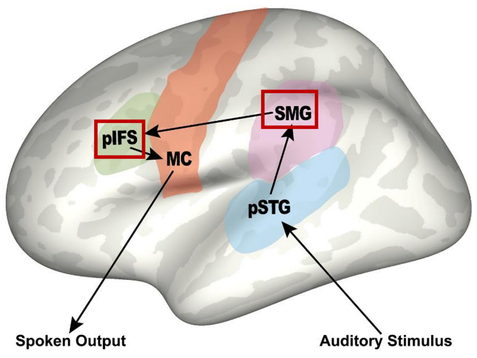
Evidence for a Phonological Output Buffer in Posterior Inferior Frontal Sulcus from Repetition Deficits in Primary Progressive Aphasia

Hilary E. Miller,[1] Claire Cordella,[2] Jessica A. Collins,[2] Rania Ezzo,[2] Megan Quimby,[2] Jason A. Tourville,[1] Frank H. Guenther,[1] & Bradford C. Dickerson[2]

[1]**Boston University** College of Health & Rehabilitation Sciences: Sargent College, Department of Speech, Language, & Hearing Sciences
[2]**Massachusetts General Hospital & Harvard Medical School** Department of Neurology, Frontotemporal Disorders Unit

Motivation



The GODIVA model of speech sequencing proposes a ***phonological output buffer*** in ***left posterior inferior frontal sulcus (pIFS)***.[1] This buffer should be heavily involved in verbal repetition tasks.

Previous studies show atrophy of ***left supramarginal gyrus (SMG)*** and ***posterior superior temporal gyrus (pSTG)*** is associated with impaired verbal repetition in ***primary progressive aphasia (PPA)*** ,[2-5] consistent with the role of a ***phonological input buffer.***

Hypothesis: Verbal repetition performance in PPA will also be correlated with cortical thickness in left pIFS (phonological output buffer).

Methods

Subjects: 42 right-handed patients in the MGH PPA Longitudinal Cohort, diagnosed according to consensus guidelines[6]

	lvPPA (n = 14)	nfvPPA (n = 13)	svPPA (n = 15)
Female, number (%)	8 F (57%)	6 F (46%)	9 F (60%)
Age, y (SD)	71.3 (8.1)	69.4 (8.4)	64.7 (7.3)
Education, y (SD)	16.2 (3.2)	15.8 (3.4)	16.3 (1.9)
Time from Diagnosis, y (SD)	0.7 (1.1)	1.0 (2.3)	0.9 (1.1)
Mean PASS score	0.5 (0.2)	0.6 (0.3)	0.5 (0.2)
WAB- Repetition score (SD)	71.3 (15.2)[b,c]	88.8 (14.0)[a]	86.5 (7.6)[a]
Forward Digit Span score (SD)	4.2 (1.6)[c]	5.5 (1.3)	6.7 (1.2)[a]
Backward Digit Span score (SD)	2.5 (1.6)[c]	3.3 (0.9)	4.0 (1.6)[a]

Behavioral measures:

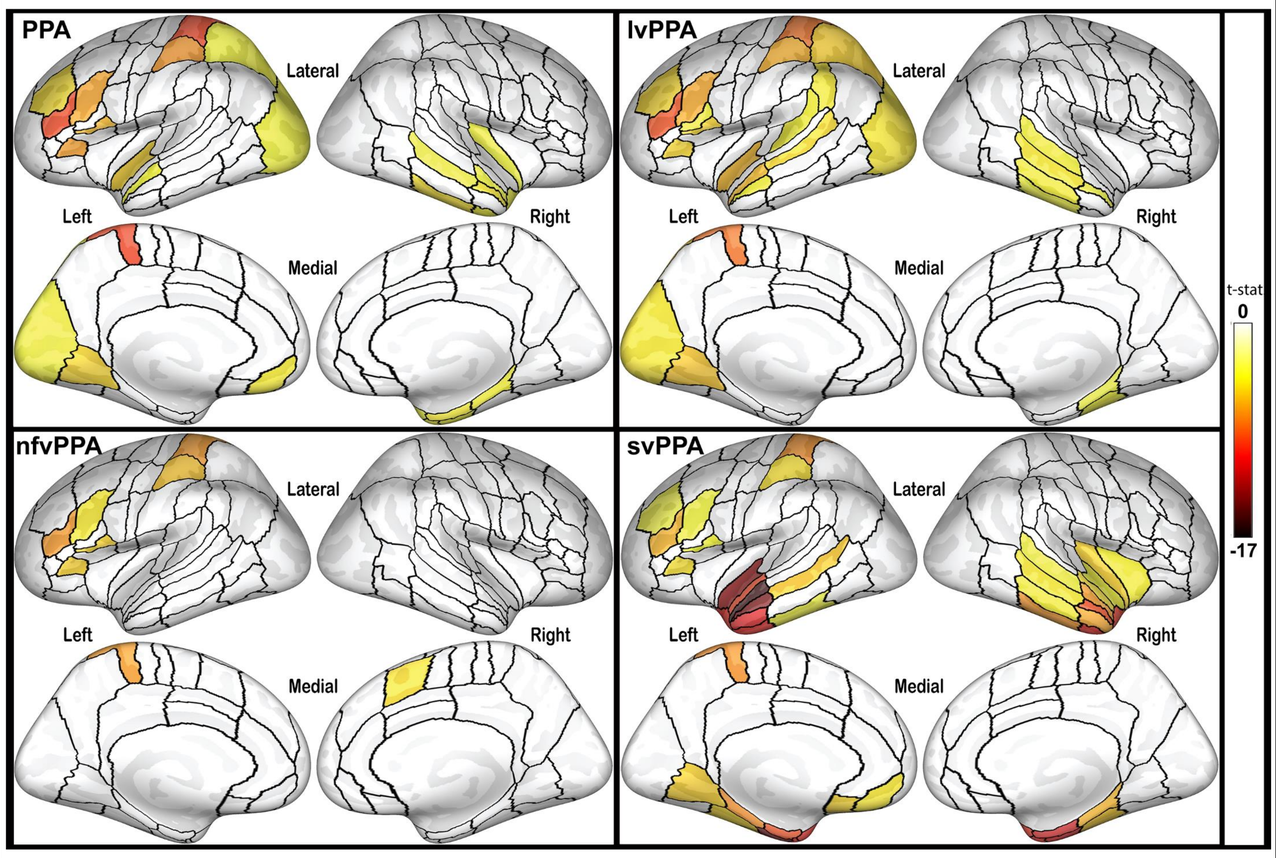
- Forward digit span[7]
- Backward digit span[7]
- Sentence Repetition subtest on Western Aphasia Battery[8]
- Average working memory score (mean of z-scores from 3 WM tests)

Neuroimaging measure:

- Cortical thickness was measured using Freesurfer software[9] within 66 anatomical ROIs in SpeechLabel parcellation[10], from T1-weighted anatomic brain scans following cortical reconstruction

Results: Atrophy by PPA Variant

One-tailed t-tests conducted to determine ***atrophy in each PPA variant*** compared to ***age-matched controls*** (FDR correction, p < 0.001; color scale represents t-statistics).



Key Findings:

- ***Nonfluent-variant***: Atrophy primarily in ***left frontal lobe***
- ***Semantic-variant***: Atrophy primarily in ***anterior temporal lobe*** (left-biased)
- ***Logopenic-variant***: Atrophy in ***temporoparietal junction*** and ***inferior frontal lobe***

References

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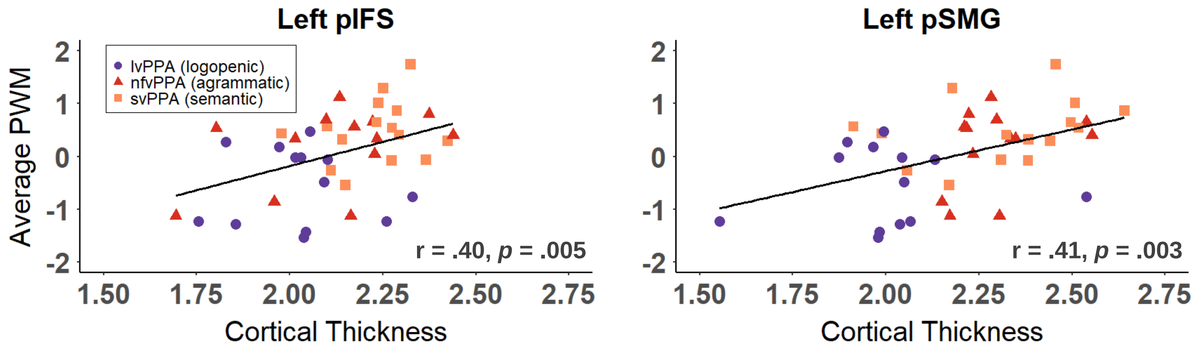
Main Result: PWM Correlations

Cortical thickness of both proposed **phonological buffers** was significantly correlated with **average PWM** score (one-tailed test, α=0.025 to correct for multiple comparisons).

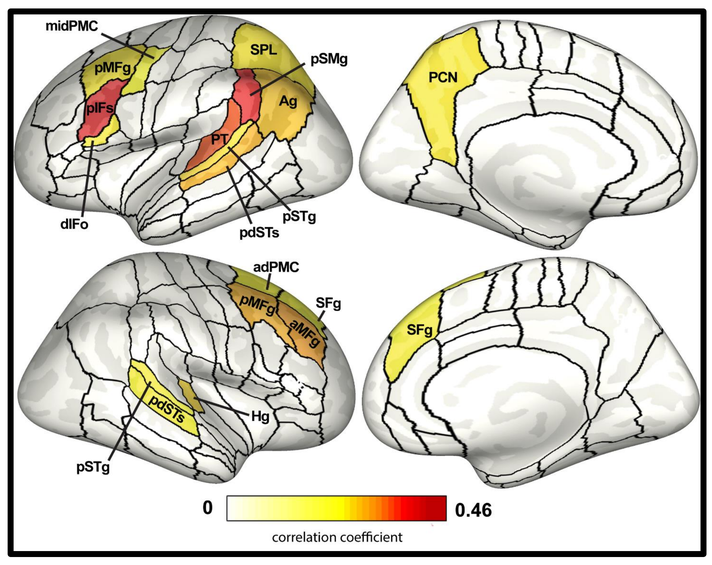


Involvement of ***left pIFS*** in verbal repetition is consistent with the role proposed by the ***GODIVA model***, where left pIFS is responsible for the ***buffering and sequencing of phonemes*** prior to spoken output.

Forward Digit Span Subtest

Key ROIs predicting Forward Digit Span:

- Left pIFS: r = .46, *p* = .001
- Left pSMG: r = .43, *p* = .002
- Left planum temporale (PT): r = .39, *p* = .006

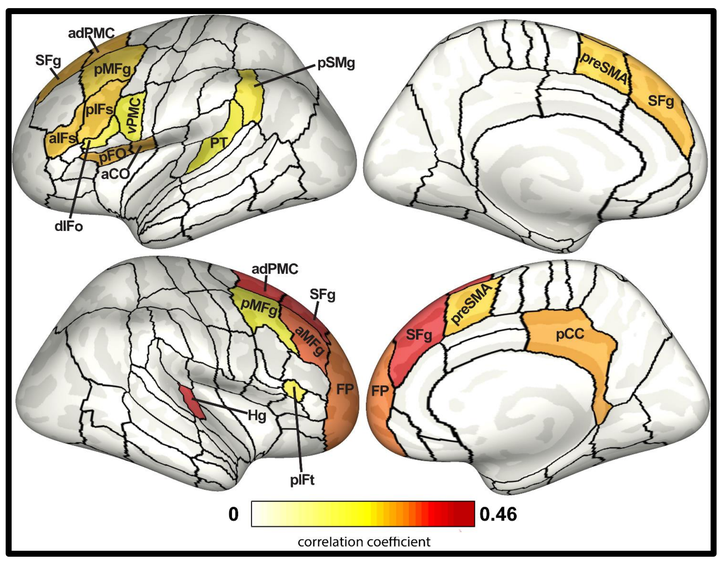


Forward digit span strongly involves proposed ***phonological input and output buffers***.

Backward Digit Span Subtest

Key ROIs predicting Backward Digit Span:

- Right superior frontal gyrus (SFg): r = .45, *p* = .001
- Right anterior dorsal premotor cortex: r = .42, *p* = .003

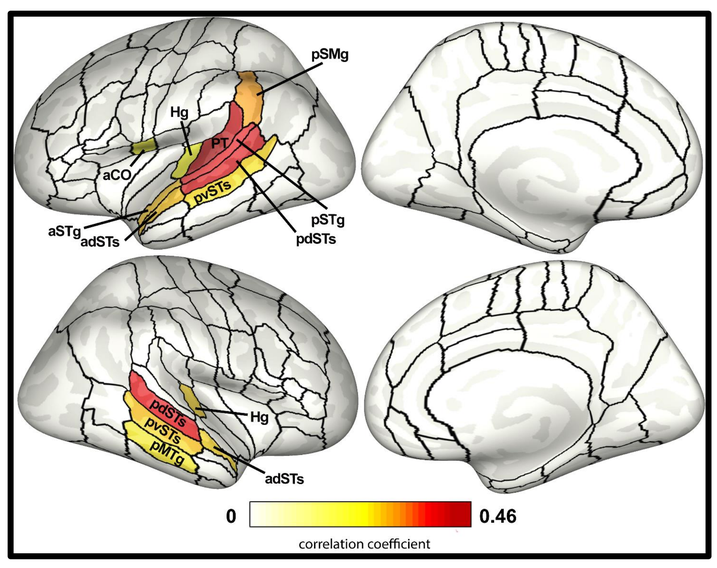


Backward digit span is more strongly correlated with ***frontal regions*** involved in ***attention and executive control***.

Sentence Repetition Subtest

Key ROIs predicting Sentence Repetition:

- Left PT: r = .48, *p* < .001
- Left posterior dorsal superior temporal sulcus (pdSTs): r = .46, *p* = .001
- Left posterior superior temporal gyrus (pSTG): r = .45, *p* = .001



Sentence repetition may be facilitated by ***syntactic and semantic knowledge*** which outweigh the contribution of the phonological output buffer to successful performance on the task.

Conclusions & Future Directions

Verbal repetition performance in PPA was significantly correlated with cortical thickness in hypothesized ***phonological input and output buffers*** in left pSMG and left pIFS, consistent with the GODIVA model.

Exploratory analysis revealed ***distinct neural correlates*** for the three analyzed PWM tasks, with implications for ***differential diagnosis*** of PPA.

Future Directions: Confirmation of the neural correlates of verbal repetition tasks in other PPA cohorts; using complementary structural and/or functional connectivity methods.

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