Speech Motor Planning Relies on Multiple Brain Areas: Evidence from Neurodegenerative Disease

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Introduction

- **Speech motor planning**: critical in speech production; takes place after phonological/phonetic encoding and before speech motor execution.
- **Apraxia of speech (AOS)**: a disorder that affects speech motor planning ➔ distorted speech sounds, substitutions, insertions, inconsistent errors, groping behaviors, and deviations in tone, stress, or rhythm.
  - ➢ Typically co-occurs with aphasia (higher-level language disorder) and dysarthria (motor execution disorder).

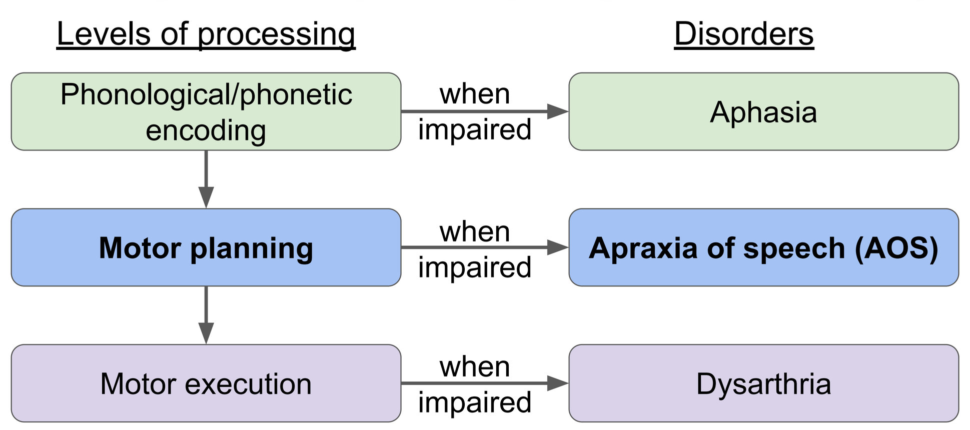

Figure 1. Processes and relevant disorders in speech production.

- However, there is **no consensus in the neural substrates** underlying speech motor planning.
  - ➢ Post-stroke AOS: associated with lesions to left precentral gyrus (PrCG) (Basilakos et al, 2015, 2018; Takakura et al., 2019).
  - ➢ Neurodegenerative disease: left premotor cortex and supplemental motor cortex (Utianski et al., 2018; Cordella et al., 2019).
- The specific **processes** involved in speech motor planning are often **underspecified**.
- This study: investigated AOS in individuals with Primary Progressive Aphasia (PPA, a neurodegenerative disorder affecting language), a less studied population.
  - ➢ Address issues specifically concerning the PPA phenotypes, evaluate if more diffuse damage profiles can provide additional insights into the nature of the speech planning processes

Research questions:

1. Which brain areas are uniquely associated with AOS in PPA?

2. What do the areas associated with AOS reveal about the specific processes that are impaired?

Methods

Participants: 34 PPA individuals (19 females; 12 lvPPA, 12 nfvPPA, 7 svPPA, 1 mixed, 2 unclassifiable)

Data:

- Behavioral data
  - ➢ **Oral picture naming**: Boston Naming Test (BNT; Williams et al., 1989)
  - ➢ **Single word repetition**: subtest 2 of Apraxia Battery for Adults (ABA2; Dabul, 2000)
    - ■ 20 triplets of words, such as "thick, thicken, thickening"
    - ■ Length effect scores (difference in total item scores between the longest and shortest words in each triplet)

Variable Mean (SD)	lvPPA (n = 12)	nfvPPA (n = 12)	svPPA (n = 7)
Age	66.75 (9.47)	67.58 (5.28)	65.14 (9.21)
Years of education	16.17 (2.89)	16.50 (2.43)	16.67 (1.03)
Years post onset	3.67 (2.45)	2.71 (1.64)	4.86 (3.13)
FTD-CDR	6.29 (3.17)	4.13 (3.16)	5.25 (3.08)

Table 1. Demographics of PPA participants.

- Speech language pathologist (SLP) ratings: for **expressive aphasia**, **AOS**, and **dysarthria**
  - ➢ Based on audio recordings of BNT, ABA2, and picture description
  - ➢ Using an in-house scale of 0-3 (0 = absent, 3 = severe)
- Neuroimaging: T1-weighted MPRAGE structural scans

Analysis 1: Neural underpinnings of speech and language disorders

- Whole-brain **voxel-based morphometry** (VBM) on the T1-weighted images using FSL-VBM (Douaud et al., 2007) ➔ identify voxels significantly correlated ($p < .05$) with each SLP ratings, controlling for the other two ratings
  - ➢ Correction for multiple comparison: permutation-based non-parametric testing using threshold-free cluster enhancement (TFCE)

Analysis 2: Relationship between volume of significant clusters and SLP ratings

- Multiple linear regression analysis ➔ test if each cluster of significant voxels accounted for unique variance in SLP ratings
  - ➢ SLP ratings ~ cluster 1 volume + cluster 2 volume + …

Analysis 3: Brain areas associated with length effect

- Multiple linear regression analysis ➔ evaluate if length effects were uniquely associated with specific brain areas
  - ➢ Length effect ~ cluster 1 volume + cluster 2 volume + …

Results

Analysis 1: Neural underpinnings of speech and language disorders

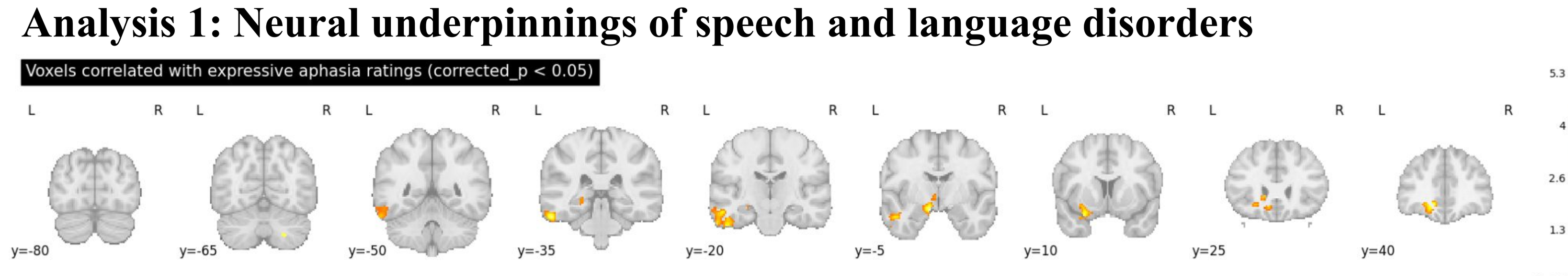

Figure 2. VBM results: Voxels significantly associated with expressive aphasia ratings.

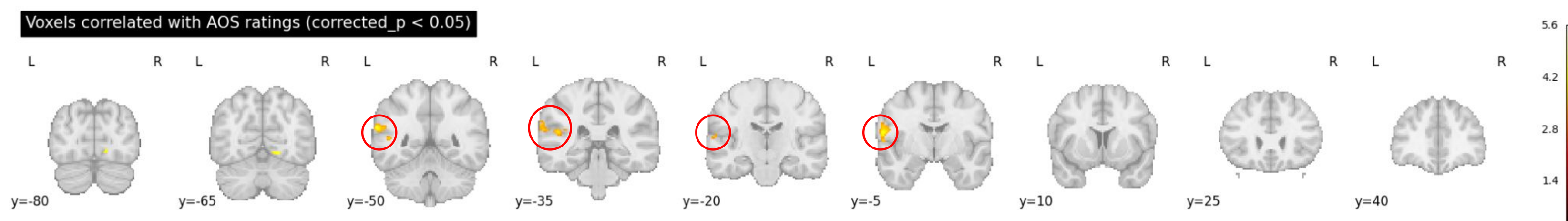

Figure 3. VBM results: Voxels significantly associated with AOS ratings.

		Size (mm3)	Center of Mass x	y	z
Expressive aphasia	cluster 1	18784	-38.2	-2.31	-18
	cluster 2	992	-25	-27.6	-9.77
AOS	cluster 1	2480	-56.2	-45.1	19.8
	cluster 2	2000	-60.1	-8.12	16.6
	cluster 3	896	14.4	-72.2	-5.82

Table 2. Clusters associated with expressive aphasia and AOS ratings.

- **Expressive aphasia**: associated with bilateral, left-lateralized cortical volumes in the temporal lobes.
- **Dysarthria:** no voxels associated with dysarthria ratings at $p < .05$, likely due to small sample size (ony 4 PPA participants with dysarthria diagnosis).
- **AOS:** associated with cortical volume in the **left PrCG**, postcentral gyrus (**PoCG**), supramarginal gyrus (**SMG**), and angular gyrus (**AG**).

Analysis 2: Relationship between volume of significant clusters and SLP ratings

- The sensorimotor PrCG/PoCG cluster ($p = 0.006$) and the parietal SMG/AG cluster ($p = 0.003$) both accounted for unique variance in AOS ratings, **suggesting** that **multiple processes** contribute to speech motor planning.

Analysis 3: Brain areas associated with length effect

- Length effect score (phonological working memory): associated with volume of the parietal cluster ($p = 0.003$) - **larger cortical volumes associated with smaller length effects**, but not with the sensorimotor cluster ($p = 0.598$).

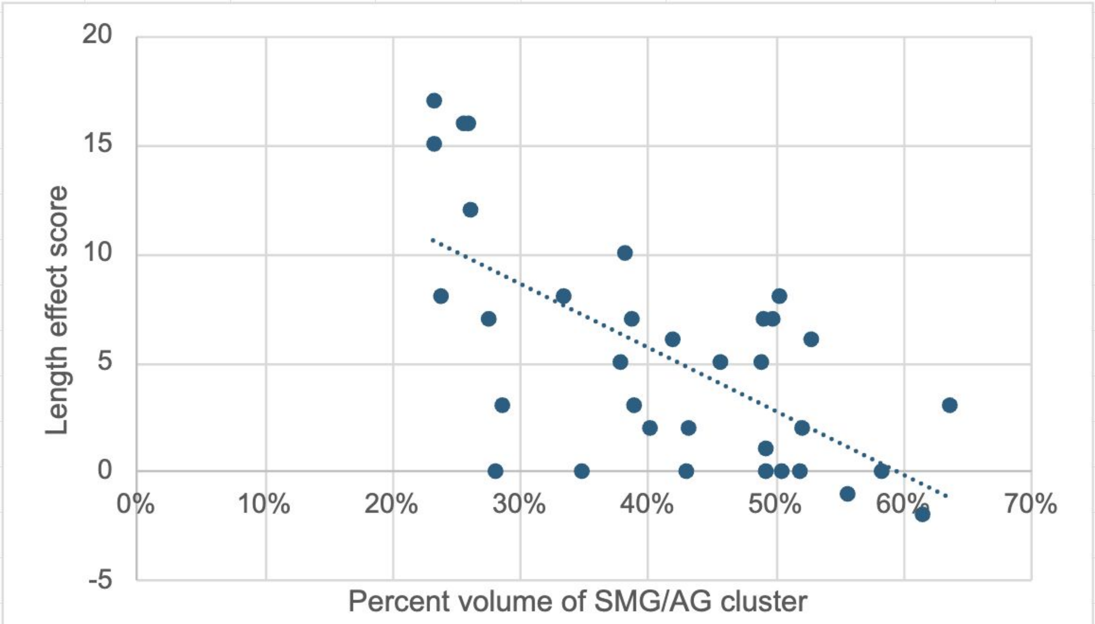

Figure 4. Volume of parietal SMG/AG cluster vs length effect scores.

Discussion

- AOS was significantly correlated with cortical volume in
  - ➢ left PrCG, the motor cortex.
  - ➢ left PoCG, the somatosensory cortex.
  - ➢ left SMG, associated with phonological WM.
  - ➢ left AG, associated with attentional control and serial order representation and processing.
  - ➢ The neural data indicates that speech motor planning consists of multiple dissociable sub-processes.
  - ➢ **Novel evidence of the role of SMG/AG in speech motor planning from PPA.**
- Phonological WM, as measured by length effect, was **uniquely** associated with the SMG/AG (and not sensorimotor areas).

Future directions

- Investigate the other processes that are involved in speech motor planning, in particular the one(s) supported by the sensorimotor cluster.
- Investigate whether if the phonological working memory involved in speech motor planning is input-/output-specific, using a picture naming task (output phonological WM) and a WM probe task (input phonological WM).

References

Basilakos, A., Rorden, C., Bonilha, L., Moser, D., & Fridriksson, J. (2015). Patterns of poststroke brain damage that predict speech production errors in apraxia of speech and aphasia dissociate. Stroke, 46(6), 1561-1566.

Basilakos, A., Smith, K. G., Fillmore, P., Fridriksson, J., & Fedorenko, E. (2018). Functional characterization of the human speech articulation network. Cerebral Cortex, 28(5), 1816-1830.

Cordella, C., Quimby, M., Touroutoglou, A., Brickhouse, M., Dickerson, B. C., & Green, J. R. (2019). Quantification of motor speech impairment and its anatomic basis in primary progressive aphasia. Neurology, 92(17), e1992-e2004.

Dabul, B. (2000). ABA-2: apraxia battery for adults. Austin, TX: Pro-ed.

Douaud, G., Smith, S., Jenkinson, M., Behrens, T., Johansen-Berg, H., Vickers, J., ... & James, A. (2007). Anatomically related grey and white matter abnormalities in adolescent-onset schizophrenia. Brain, 130(9), 2375-2386.

Guenther, F. H. (2016). Neural control of speech. Mit Press.

Takakura, Y., Otsuki, M., Sakai, S., Tajima, Y., Mito, Y., Ogata, A., ... & Nakagawa, Y. (2019). Sub-classification of apraxia of speech in patients with cerebrovascular and neurodegenerative diseases. Brain and cognition, 130, 1-10.

Utianski, R. L., Duffy, J. R., Clark, H. M., Strand, E. A., Boland, S. M., Machulda, M. M., ... & Josephs, K. A. (2018). Clinical progression in four cases of primary progressive apraxia of speech. American Journal of Speech-Language Pathology, 27(4), 1303-1318.

Williams, B. W., Mack, W., & Henderson, V. W. (1989). Boston naming test in Alzheimer's disease. Neuropsychologia, 27(8), 1073-1079.

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