

Speech Changes in Objective and Subjective Cognitive Decline and Associations with Blood Biomarkers

Laili Soleimani ¹, Nadia Ramsingh¹, Sunghye Cho ², Nikolaos Karvelas ¹, Sai Vendidandi ³, Faye Sheppard¹, Anna Torten Rabinowitz ¹, Judith Neugroschl ¹, Jimmy Akrivos ¹, Maria Loizos¹, Margaret Sewell ¹, Michal Schnaider Beerl ³, Mark Liberman ², Fanny Elahi ¹, Mary Sano ¹, Carolyn Zhu ¹

1. Icahn school of Medicine at Mount Sinai, New York, NY, USA. 2. Linguistic Data Consortium, University of Pennsylvania, Philadelphia, PA, USA.
3. Rutgers New Jersey Medical School, Newark, NJ, USA.

INTRODUCTION

- There is a critical need for accessible and reliable tools for dementia diagnosis.
- Current approaches rely heavily on neuroimaging and CSF analyses, which are costly, invasive, limited in access.
- Speech and language offer non-invasive and scalable markers for cognitive decline, with potential for remote monitoring.
- Here, we examined speech changes across cognitive status function in relation to objective and subjective cognitive decline and blood biomarkers.

METHODS

Participants:

- Normal controls (NC= 105) and individuals with MCI (N= 60) or Alzheimer's Disease and related disorders (ADRD; N=47).
- MCI and ADRD subjects were grouped into a single Cognitively impaired group.

Scales:

- Objective Cognitive Decline: Clinical Dementia Rating (CDR)¹
- Subjective Memory Complaint: Subjective Memory Complaint (SMC) item in the Geriatric Depression Scale-15 (GDS-15) ²

Speech Task: Picture Description Task: Cookie Theft (neutral), one negative, and one positive image from International Affective Picture System (IAPS) ³

Blood Biomarkers (pTau181/217, GFAP, NfL, Aβ): Ultrasensitive immunoassay platforms in a subset of participants ⁴

Statistical Analysis:

- Logistic regression (AUC) classified cognitive impairment
- Mixed models: Speech variables and Objective/ Subjective Cognitive Decline
- Partial correlations: Speech - Blood Biomarker
Covariates: age, sex, and education.
GDS analyses controlled for CDR

RESULTS

Table 1. Demographic and Clinical Characteristics

Variable	Non-impaired n = 105	Impaired n = 107
Age	75.98 (7.22)	78.36 (7.80)
Education (years)	16.63 (2.72)	16.49 (2.64)
MMSE total	28.32 (1.55) n=87	23.93 (4.25) n=84
CDR sum of boxes	0.05 (0.19)	2.60 (2.11)
NPI-Q total	1.13 (2.34) n=104	4.20 (4.26) n=105
GDS total	2.42 (2.82)	2.78 (2.81) n=101
FAQ total	0.18 (0.80) n=104	7.45 (7.51) n=106
Sex (Male: n, %)	39 (37.1%)	54 (50.5%)
CDR global		
0 (no impairment)	101 (96.2%)	0 (0%)
0.5 questionable	4 (3.8%)	81 (75.7%)
1 (mild)	0 (0%)	19 (17.8%)
2 (moderate)	0 (0%)	1 (0.9%)

Table 3. Association of CDR and Speech Variables

Domain	Variable	b	Effect
Time / Fluency	Mean pause	0.04	↑ *
	Total syllable count	-11.37	↓ *
	Partial words	0.106	↑ **
	Repetitions	0.207	↑ ***
	Words per minute	-2.861	↓ **
	Articulatory rate	-0.071	↓ *
Lexical Semantics	Frequency Content	0.031	↑ ***
	Age of acquisition	-0.045	↓ ***
	Phonemic content	-0.033	↓ **
	Valence	0.013	↑ *
	Dominance	0.013	↑ **
	Lexical diversity	-0.002	↓ *
Syntax	Nouns	-0.275	↓ *
	Adjectives	-0.151	↓ **
	Determiners	-0.171	↓ *
	Pronouns	0.388	↑ ***
	Tense-inflected verbs	0.137	↑ *

Table 4. Association of GDS-SMC and Speech Variables

Domain	Variable	b	Effect
Lexical/Semantic	Age of acquisition	-0.112	* ↓
Syntax	Tense-inflected verbs	-0.577	* ↓

Table 2. Speech-Derived Predictors of Cognitive Impairment

Rank	Predictor	AUC	OR	Effect
1	Age of Acquisition	0.683	0.212	↓ ***
2	Words per min	0.676	0.985	↓ ***
3	Frequency content	0.666	8.57	↑ ***
4	Articulatory rate	0.665	0.665	↓ *

Included all, controlling for picture task

Table 5. Partial Correlation of Speech Variables and Blood Biomarker

Task	Speech Variable	Biomarker	Partial Spearman r	P Value
Neutral	Adjectives	ptau217	-0.225	0.0369*
	Frequency content	GFAP	0.208	0.0358*
	Frequency content	Aβ40	-0.222	0.0283*
	Mean Speech	ptau217	-0.381	0.0003***
Negative	Mean Speech	NfL	-0.229	0.0195*
	Frequency content	Aβ40	-0.207	0.0399*
	Mean Speech	ptau217	-0.217	0.0434*
	Mean Speech	GFAP	-0.198	0.0446*
	Mean Speech	NfL	-0.232	0.0171*

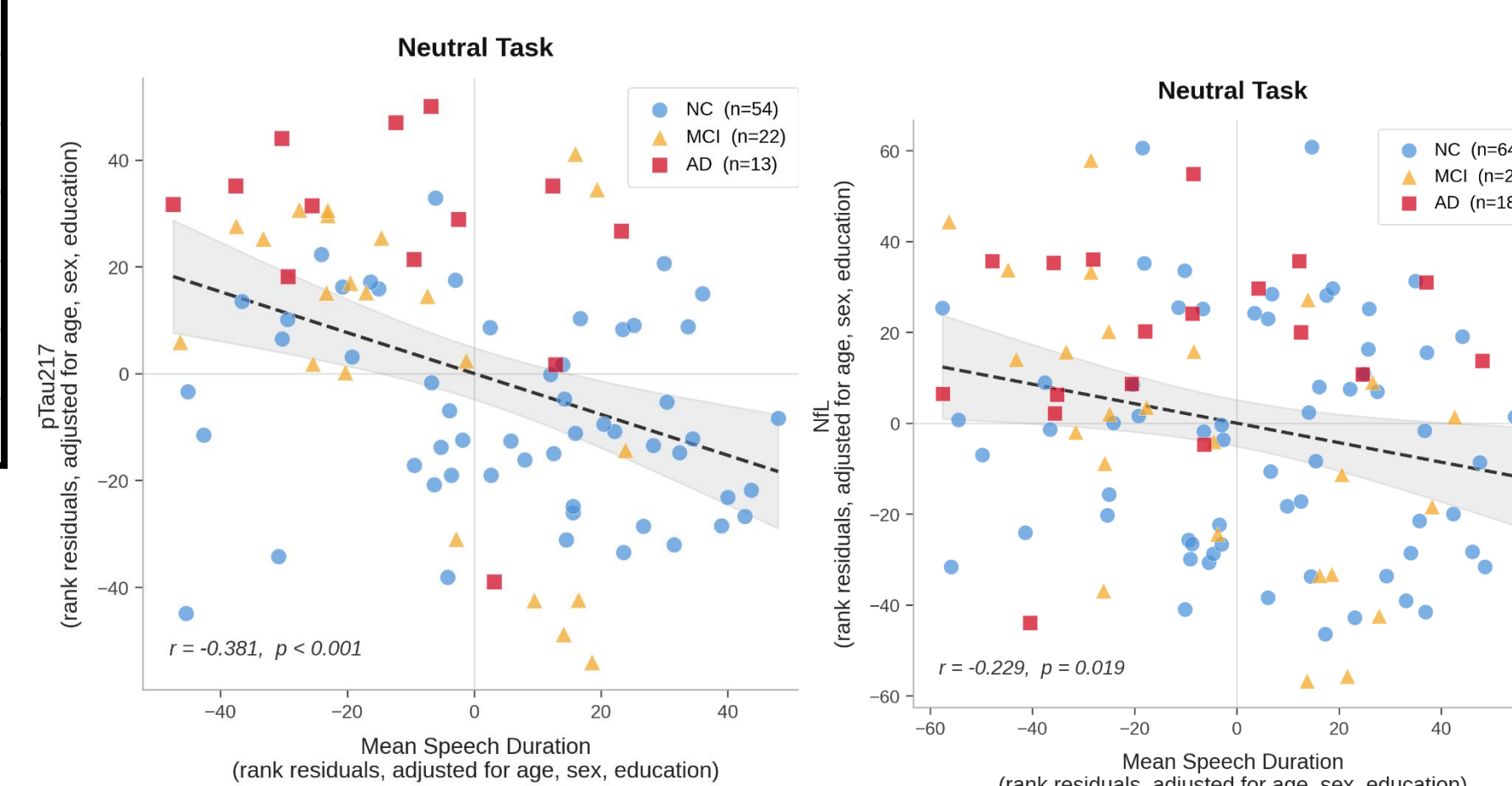


Figure 1. Distribution of Speech Variables (Mean Speech) and Blood Biomarker (pTau217 and NfL)

DISCUSSION

- Speech changes can serve as a reliable predictor for cognitive impairment, with strongest contributions from lexical-semantic variables and speech rate (AUC up to 0.73).
- CDR as an objective measure of cognitive decline is associated with series of changes that include dysfluencies, increased repetitions and simplified content words.
- SMC is associated with changes in speech variables beyond explained by objective measures.
- Overall, speech may be a promising, non-invasive, digital biomarker for detecting both objective and subjective cognitive decline.
- The strongest speech–biomarker association was observed between mean speech duration and p-tau217 during the neutral task ($r = -0.381$, $p < .001$), suggesting that individuals with higher p-tau217 levels produced shorter speech segments.

REFERENCES



ALZHEIMER'S ASSOCIATION

ISTAART
alzheimer's association

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Contact: Laili.Soleimani@mssm.edu