickerson, B, Wolff P, in revision

Natural language processing helps use understand the linguistic features that are similar between subtypes of PPA, including many that have been identified before and some novel linguistic features

- We then used NLP to identify linguistic features that best dissociate the three PPA variants.

- Seventeen features emerged as most valuable for this purpose.

- Using these linguistic features derived from the analysis of brief connected speech samples, we developed a classifier that achieved 97.9% accuracy in predicting PPA subtypes and healthy controls.

- One of the important features we identified was low- vs. high-frequency verbs, a novel feature for this patient population.

Rezaii N, et al., Dickerson, B, Wolff P, in revision

NLP confirms and identifies new linguistic features in PPA

nfvPPA patients tend to use more low-frequency verbs

lvPPA patients tend to use more high-frequency verbs

As has been shown before, svPPA patients tend to use more pronouns and fewer nouns.

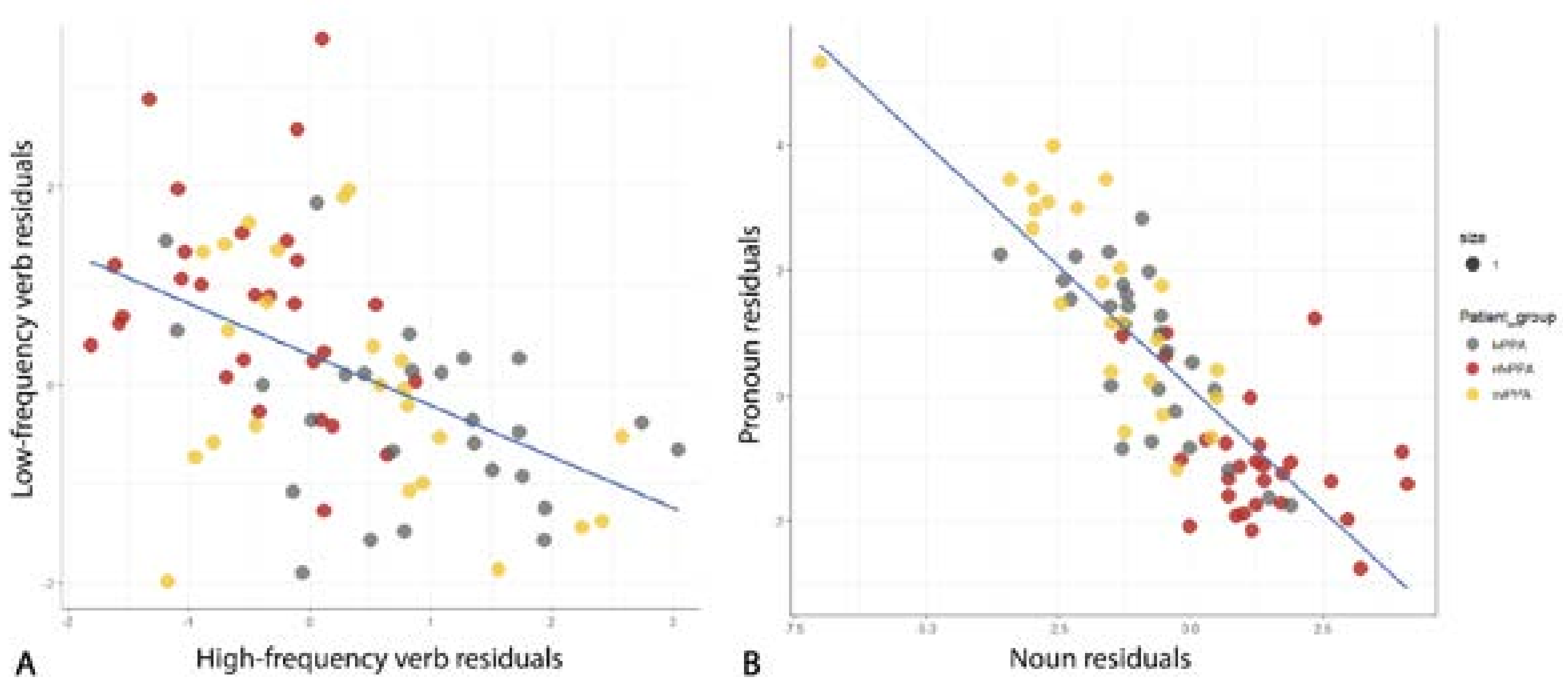


Fig 5. Scatterplots showing trade-offs between low- and high-frequency verbs (A) and nouns and prepositions (B). In panel A, nfvPPA patients tend to occupy the upper left corner, indicating relatively few high-frequency verbs, while lvPPA patients tend to occupy the lower right corner, indicating relatively few low-frequency verbs.

Rezaii N, et al., Dickerson, B, Wolff P, in revision

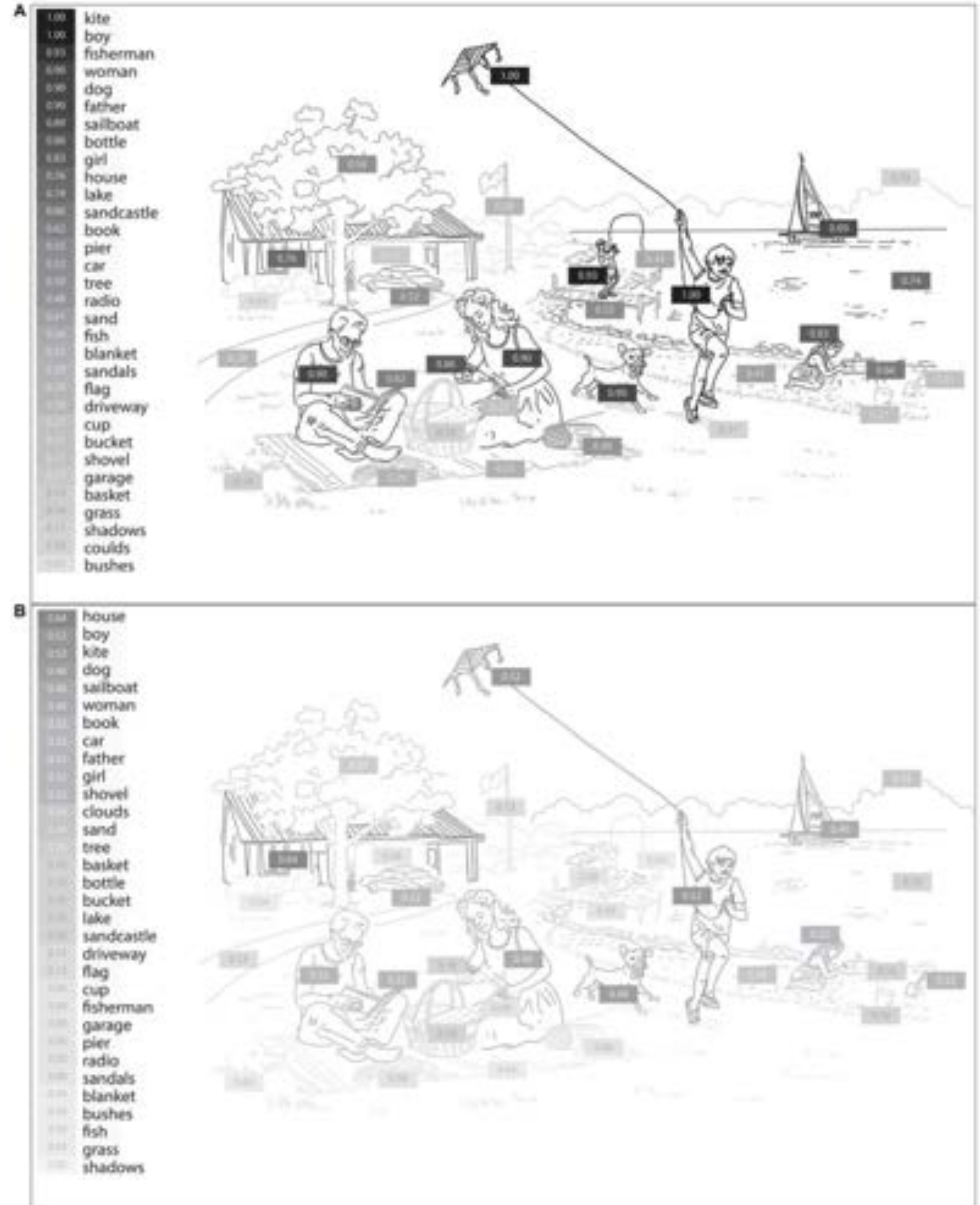
PCA patients' language is abnormal when describing a picture but not when describing their occupation from memory

- We compared the language samples of PCA patients with controls across two distinct tasks: a visually-dependent picture description and a visually-independent job description task.
- Patients with PCA showed significant language deficits in the visually-dependent task, characterized by higher word frequency, prolonged utterance latency, and fewer spatial relational words, but not in the visually-independent task.
- PCA patients struggled to identify certain visual elements as well as the overall theme of the picture.
- A predictive model based on these language features distinguished PCA patients from controls with high classification accuracy (0.96).

Rezaii N, et al., Dickerson B, Putcha, Frontier in Neurosci, 2024

Likelihood of mentioning each content unit in picture by controls.

Likelihood of mentioning each content unit in picture by persons with PCA.



...URE 3
...e likelihood of mentioning each content unit of the WAB Picnic Scene by healthy individuals (A) and PCA patients (B). The shading intensity of each ...m corresponds to its verbalization probability by participants, with d... ...gher likelihood of being mentioned by PCA patients ...d healthy individuals.

Screenshot

In early AD, language informativeness declines similarly in both English and Persian

- We introduced a machine learning-based metric, Language Informativeness Index (LII), to quantify informativeness.
- From a language sample describing the Cookie Theft Picture, indicators of AD in English were found to be highly predictive of AD in Persian, with a 92.3% classification accuracy.
- Additionally, we found robust correlations between the typical linguistic abnormalities of AD and language emptiness (low LII) across both languages.

Bayat, Dickerson, Golberg, Rezaii et al., medRxiv

Testing the measure: Language Informativeness declines as key words are removed

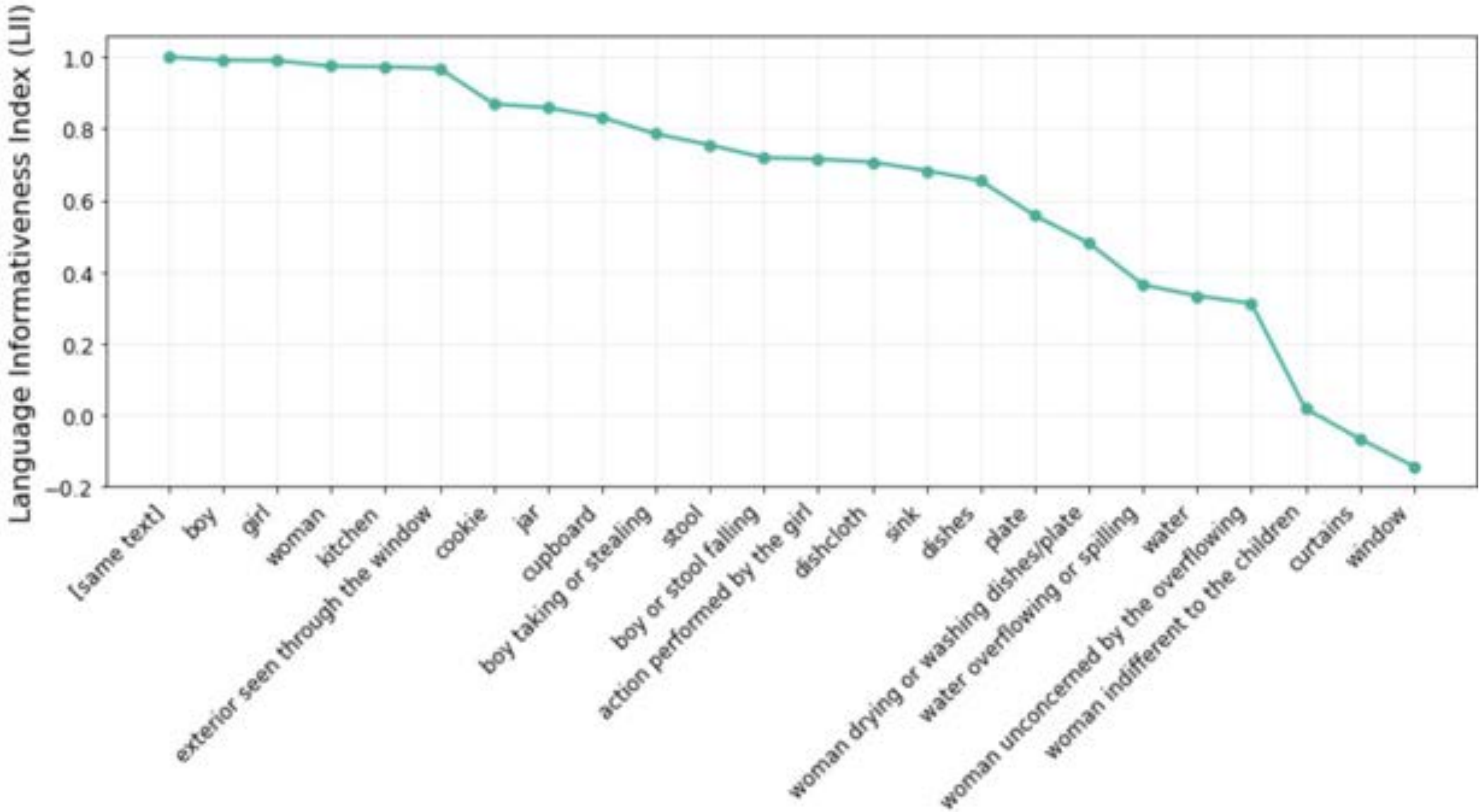


Figure 4. The reduction of LII as a function of excluding various content units in the Cookie Theft Picture. As each information unit is sequentially eliminated from the target text, its similarity to the reference text declines.

Bayat, Dickerson, Golberg, Rezaii et al., medRxiv

In early AD, language informativeness declines similarly in both English and Persian

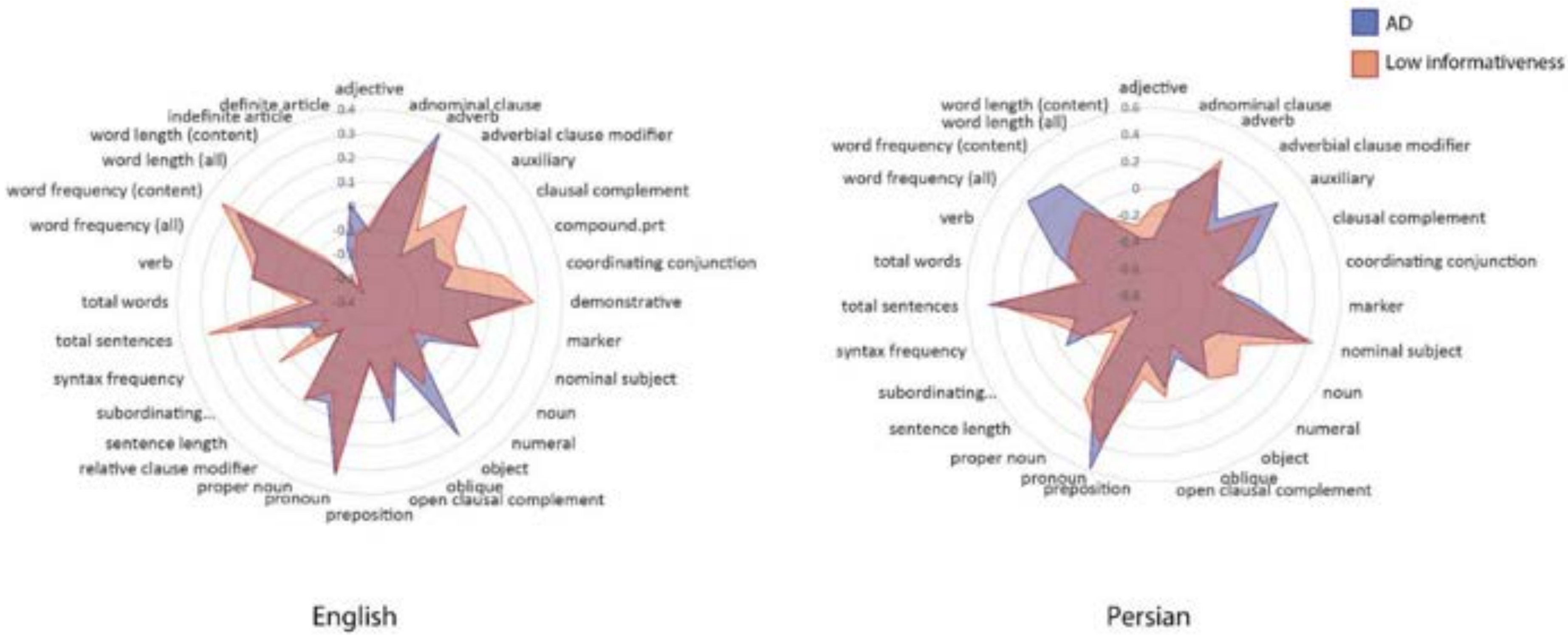


Figure 6. Radar charts depicting correlation coefficients between Alzheimer's Disease (AD) and low informativeness (emptiness) across various linguistic features in English and Persian. Substantial overlap exists between the two variables with respect to linguistic features in both languages

Bayat, Dickerson, Golberg, Rezaii et al., medRxiv

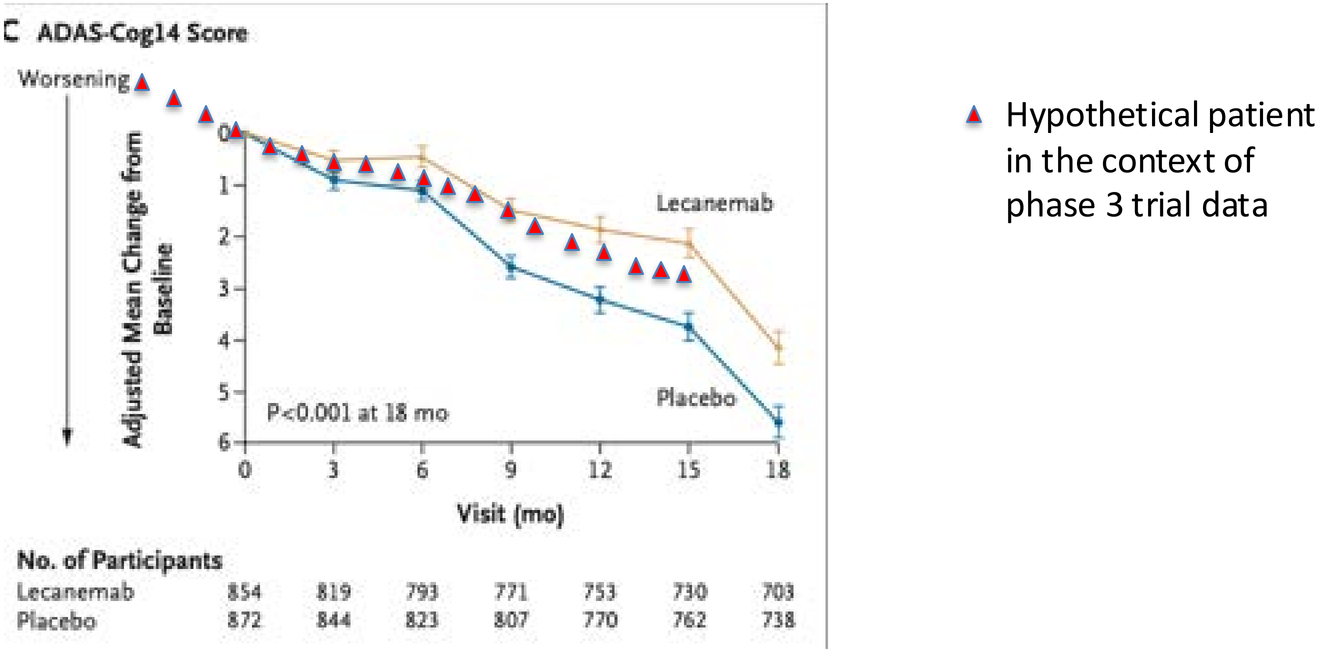
In early AD, language impairments reflect the disease as well as the spoken language (e.g., English vs. Persian)

- Conventional thinking: impaired verb usage -> frontal damage, impaired noun usage -> temporoparietal damage. BUT AD patients--typically more prominent posterior cortical degeneration--have reduced usage of both nouns and verbs.
- We hypothesized that this reflects the distributional properties of words within a language rather than distinct neural processing for noun vs. verb word classes.
- English has a set of particularly high-frequency verbs that surpass most nouns in usage frequency: *be, do, have, know, go, get, think, come, see, think*.
- Since AD patients tend to use high-frequency words, the byproduct of this word distribution in the English language would be an over-usage of high-frequency verbs.
- In contrast, Persian features complex verbs with a distribution lacking extremely high-frequency verbs like those found in English.
- Employing uniform automated natural language processing methods, we measured the usage rates of nouns, verbs, and word frequencies.
- English-speaking persons with AD (pwAD) use higher-frequency verbs than healthy individuals, a pattern not mirrored by Persian-speaking pwAD.
- Regression models that treated noun and verb frequencies as separate predictors did not outperform models that considered overall word frequency alone in classifying AD vs. controls.
- Some language abnormalities among English-speaking pwAD reflect the unique distributional properties of words in English rather than a universal noun-verb class distinction.

Sanati, Goldberg, Dickerson, Rezaii et al., medRxiv

REmote Assessment of cLinical outcomes in AD patients treated with Disease-Modifying Therapy (REAL outcomes AD)

- We developed a brief (20 min) remote cognitive assessment protocol employing on-line testing with digital audio recording of responses for use in people in the evaluation stage for lecanemab therapy.
- We collect monthly assessments, aiming to capture at least 3 measures prior to treatment and then monthly measures following the start of lecanemab.
- The goal is to try to measure a flattening of the trajectory of decline in individual patients with early-stage AD who are treated with disease-modifying therapies.



MGH-Sonde pilot project: Brief cognitive assessment iPhone app

Exploring feasibility of voice biomarker remote monitoring platform in clinical population with cognitive symptoms

Participant downloads and installs Sonde One app on their own phone

After initial training session, they conduct weekly study sessions on their own at home

Weekly sessions for 4 weeks

Participant feedback after 4 weeks

Study design

- Developed novel app for use on Sonde One platform
- Enrolled 53 patients from the MGH FTDU
- Used Sonde One app during 4-week study duration once a week (optional longer-term continuation)
- Gathered feedback from participants through end-of-study feedback

Study goals

1. Determine engagement with voice platform among cognitively impaired population
2. Learn how participants view the technology and its uses
3. Assess quality and consistency of voice samples and vocal features extracted in naturalistic conditions

The overall outcomes will help to assess the readiness of the technology as a remote monitoring platform for patients or at-risk older adults

MassAITC
Massachusetts AI and Technology Center for Connected Care in Aging & Alzheimer's Disease

P30AG073107

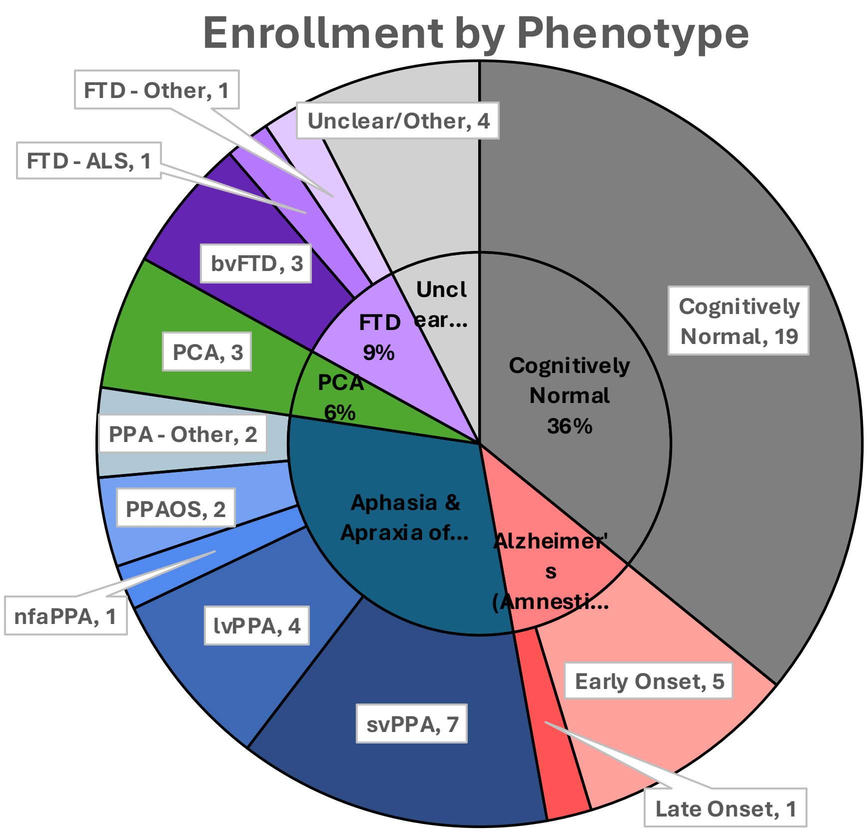
Bonnie Wong, PhD, Erik Larsen, Brad Dickerson

Dataset & analysis

- **Participants enrolled: 53** (3 withdrawn)
- **Data collected**: 2,718 voice samples across 250 study sessions
- **Tasks:** story encoding, alphabet & counting, alternating alphabet/counting, reading, category fluency, story recall (10-15 minutes)
- **Feedback questionnaires**: 22 collected
- **Vocal biomarker analysis:** all samples had feature extraction conducted (mental fitness related features), indicating good potential for future analysis and modeling
- **Other follow up**:
  - Generated subject data records with clinical data (phenotype, level of impairment)
  - Continuing quality control & transcriptions for language analysis
  - Continuing analysis & modeling including relationship with neuropsychological measures

P30AG073107
Bonnie Wong, PhD, Erik Larsen, Brad Dickerson

Enrollment: Participant Characteristics

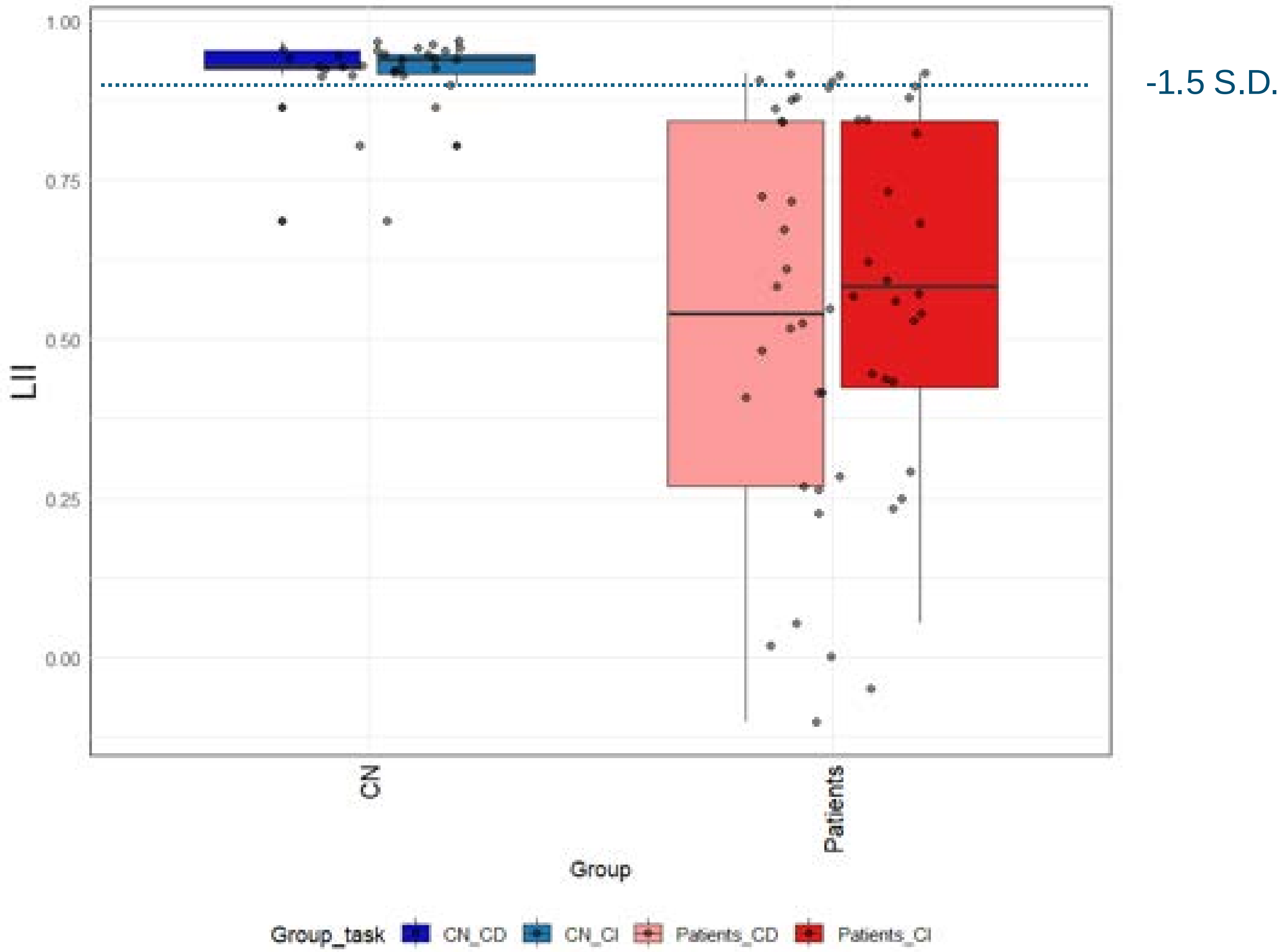


Mean Age: 67.3 +/- 7.2 yrs
Patients: 66.6 +/- 7.9 yrs (CDR 0, 0.5, or 1)
Cognitively Normal (CN): 68.9 +/- 5.3 yrs

Sex: 53% Female
Patients: 44% Female
CN: 71% Female

P30AG073107
Bonnie Wong, PhD, Erik Larsen, Brad Dickerson

Screening for cognitive impairment:
Language Informative Index analysis of immediate (CI) and delayed (CD) recall of short story



P30AG073107

Neguine Rezaii, Bonnie Wong, Erik Larsen, Brad Dickerson

Characterizing profile of cognitive impairment:

Feature value profiles reflect specific cognitive impairments within each major category of diagnosis

Speech rate by task type

(2,041 samples total, words/min)

Task type	Control	ADRD	PPA	FTD	PCA
Alphabet + counting	138	116	113	102	125
Passage reading	133	113	105	100	105
Free response question	126	109	101	77	102
Immediate recall	118	99	99	72	92
Delayed recall	116	93	93	63	82
Count backwards	95	62	80	62	60
Alternate alphabet and counting	91	61	76	58	50
Category fluency	79	57	63	48	38
Average	***112***	***89***	***91***	***73***	***82***

Task type impacts speaking rate

- Speaking rate varies significantly (~2x) by task type, reflecting varying cognitive demand

Diagnosis category profiles

- **ADRD** has lower speech rates across all tasks, primarily for higher complexity tasks, reflecting memory and cognitive impairments
- **PPA** has lower speech rates especially in language-dependent tasks such as passage reading and free response, with better performance in structured tasks
- **FTD** has lowest speech rates overall, particularly in recall and free response, reflective of executive dysfunction and language impairments
- **PCA** similar to PPA, but greater deficits in structured tasks

Speech rate profiles (or more complex profiles with multiple features) might capture significant phenotype information that will reflect typical impairments in different pathologies

Sample inclusion criteria: QoS <= 4 (if available), speech rate: 5-180 words/min

P30AG073107

Bonnie Wong, PhD, Erik Larsen, Brad Dickerson

LEADS Longitudinal Early-Onset Alzheimer's Disease Study experience with digital voice

- We have been recording digital audio samples of verbal NACC UDS 3.0 assessments in the LEADS consortium since 2018
- The LEADS consortium includes 18 US sites, 14 of which are ADRCs
- In LEADS, coordinators at each site are trained on procedures and a digital audio recorder is provided to each site. The following UDS tests are recorded: Craft Story immediate and recall, Category fluency (animals and vegetables), Lexical fluency (Fs and Ls), FTLD battery word reading, sentence repetition, noun and verb naming, and sentence reading; Rey AVLT is also recorded
- Essentially no additional time is added to participant visits for these recordings
- Our experience in LEADS has been that, once trained, coordinators require a total of approximately 15-20 additional minutes per participant session for file management
- Participants are consented for recording & sharing of digital audio (>99% opt in)
- Digital audio files are stripped of any PHI/PII
- Files are stored locally and copies are shared with Indiana University (prime site) for distribution to other investigators
- One publication (Bushnell J, et al. Alzheimers Dement. 2023) with multiple analyses in progress

UCSF Weill Institute for Neurosciences Memory and Aging Center · MGH 1811 · alzheimer's association · NACC · Keck School of Medicine of USC Alzheimer's Therapeutic Research Institute

Potential opportunities:
ADRCs digital recording of NACC UDS assessments

- Based on experience to date, staff training and burden would be low
- No additional participant burden
- The vast majority of participants understand the value of recordings with brief explanation and provide consent
- The information available is incredibly rich and would lend itself to increasingly sophisticated analyses of a variety of types as technology advances
- The clinical and demographic diversity of NACC participants, along with the depth of additional data available, would make digital recordings an incredibly valuable dataset

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Thank you!

MGH FTD Unit & Center for Translational Brain Mapping

Affiliated with the Mass ADRC and Martinos Center for Biomedical Imaging

Thanks for funding to:

With collaborators: P50 AG005134, R01 AG045390, U54 NS092089, R01 AG048351, R01 AG038791, U01 AG052943

Dickerson PI or MPI: R01 DC014296, R01 AG056015, R01 AG054081, R01 MH113234, R21 AG056958, U01 AG057195, Alzheimer's Drug Disc Foundation , Krupp Foundation

Digital Voice: Consent & IRB Protocol

Sudeshna Das, PhD
Hiroko Dodge, PhD

June 26, 2024

MGB ADRC

Mass General Brigham

MASSACHUSETTS Alzheimer's Disease Research Center

Informed Consent

- **Purpose**: Clearly explain the reason for the audio recording and how it will be used.
- **Confidentiality**: Describe how the recordings will be kept confidential and the measures in place to protect the participant's privacy.
- **Data Sharing**: Specify who will have access to the recordings and who will the data be shared with.
- **Benefits and Risks**: Explain any potential benefits and risks associated with the audio recording.

Example: LEADS Study

Memory and thinking tests: You will be asked to do activities which include remembering information, naming and drawing pictures, connecting symbols, and other similar tasks. The tests will be a combination of written, verbal, and computerized tests using a device like an iPad. The tests will take up to 5 hours to complete and can be split over multiple days. You can skip any questions you do not want to answer and take breaks if needed. We will audio record your responses to some of the memory and language tests. Recording your responses will allow researchers to write out (transcribe) your responses exactly as they were spoken. These audio recordings and transcriptions will allow researchers to analyze your responses in order to answer important questions about (such as) behavioral markers of speech, language and cognitive decline. Your recordings will be maintained on secure servers used for this study and only those with privacy training and permission from the study team will have access to them. While your voice can identify you, all other information which might identify you will be removed to protect you.

Example: LEADS Study

Memory and thinking tests: You will be asked to do activities which include remembering information, naming and drawing pictures, connecting symbols, and other similar tasks. The tests will be a combination of written, verbal, and computerized tests using a device like an iPad. The tests will take up to 5 hours to complete and can be split over multiple days. You can skip any questions you do not want to answer and take breaks if needed. We will audio record your responses to some of the memory and language tests. Recording your responses will allow researchers to write out (transcribe) your responses exactly as they were spoken. These audio recordings and transcriptions will allow researchers to analyze your responses in order to answer important questions about behavioral markers of speech, language and cognitive decline. Your recordings will be maintained on secure servers used for this study and only those with privacy training and permission from the study team will have access to them. While your voice can identify you, all other information which might identify you will be removed to protect you.

Example: I-CONECT Study

Informed Consent Form Extract:

All video chats in this study will be video and audio recorded. Parts of the testing calls will be audio recorded. The weekly phone call will also be audio recorded. We will use these recordings for educational materials and research analysis.

In the future, your saliva and information and recordings may be given to researchers for other research studies. These studies may include genetic research.

We will protect your privacy when sharing audio recordings by only sharing the recordings with approved researchers. We will not share any parts of the audio recordings that contain identifying information like your name, telephone number, or other information we think could be used to tell your identity. However, because everyone's voice is unique, it's possible that someone listening to the recording could identify you from the sound or pattern of your voice.

Additional Consent

Do you give us permission to audio record your responses to some of the memory and language tests?

☑ Yes, you have my permission
☐ No, you do not have my permission:

Additional consent is required if the audio recording is not an essential part of the study

IRB Study Protocol

- **Objective**: Clearly state the purpose of the study and the role of audio recordings in achieving the study objectives.
- **Recording Procedure**:
  - Specify what will be recorded
  - Specify the setting and method for audio recording (e.g., office or virtual visits).
  - Detail the equipment to be used for recording.
- **Storage**: Describe measures to protect participant confidentiality
- **Data Sharing**: Specify who will have access to the recordings and who will the data be shared with.

Example: LEADS Study

7.3.3 Audio Recording

The administration of select language and memory tests will be audio recorded for every participant, at every visit. This data will be collected to allow for additional analyses. A recording device, such as the Olympus VN-722PC digital voice recorder or a similar digital recording device, will be used.

15.4 Audio Recording Storage

The audio files acquired in this study will be securely transmitted and stored in databases being used for the study. The audio recorded during the administration of select assessments should not contain PHI. Sites will be responsible for ensuring that no PHI is included in the recordings prior to upload.

Example: I-CONECT Study

Audio/Video Recording

The I-CONECT video chat system is a secure, scalable, and cost-effective video chat platform for conducting in-home telehealth with geriatric populations. It enables researchers, clinicians and older participants (age 75+) easy access to private meeting spaces at the touch of a button. I-CONECT uses highly modified 2-in-1 style Chromebooks with functional touchscreens and webcams. The devices are folded to hide the keyboard, leaving only the touchscreen usable. The device is customized with Google G-Suite Enterprise, to enable remote management, updates, restricted access, and automatically load up the I-CONECT video chat app. They are installed with needed peripherals, several audio options, and a cover. The I-CONECT video chat app is a javascript interface built to run on top of commercial video chat software which uses a Web RTC interface. Essentially, it facilitates joining video-chat services by automatically entering required join commands for the subject with one click. Users have two UI options: “Join” or “Restart”. Researchers and clinicians join video chats through the commercial platform interface on their personal computers, which allows them to record chat audio using installed software. I-CONECT uses MacBook Air’s, with Audio Hijack installed, which allows individual channels to be isolated, recording input and outputs separately.

Audio/Video Recording Storage

All the recordings are stored in the HIPAA-compliant institution-supported cloud sources.

Helpful Suggestions

1. Keep purpose and details of study procedure general and non-specific to avoid limiting yourself in the future
   - Use examples, with "such as", as opposed to blanket statements
2. Privacy and security of data should be protected in the same manner as other data types (e.g., imaging, genotyping)
   - Locally stored in HIPAA compliant storage solutions
   - Access limited to IRB-approved study-staff
   - Transmitted securely to NACC (NIH certificate of confidentiality)
3. The deidentification tools are still under development - this data will not be shared by NACC until we are 100% confident that the data has been adequately deidentified.

Questions?

BOSTON UNIVERSITY

Digital Voice Processing, Analysis, and Results

UDS 4.0 Digital Voice Training Workshop
Rhoda Au, PhD, MBA
Cody Karjadi, MS
2024-06-26

Overview

- Intake and Quality Control
- Preprocessing and Standardization
- Feature Generation
- Publications

Intake and Quality Control

Record audio → Save and rename audio file → Compare schedule records to audio filenames

Save and rename audio file → NACCID_DATE_TESTNAME_TESTERID.wav
(e.g., NACC025360_20220302_MOCA_853.wav)

Compare schedule records to audio filenames — Passed Audio → Final storage

Compare schedule records to audio filenames — Flagged Audio → Resolve flagged cases

Resolve flagged cases — Resolved Audio → Final storage

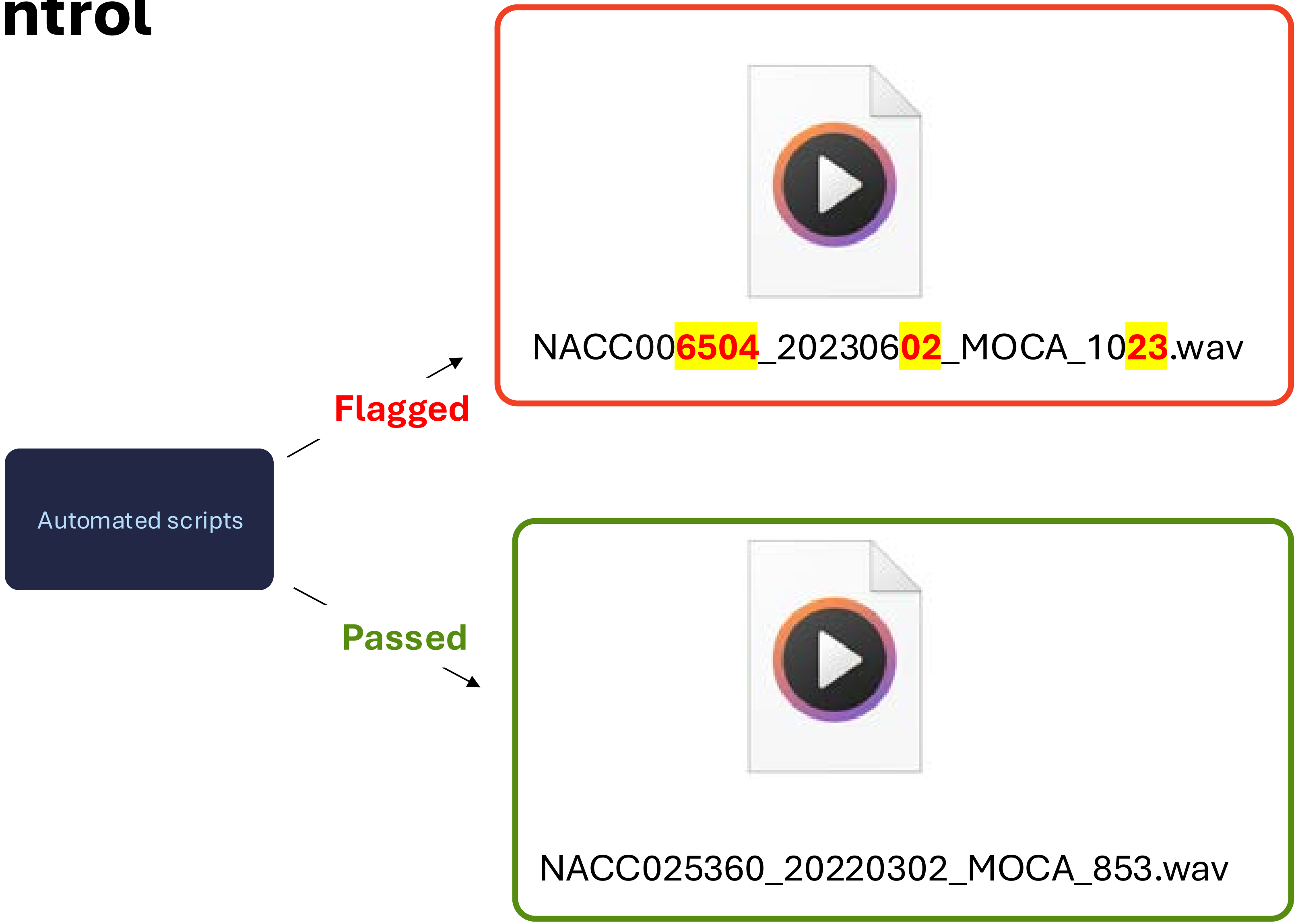
Resolve flagged cases ← Unresolved Audio → Flagged storage

Layers of Confirmation:

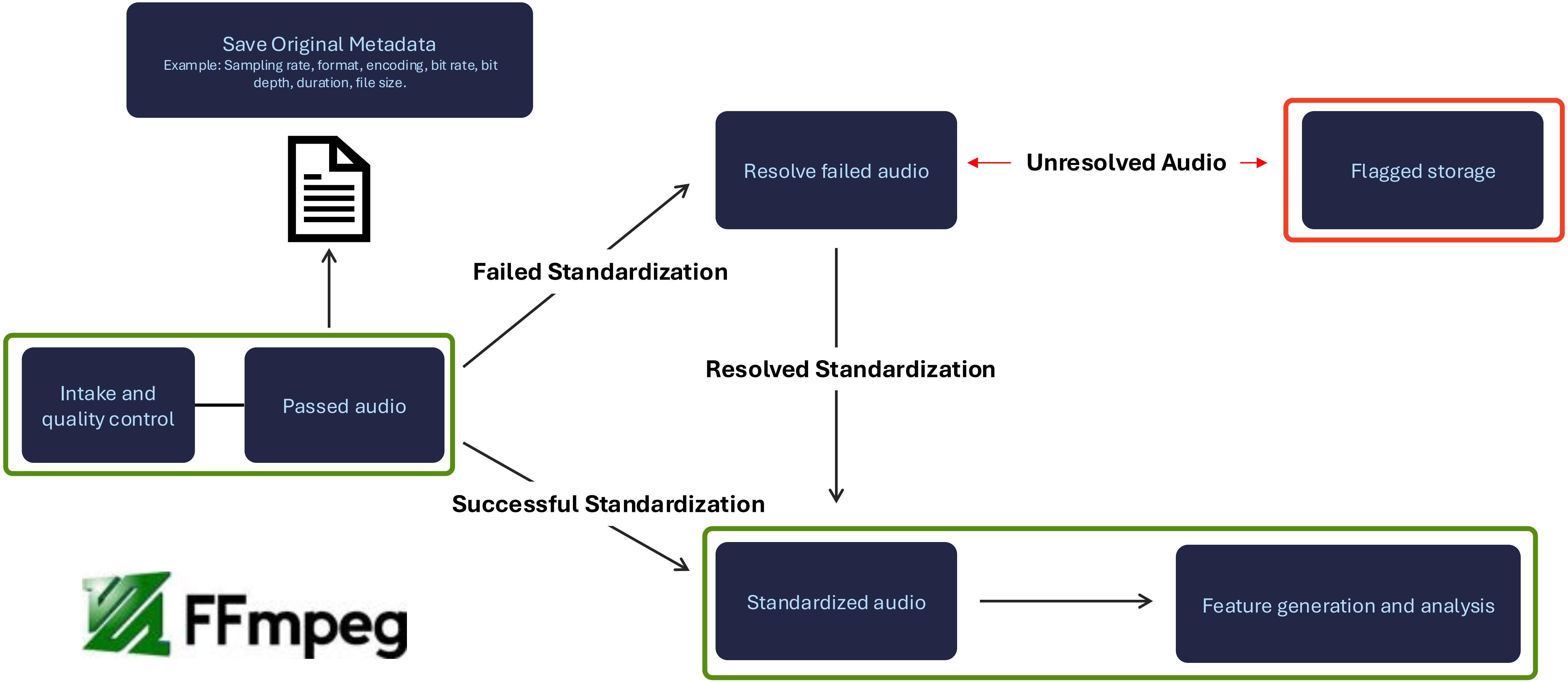
- Start of exam identifier
- Recording vs. battery results

Intake and Quality Control

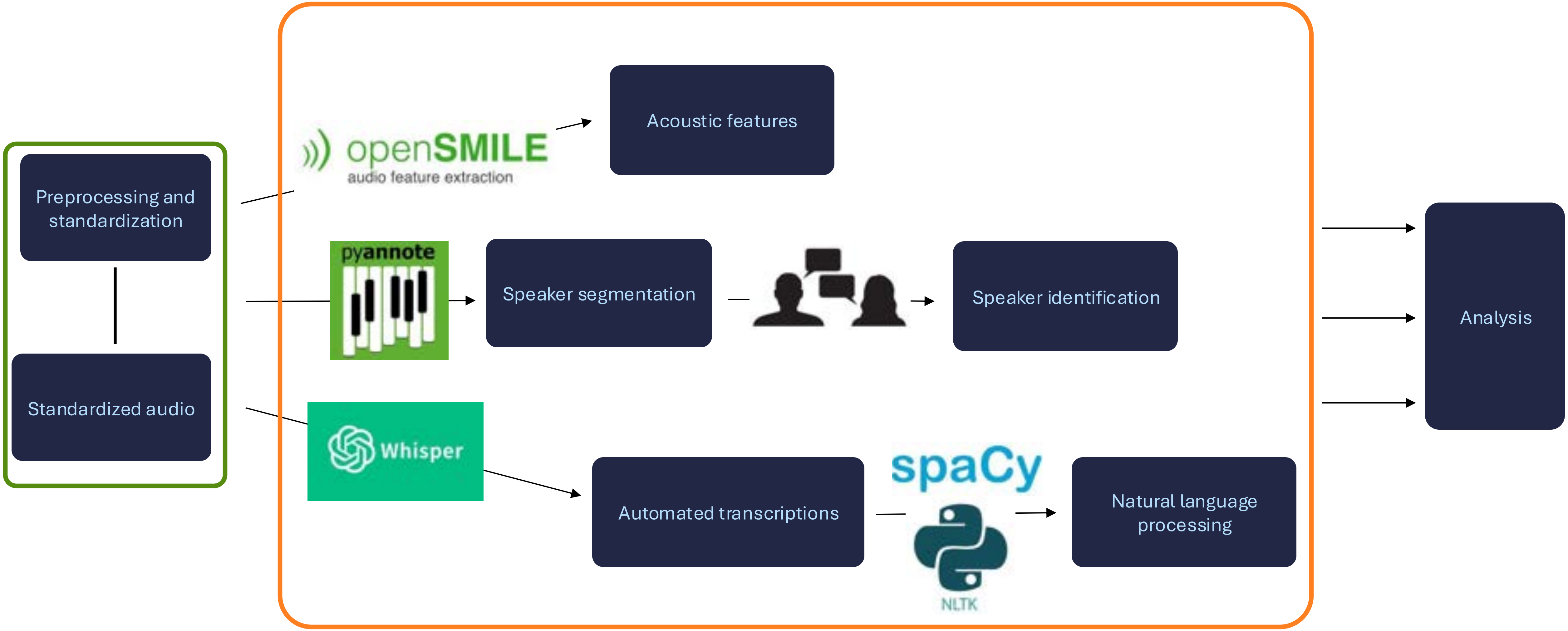
	A	B	C
1	**nacc_id**	**date**	**tech_id**
2	NACC025360	3/2/2022	853
3	NACC005604	6/3/2023	1032



Preprocessing and Standardization



Feature Generation



Postprocessing - More to Come!

- De-identification:
  - Voice Masking, PII Splicing.

Publications

- Amini S, Hao B, Yang J, et al. **Prediction of Alzheimer's disease progression within 6 years using speech: A novel approach leveraging language models.** *Alzheimer's Dement*. 2024; 1-9. https://doi.org/10.1002/alz.13886
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- Rezaii N, Mahowald K, Ryskin R, Dickerson B, Gibson E. **A syntax-lexicon trade-off in language production.** Proc Natl Acad Sci U S A. 2022 Jun 21;119(25):e2120203119. doi: 10.1073/pnas.2120203119. Epub 2022 Jun 16. PMID: 35709321; PMCID: PMC9231468.
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Visit the UDSv4 Digital Voice Webpage!

- Includes useful resources such as:
  - Information about the work the CTF Technology Workgroup is doing to support digital voice adoption across the ADRC program
  - Resources for ADRCs
  - Sign-up for CTF Tech WG Sub-Committees
  - Events and training opportunities will be posted here
- **Visit:** https://bit.ly/UDSv4_DigitalVoice

bitly

SCAN ME

Thank you!

June 26, 2024

UDSv4 Digital Voice Workshop

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Flexibility in data collection protocol adherence...

ADRCs Collecting Audio Files During Cognitive Assessments - *Basic Considerations*

- There is flexibility around devices used, file type, recording windows, etc.
- If sharing of these data for research going forward is a common goal, the ideal is to have common documentation and standardization
- Encourage standardization (e.g., record cognitive assessment, metadata assignment) and share things that are important to capture (provide a checklist, etc.)
- Need to understand what is currently being done - identify where commonalities lie
- Consider other - beyond cognitive test sessions - audio (and video) files

ADRCs Collecting Audio Files During Cognitive Assessments: *Current Activities*

- Fall, 2023 ADRC survey:
  - 18 ADRC's collecting audio files during cognitive assessments (mostly?) in 2023
  - 8 "No, but we plan to collect this data in the future"
  - 8 "No, we do not plan to collect this data"
- Current reasons for collection and protocols to be clarified

Other Ongoing Studies Recording Cognitive Testing

The Storyteller Memory Test by Novoic Ltd.

ADNI4

V-COG

Alzheimer's & Dementia
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

CLINICAL MANIFESTATIONS | Free Access

Validation of a Video Adaptation of the UDSv3 Cognitive Battery (VCog): Study Design and Preliminary Participant Satisfaction Results

Bonnie C. Sachs, Lauren Latham, Suzanne Craft, Lisa L. Barnes, Lindsay R. Clark, Hiroko H Dodge, Kevin Duff, Sarah Tomaszewski Farias, Eric Fischer, Sarah A. Gaussoin, Felicia C Goldstein, Benjamin M. Hampstead, Suman Jayadev, Gregory A Jicha, Jeffrey A Kaye, Walter A. Kukull, Abigail H O'Connell, Dawn Mechanic-Hamilton, Judith A. Neugroschl, Kathryn V. Papp, Andrew J. Saykin, Margaret Sewell, Stephen R. Rapp ... See fewer authors

First published: 25 December 2023 | https://doi.org/10.1002/alz.079840

LEADS

Alzheimer's & Dementia
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

RESEARCH ARTICLE | Open Access

Influence of amyloid and diagnostic syndrome on non-traditional memory scores in early-onset Alzheimer's disease

Justin Bushnell, Dustin B. Hammers, Paul Aisen, Jeffrey L. Dage, Ani Eloyan, Tatiana Foroud, Lea T. Grinberg, Leonardo Iaccarino, Clifford R. Jack Jr, Kala Kirby, Joel Kramer, Robert Koeppe, Walter A. Kukull, Renaud La Joie, Nidhi S. Mundada, Melissa E. Murray, Kelly Nudelman, Malia Rumbaugh, David N. Soleimani-Meigooni, Arthur Toga, Alexandra Touroutoglou, Prashanthi Vemuri, Alireza Atri, Gregory S. Day, Ranjan Duara, Neill R. Graff-Radford, Lawrence S. Honig, David T. Jones, Joseph Masdeu, Mario Mendez, Erik Musiek, Chiadi U. Onyike, Meghan Riddle, Emily Rogalski, Steven Salloway, Sharon Sha, Raymond S. Turner, Thomas S. Wingo, David A. Wolk, Maria C. Carrillo, Bradford C. Dickerson, Gil D. Rabinovici, Liana G. Apostolova, David G. Clark, the LEADS Consortium ... See fewer authors

First published: 31 August 2023 | https://doi.org/10.1002/alz.13434

Other Potential Recordings?

Use Cases - Recording Methods – Recording Setting/Conditions

https://www.moonlightsonatadoc.com/

REMOTE ADRC CLINIC VISITS

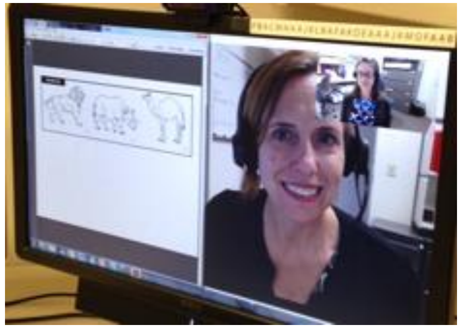
Feature Set	AUC	σ
Test scores 1–9	0.815	0.050
Test scores 1–9 + automated language features 4, 7–9, 12	0.854	0.045
Test scores 1–9 + automated language features 4, 7–9, 12 + automated speech features 16–19	0.861	0.044

Roark B, Mitchell M, Hosom JP, Hollingshead K, Kaye J. Spoken Language Derived Measures for Detecting Mild Cognitive Impairment. IEEE Trans Audio Speech Lang Process. 2011 Sep 1;19(7):2081-2090.

TELE-STELLA VIDEO CHAT

Figure 3: Screen view when Chromebook is opened

Allison Lindauer, PI



NCT04335110

ICONECT VIDEO CHAT

Hiroko Dodge, PI

MCI participants generate a greater proportion of words
(x= 2985 vs. 2423 words)

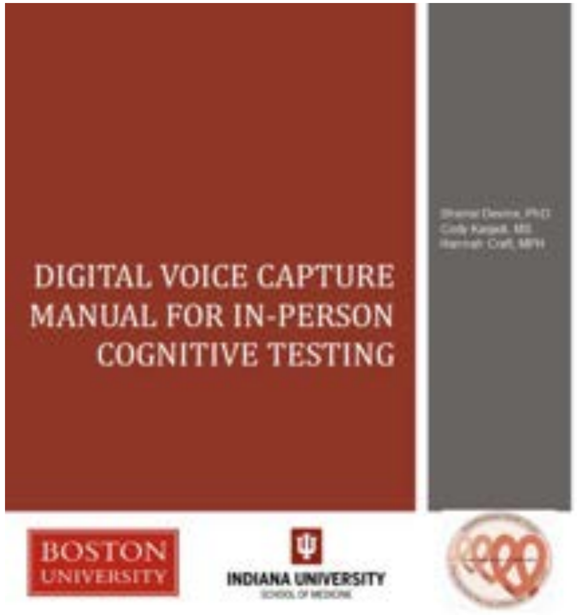
NCT02871921, NCT01571427

SHARP AUDIO RECORDS

Raina Croff, PI

NCT05658328

Towards Standardization:
Manuals/Roadmaps for Considering What to Do & Document



6/5/2023

Table of Contents

• **INFORMED CONSENT**

It is crucial to provide an in-depth description of the audio recording implementation and use of the data as part of the informed consent process. In addition, it is important to provide detailed information regarding data usage, storage, and protection. A copy of the FHS-BAP consent form can be found under Appendix B: FHS-BAP Consent Form.

• **SELECTING AUDIO RECORDING EQUIPMENT**

For audio recording equipment, consider the following factors: portability, data storage space, battery life, ease of set up, sampling rate, etc. FHS-BAP uses the Zoom H4N recorder. Refer to here for alternative models.

• **STORAGE AND RETRIEVAL OF AUDIO RECORDINGS**

Use a standardized naming convention for the audio recording files and maintain a data log for inventory management.

• **POST DATA COLLECTION PROCESSING**

Generating analysis-ready files is resource intensive. It may not be possible for all researchers, especially if funding may be an issue. Personally identifiable information is a common concern for audio recordings; hence these files must undergo post data-collection processing before they can be made available for analysis, especially in situations where the sensitive data are being shared with other researchers.

Examples of Considerations

Basic Data Elements to Collect and Record

GENERAL METADATA ELEMENTS (HARMONIZABLE)			
Metadata Title	**Data description**	**Data format**	**Allowable codes (if applicable)**
Collection Date	Date that data was collected	Integer	MM/DD/YYYY
Collection Time	Time that data was collected	Integer	HH:MM:SS
Collection Tool	Tool that data was collected on	String	Limit to list of specific tools
Tool Version	Model or version of tool	String	Limit to list of specific tool versions
Device model		String	
Operating System	Software and/or OS used on tool	String	Limit to list of specific OS
Raw data format	Data format of raw data (voice recording, image capture, video recording, CSV file)		Limit to list of options specific to this data (voice file, image file, video file, etc.)

Editing / Annotation of Files

- Personally Identifying Information
- Labeling cognitive tests, spontaneous speech segments
- QC (review of files)

ADRC Digital Biomarker FAQs

Can I use any recorder to capture voice data for the UDSv4?

While many devices will record voice data, NACC has certain requirements for recording UDSv4 voice data

- Zoom H4N recorders are preferred
- Limited background noise
- At the beginning of the recording state staff ID, participant ID, study visit date and number, and what is being recorded

Do I need to process the voice data at my ADRC?

While all ADRCs are encouraged to keep voice files for their own use, all voice data will be uploaded to NACC

- Use NACC naming conventions: NACCID_DATE_TESTNAME
- Store in WAV format
- Enter meta-data of the test in UDS4 dVoice form

What is UDS4 dVoice form?

This is the form that will accompany voice data uploads; it includes

- NACC ID
- Tester ID
- Recording Date
- Name of file with full path
- Recording device details
- QC details

ADRC Digital Biomarker FAQs

What are the benefits of digital biomarkers to my ADRC?

There are many practical benefits to adding voice recording to your ADRC, they include

- Acting as a QC tool to determine natural drift in standardization in any longitudinal study
- Providing an easy, low-cost collection of data that can be done in a participant's preferred language
- Allowing additional scientific enablement at no additional participant burden
- Increasing opportunities to explore acoustic and semantic features in novel forms

What are the benefits of digital biomarkers to participants?

While direct participant benefit may be low at the outset, over time features of voice data may be able to

- Provide early indicators of cognitive impairment in preclinical or prodromal Alzheimer's dementia
- Help track disease progression and predict conversion to dementia

What are the benefits of digital biomarkers to science?

Features of voice data are already showing promise in

- Serving as a dementia screening tool to detect those at risk for dementia
- Indicating the effectiveness of clinical trials
- Associating with CSF biomarkers of disease

Any additional questions?