ASSOCIATION BETWEEN SPEECH CHARACTERISTICS AND CORTICAL [18F]GTP1 TAU PET TAU LEVELS IN PRODROMAL-TO-MILD ALZHEIMER'S DISEASE

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Jessica Robin[1], Mengdan Xu[1], Aparna Balagopalan[1], Jekaterina Novikova[1], Somaye Hashemifar[2], Abdi Oday[2], Laura Kahn[2], Mohsen Hejrati[2], Rainier Amora[2], Sandra Sanabria Bohorquez[2], William Simpson[1], Edmond Teng[2]

(1) Winterlight Labs, Toronto, ON, Canada; (2) Early Clinical Development, Genentech, Inc

Background

Speech changes in Alzheimer's disease (AD) are potential early indicators of disease, but their validation against established AD biomarkers is lacking[1]. Tau pathology has been associated with the degree of cognitive impairment in AD[2,3,4]. We examined associations between speech and language characteristics and cerebral tau accumulation measured by tau PET in prodromal-to-mild AD.

Methods

- Baseline (N=88) and 18-month (N=46) longitudinal data from a subset of right-handed English-speaking participants in the Tauriel trial of semorinemab (NCT03289143) in prodromal-to-mild AD were analyzed.
- Speech samples recorded from Clinical Dementia Rating (CDR) administrations were analyzed using the Winterlight speech processing pipeline, generating over 500 acoustic and linguistic speech variables.
- Pearson correlations were computed to determine univariate associations between baseline speech features and cognitive scores with both baseline and baseline-to-endpoint change in [18F]GTP1 tau PET SUVR values in whole cortical grey and other regions of interest (ROIs). Correlation coefficients (R) and uncorrected p-values (p) are included in Figures 1-4.

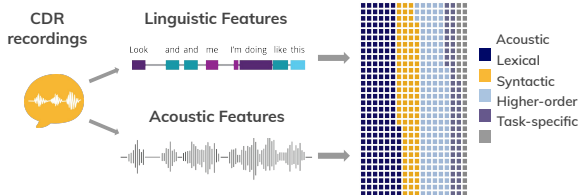### Winterlight Speech Analysis Pipeline

CDR recordings → Linguistic Features / Acoustic Features → Acoustic, Lexical, Syntactic, Higher-order, Task-specific

Figure 1: Cross-sectional correlations between whole cortical grey [18F]GTP1 SUVR and global clinical scores (n=88)

Tau-WCGS	CDR-SB	ADAS-Cog	RBANS	MMSE	ADCS-ADL
	0.19	0.41	-0.44	-0.23	-0.07

Pearson correlation: 1.0, 0.5, 0.0, -0.5, -1.0

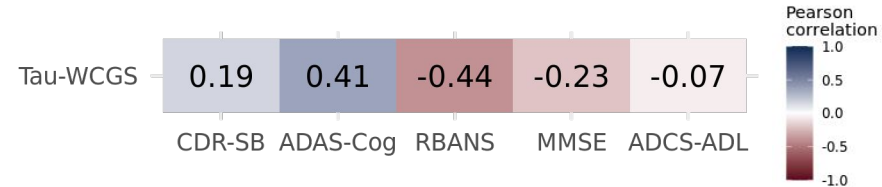## Figure 2: Cross-sectional correlations between whole cortical grey [18F]GTP1 SUVR and speech characteristics (n=83)

Filled pauses (um) R = 0.46 p = 1.36e-05

Word frequency R = 0.3 p = 0.00506

Vocabulary diversity R = -0.28 p = 0.0093

Whole cortical gray matter [18F]GTP1 tau PET SUVR

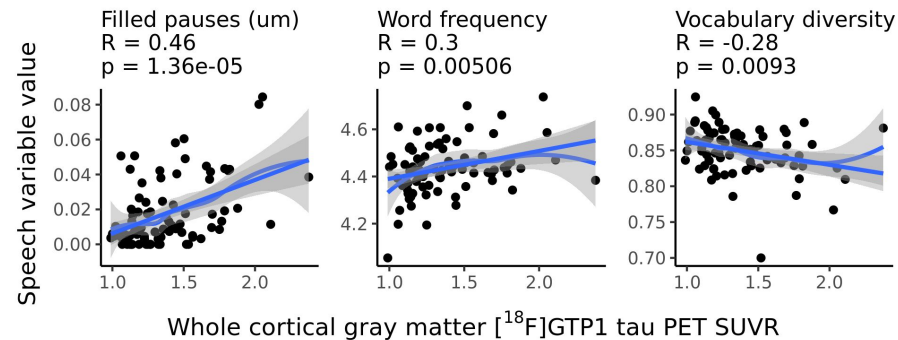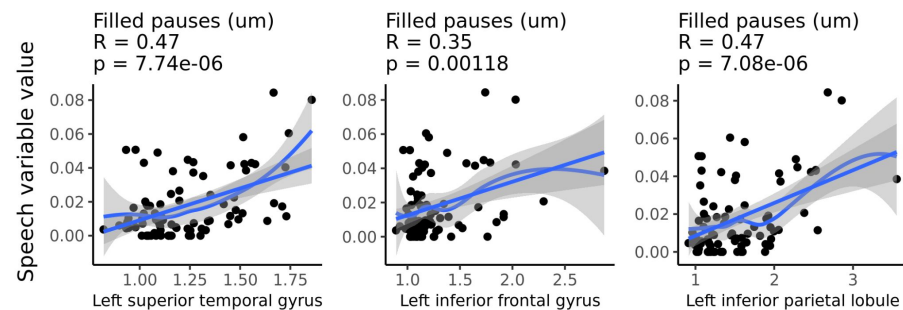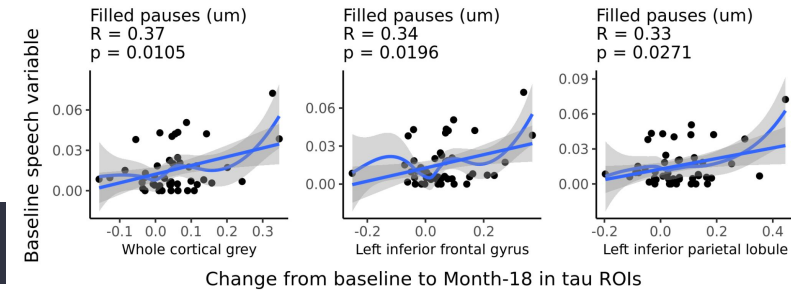## Figure 3: Cross-sectional correlations between [18F]GTP1 SUVR and filled pauses generalize across ROIs (n=83)

Filled pauses (um) R = 0.47 p = 7.74e-06 — Left superior temporal gyrus

Filled pauses (um) R = 0.35 p = 0.00118 — Left inferior frontal gyrus

Filled pauses (um) R = 0.47 p = 7.08e-06 — Left inferior parietal lobule

Figure 4: Baseline filled pauses correlate with increases in [18F]GTP1 SUVR over 18 months (n=46)

Filled pauses (um) R = 0.37 p = 0.0105 — Whole cortical grey

Filled pauses (um) R = 0.34 p = 0.0196 — Left inferior frontal gyrus

Filled pauses (um) R = 0.33 p = 0.0271 — Left inferior parietal lobule

Change from baseline to Month-18 in tau ROIs

Summary

- Speech and language features relating to pauses and vocabulary were associated with tau PET SUVR.
- Increased use of filled pauses, more frequent words and simpler vocabularies may indicate word finding difficulty and/or memory impairment related to increased underlying tau pathology.
- Associations were also observed between global clinical outcome measures and tau PET SUVR.
- These associations between speech and tau pathology are consistent with the hypothesis that increased cortical tau deposition may drive altered speech patterns associated with disease progression.

References

1. Robin, J. et al. Evaluation of Speech-Based Digital Biomarkers: Review and Recommendations. Digit. Biomark. 99–108 (2020) doi:10.1159/000510820.
2. Arriagada, P. V., Growdon, J. H., Hedley-Whyte, E. T. & Hyman, B. T. Neurofibrillary tangles but not senile plaques parallel duration and severity of Alzheimer's disease. Neurology 42, 631 (1992).
3. Bejanin, A. et al. Tau pathology and neurodegeneration contribute to cognitive impairment in Alzheimer's disease. Brain 140, 3286–3300 (2017).
4. Nelson, P. T. et al. Correlation of Alzheimer Disease Neuropathologic Changes With Cognitive Status: A Review of the Literature. J. Neuropathol. Exp. Neurol. 71, 362–381 (2012).

Contact: jessica@winterlightlabs.com

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