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SHORT REPORT

Speech markers of depression dimensions across cognitive status

Laili Soleimani[1] | **Yuxia Ouyang**[1] | **Sunghye Cho**[2] | **Arash Kia**[1] | **Michal Schnaider Beeri**[3] | **Hung-Mo Lin**[4] | **Ramit Ravona-Springer**[5,6] | **Nadia Ramsingh**[1] | **Mark Y Liberman**[2] | **Murray Grossman**[7,†] | **Naomi Nevler**[7]

[1]Icahn School of Medicine at Mount Sinai, New York, New York, USA

[2]Linguistic Data Consortium, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[3]Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA

[4]Department of Anesthesiology, Yale School of Medicine, New Haven, Connecticut, USA

[5]The Joseph Sagol Neuroscience Center, Sheba Medical Center, Tel-Hashomer, Israel

[6]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

[7]Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Correspondence
Laili Soleimani, Icahn School of Medicine at Mount Sinai, 1 Gustave L. Levy Pl, New York, NY 10029, USA.
Email: laili.soleimani@mssm.edu

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Abstract

Introduction: Depression and its components significantly impact dementia prediction and severity, necessitating reliable objective measures for quantification.

Methods: We investigated associations between emotion-based speech measures (valence, arousal, and dominance) during picture descriptions and depression dimensions derived from the geriatric depression scale (GDS, dysphoria, withdrawal-apathy-vigor (WAV), anxiety, hopelessness, and subjective memory complaint).

Results: Higher WAV was associated with more negative valence (estimate = -0.133, $p = 0.030$). While interactions of apolipoprotein E (APOE) 4 status with depression dimensions on emotional valence did not reach significance, there was a trend for more negative valence with higher dysphoria in those with at least one APOE4 allele (estimate = −0.404, $p = 0.0846$). Associations were similar irrespective of dementia severity.

Discussion: Our study underscores the potential utility of speech biomarkers in characterizing depression dimensions. In future research, using emotionally charged stimuli may enhance emotional measure elicitation. The role of APOE on the interaction of speech markers and depression dimensions warrants further exploration with greater sample sizes.

KEYWORDS
apathy, cognitive decline, dementia, depression, neuropsychiatric symptoms, speech

Highlights

- Participants reporting higher apathy used more negative words to describe a neutral picture.
- Those with higher dysphoria and at least one APOE4 allele also tended to use more negative words.

- Our results suggest the potential use of speech biomarkers in characterizing depression dimensions.

1 | INTRODUCTION

Depression and its respective dimensions (e.g., apathy, anxiety) are common in older adults with cognitive impairment across various stages including the preclinical phase. This highlights the value of using these symptoms for improving detection at the preclinical stages of dementia.[1] Depression as a whole and apathy specifically, have also been shown to be associated with faster cognitive decline,[2] hence hold predictive value.[3]

Leveraging large datasets with extensive cognitive information, our previous research has demonstrated that specific depression dimensions derived from the Geriatric Depression Scale (GDS-15), including dysphoria, apathy, anxiety, helplessness, and subjective memory complaint, are associated with cognitive decline.[4,5] However, the use of questionnaires to define these dimensions is constrained by subjectivity and limited reliability of participants and informants.[1]

This study investigates the use of speech biomarkers to identify specific dimensions within the depression phenotype in dementia, leveraging the significant role of language in psychiatric evaluation and recent advancements in speech technology. In a prior study by Konig et al., automated analysis of speech features revealed connections between neuropsychiatric symptoms. Apathy was linked to slower speech, indicating greater severity, while anxiety showed a correlation with voice quality measures like sound-to-noise ratio.[3] Given the significance of emotional processing in the depression dimensions, we tried to use the quantifiable emotion-based speech measures extracted from speech data and explore their association with depression dimensions from the population at risk of dementia.[6] Additionally, we investigated whether the apolipoprotein E4 (APOE4) genotype has an impact on these observed associations.

2 | MATERIALS AND METHOD

2.1 | Participants

We analyzed cross-sectional speech data from participants at the University of Pennsylvania, who were native English speakers and were recruited to Penn's Institutional Review Board (IRB)-approved longitudinal frontotemporal dementia (FTD) cohort study. The diagnosis was determined based on published criteria[7] and validated in a multidisciplinary consensus, with no additional exclusion criteria. A total of 112 samples were included in this analysis (Alzheimer's disease [AD]: 76; mild cognitive impairment [MCI]: 16; and healthy age-matched participants: 20).

2.2 | Speech collection and processing

Detailed methodology on a collection of semi-structured narrative speech samples was previously described.[8] Briefly, an interviewer instructed participants to provide a detailed description of the "Cookie Theft" scene from the Boston Diagnostic Aphasia Examination.[9] For the purpose of this study, only the earliest available recordings from each participant were analyzed. Recordings were transcribed by trained annotators at the Linguistic Data Consortium (LDC) of the University of Pennsylvania who were blinded to the cognitive or emotional status of the speaker and tokenized with spaCy[10] open-source libraries.

2.3 | Emotion-based measures

Emotion-based measures, including valence, arousal, and dominance, for each word were calculated based on a previously published database.[11] Valence is defined as the pleasantness of a stimulus, arousal as the intensity of emotion elicited, and dominance as the degree of power exerted by the word. Based on this database, higher scores correspond to positive valence, more arousal, and more control, respectively. For each subject, we rated valence, arousal, and dominance of all content words including nouns, verbs, adjectives, and adverbs that were automatically tagged by spaCy and averaged per participant. We excluded all function words as well as the copula verb "to be" from the analysis, since these categories do not have any semantic content but only serve their grammatical roles in sentences.

2.4 | Depression dimensions

The depression dimension scores were calculated for dysphoria, withdrawal-apathy-vigor (WAV), anxiety, hopelessness, and subjective memory complaint based on the mean of itemized Geriatric Depression Scale—15 item (GDS-15)[4,5] for each dimension. The resulting score ranged from 0 to 1, with 0 indicating the absence of any symptom and 1 indicating the presence of all symptoms.

2.5 | APOE 4 carrier's status

DNA was extracted from blood and APOE4 genotype was available for a subsample of the participants ($n = 79$). APOE status was categorized based on the presence of at least one epsilon 4 ($\varepsilon 4$) allele.

RESEARCH IN CONTEXT

1. **Systematic Review**: PubMed was used to review the literature. Findings highlight the potential value of depression and its associated dimensions in predicting the trajectory of cognitive decline and call for a need for objective quantification. This study explores the associations of emotion-based speech measures and these depression dimensions derived from the Geriatric Depression Scale (GDS-15).
2. **Interpretation**: This study underscores the potential utility of speech biomarkers (including valence) in characterizing depression dimensions.
3. **Future Directions**: In future research, using emotionally charged stimuli rather than neutral ones may enhance emotional measure elicitation.

2.6 | Statistical analysis

Linear regression was used to assess the association between baseline depression score (total GDS) and for each depression dimension as independent variable and speech features (i.e., valence, arousal, and dominance) as dependent variable, adjusting for age, sex, years of education, and Mini-Mental Status Examination (MMSE) score. All analyses were done with SAS 121 9.4 (SAS Institute Inc., Cary, NC). A two-sided $p < 0.05$ was defined as the significance level in all statistical tests. All results are reported in Table 1.

2.7 | Consent statement

All human subjects provided written informed consent approved by the IRB at the University of Pennsylvania. All patient data were handled by Health Insurance Portability and Accountability Act (HIPPA) -certified personnel and stored on HIPPA-compliant servers.

3 | RESULTS

3.1 | Description of the sample

Demographic and clinical characteristics of the patient groups are summarized in Table S1.

The study included 112 subjects (49.0% female) with a mean age of 66.95 (SD 9.29) years, 16.39 (SD 2.80) years of education, and a baseline MMSE score of 23.69 (SD 5.23).

On average, the sample had a GDS score of 2.14 (SD 2.39) at baseline, reflecting a relatively low number of depressive symptoms. The most reported GDS-15 items at baseline among the participants was item 10 (memory problems), reported by 55.36% of the participants as expected from the nature of the study cohort. The subsequent items included item 2 (drop activities), reported by 24.11% of the participants, and item 13 (decreased energy), reported by 22.32% of the participants (Figure 1).

3.2 | Emotion-based measures

Scores for the lowest and highest-rated words for valence, arousal, and dominance are listed in Table S2.

Table 1 summarizes the results of the regression models. A high WAV score was associated with more negative valence (apathy: estimate = −0.133, $p = 0.03$). We did not find a significant association between valence with total GDS or other depression dimensions. Similarly, other emotion-based measures (arousal and dominance) did not show a significant association with depression dimensions.

When exploring the interaction of emotional measures with APOE4 and depression dimensions, none of the associations reached statistical significance. However, there was a trend for significant interaction between dysphoria and APOE4 on valence (estimate = −0.404, $p = 0.084$) suggesting that carriers of the APOE4 allele with higher reported dysphoria may be using language with more negative valence when compared to those with no APOE4 allele (Figure S1). There were no interactions between dementia severity and depression dimensions on emotion measures.

4 | DISCUSSION

Our study revealed a noteworthy association between the emotional aspects of speech and specific facets of depression, particularly the WAV dimension (related to apathy). Notably, participants with high apathy scores used words with less positive emotional meaning even when describing neutral stimuli. No similar associations were found with other dimensions of depression. These associations persisted after controlling for severity of impairment (i.e., MMSE score), suggesting that they are maintained during the disease course. The progressive and persistent nature of apathy coupled with its predictive value for cognitive decline, adds to the clinical value of this finding for detecting apathy at the preclinical stage.[12]

Apathy is a multi-dimensional construct encompassing domains of behavior, cognition, and emotions. The latter encompasses emotional blunting in response to positive and negative stimuli. In our study, the three GDS-15 items constituting the WAV dimension primarily describe the behavioral and cognitive components of apathy, not the emotional domain.[13] Therefore, subjects with high WAV scores using fewer positive words may not necessarily score high on emotional apathy. Moreover, apathy is linked to an altered meso-cortico-limbic dopaminergic system, leading to reduced salience of the positive stimuli.[14] This potential alteration in the reward network of those reporting higher apathy items, may steer them away from positive elements of the relatively neutral image.

There is a growing body of literature on the use of different aspects of speech (including acoustic and lexical features as well as emotional

TABLE 1 Association of GDS dimensions with speech parameters

Parameter		Valence	Arousal	Dominance
Total GDS	Main effect	Estimate = −0.012, $p = 0.120$	Estimate = 0.006, $p = 0.305$	Estimate = 0.0006, $p = 0.901$
	X APOE4	$p = 0.269$ APOE4 [1 vs. 0] Estímate = −0.019	$p = 0.582$ APOE4 (1 vs. 0] Estimate = −0.008	$p = 0.782$ APOE4 (1 vs. 0] Estimate = −0.003
Dysphoria	Main effect	Estimate = −0.048, $p = 0.655$	Estimate = 0.083, $p = 0.296$	Estimate = 0.109, $p = 0.131$
	X APOE4	$p = 0.084$ APOE4 [1 vs. 0] Estimate = −0.404	$p = 0.323$ APOE4 [1 vs. 0] Estimate = −0.184	$p = 0.163$ APOE4 [1 vs. 0] Estimate = −0.231
Withdrawal-apathy–vigor (WAV)	Main effect	Estimate = −0.133, $p = 0.030$ *	Estimate = 0.022, $p = 0.635$	Estimate = −0.045, $p = 0.280$
	X APOE4	$p = 0.262$ APOE4 [1 vs. 0] Estimate = −0.158	$p = 0.994$ APOE4 [1 vs. 0] Estimate = −0.00082	$p = 0.898$ APOE4 [1 vs. 0] Estimate = −0.013
Anxiety	Main Effect	Estimate = −0.005, $p = 0.909$	Estimate = 0.039, $p = 0.233$	Estimate = −0.013, $p = 0.648$
	X APOE4	$p = 0.988$ APOE4 [1 vs. 0] Estimate = −0.0015	$p = 0.465$ APOE4 [1 vs. 0] Estimate = 0.058	$p = 0.507$ APOE4 [1 vs. 0] Estimate = 0.046
Hopelessness	Main Effect	Estimate = −0.139, $p = 0.198$	Estimate = 0.043, $p = 0.596$	Estimate = −0.025, $p = 0.729$
	X APOE4	$p = 0.898$ APOE4 [1 vs. 0] Estimate = 0.306	$p = 0.320$ APOE4 [1 vs. 0] Estimate = 0.191	$p = 0.751$ APOE4 [1 vs. 0] Estimate = 0.054
Subjective memory complaint	Main Effect	Estimate = −0.037, $p = 0.312$	Estimate = −0.0007, $p = 0.979$,	Estimate = −0.026, $p = 0.286$
	X APOE4	$p = 0.867$ APOE4 [1 vs. 0] Estimate = −0.013	$p = 0.410$ APOE4 [1 vs. 0] Estimate = −0.052	$p = 0.236$ APOE4 [1 vs. 0] Estimate = 0.065

Note: Summary of the regression models controlled for age, sex, education, and MMSE. APOE4 1: at least one epsilon 4 (ε4) allele. 0: no ε4 allele. Estimate: the coefficient of the correlation.
Abbreviations: GDS, Geriatric Depression Scale; MMSE, Mini-Mental State Examination; WAV, withdrawal-apathy-vigor.
*$p < 0.05$.

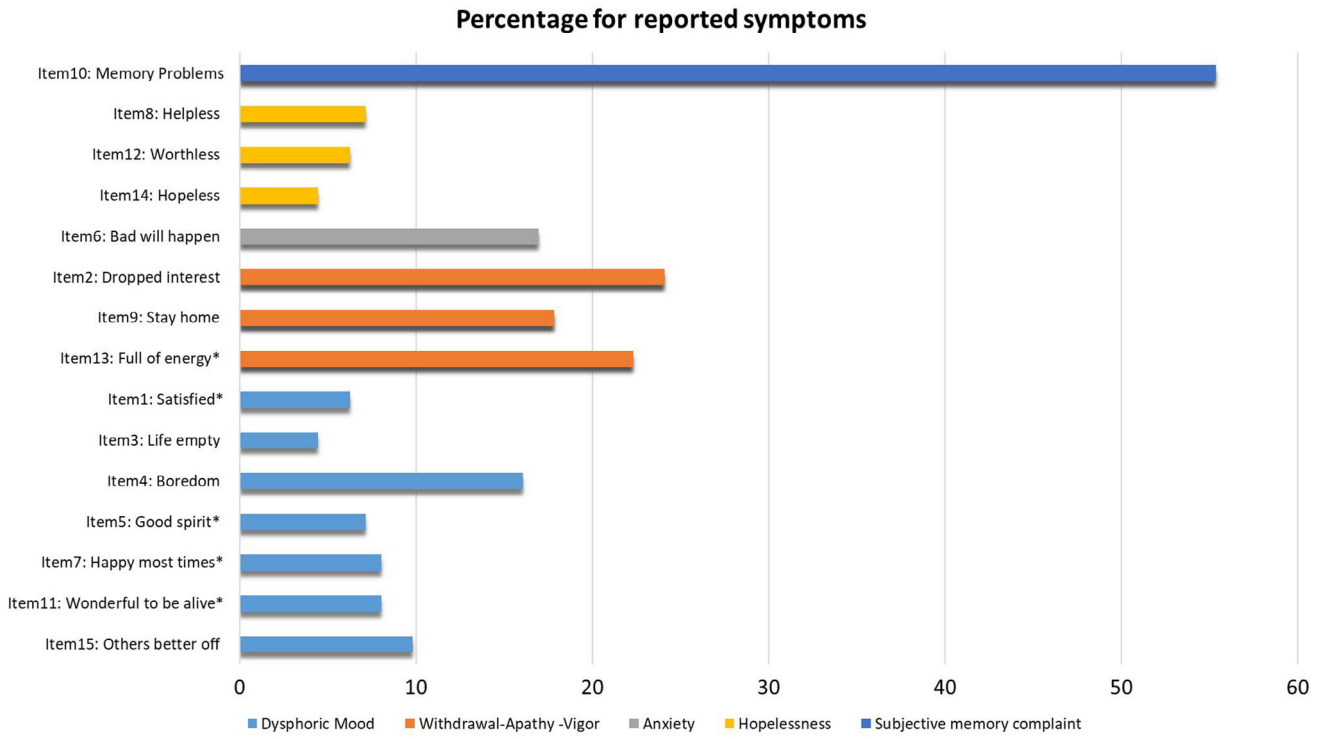

FIGURE 1 Percentage of reported symptoms from Geriatric Depression Scale-15 items (GDS-15). *GDS score was reversed such that a higher score represents a higher depression score

content) for detecting psychiatric symptoms including depression[15–17] and anxiety.[16,18] Alteration in cognitive processing, leading to an automatic preference for negative stimuli (i.e., negative attention bias) has been shown both for depression and anxiety [19,20] and speech may be a sensitive and objective measure to capture these subtle changes.[21] The three-dimensional representation of emotion (i.e., valence, arousal, and dominance) allows for a refined description of emotional content in speech.[11] Higher scores of depression and anxiety were previously shown to be associated with higher frequency of negative valence words.[16–18] The absence of such association in our study for total GDS, dysphoria, or anxiety may stem from the neutral nature of the "cookie theft" picture, the fact that our population is not clinically depressed with low depression scores, or the limitations of questionnaires to adequately capture these depression dimensions. While dysphoria, per se, was not associated with more negative valence in speech, those with higher dysphoria who were carriers of the APOE4 genotype tended to express more negative emotional valence. This finding should be replicated in larger sample sizes as it suggests that APOE4 may be a modulator for the expression of behavioral phenotypes.

Although preliminary, our study findings offer promising insights into objective and quantifiable speech-emotional measures. Yet, this study has a few limitations, including the use of subjective self-report questionnaires to delineate depression dimensions, which may be influenced by variable symptom awareness across the spectrum of cognitive disorder.[22] This can be addressed in future studies by using more in-depth questionnaires that incorporate collateral information from study informants. The small sample size of the study may limit the generalizability of the findings to a larger population. In addition, using neutral stimuli may have contributed to the sparsity of associations with emotional speech measures. In future studies, using positively or negatively charged pictures may be helpful to explore the differential effect of emotional stimuli on the speech measures given the expected cognitive bias in patients with dominant depression and anxiety symptoms in comparison with those with prominent apathy who may be experiencing emotional blunting.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare. Disclosures are available in the supporting information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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