

## **Phonological processing in primary progressive aphasia**

### Introduction

Primary progressive aphasia (PPA) is a debilitating condition wherein speech and language deteriorate as a result of neurodegenerative disease. Three variants of PPA are now recognized, each of which shows a unique constellation of speech-language deficits and pattern of underlying atrophy in the brain (Gorno-Tempini et al., 2011). The variants include a nonfluent/agrammatic type (nfvPPA), characterized by syntactic and motor speech deficits and fronto-insular atrophy in the left hemisphere. The semantic variant (svPPA) shows degradation of semantic knowledge in the context of anterior and inferior temporal lobe atrophy (left hemisphere greater than right). Finally, the more recently characterized logopenic variant (lvPPA) shows impairments in naming and repetition that are thought to be phonological in nature. This variant, associated with atrophy of temporoparietal regions in the left hemisphere, has also been referred to as the “phonological” variant of PPA due to observed deficits on tasks that require phonological storage (i.e., the “phonological loop”) and to the presence of phonological paraphasias in connected speech (Gorno-Tempini et al., 2008). Impaired phonological processing has been considered a unique feature of the logopenic variant of PPA, however, phonological skills have not been thoroughly characterized across the three variants.

Recent models of the functional neuroanatomy of language propose two pathways by which speech is processed in the brain (Hickok & Poeppel, 2007). A dorsal pathway involving temporoparietal and posterior frontal structures is thought to be involved in mapping phonological representations onto articulatory representations. A ventral pathway located in the middle and inferior temporal lobes is considered crucial for mapping phonological representations onto lexical-semantic representations. Both the dorsal and ventral streams emanate from a common cortical region in posterior, superior temporal cortex/sulcus that appears critical to the mental representation of phonology. We investigated phonological processing in PPA, with the goal of identifying whether patterns of performance in the different variants support this functional-anatomical framework. Based on our knowledge of the locus of anatomical damage in the subtypes of PPA, we hypothesized that patients with damage to dorsal route structures (nonfluent and logopenic variants) would show greater impairment on phonological processing tasks, whereas patients with damage to ventral route structures (semantic variant) would show relative preservation of phonological abilities.

### Methods

Thirty-three individuals with PPA (15 individuals with semantic variant, 11 individuals with logopenic variant, and seven individuals with nonfluent variant) and 15 normal controls were included in the study. PPA diagnosis by variant was reached by consensus, following a multi-disciplinary evaluation comprising language and neuropsychological testing, neurological examination, and structural neuroimaging. Each individual was administered a battery of

phonological tasks (Arizona Phonological Battery; Beeson, Rising, Kim, & Rapcsak, 2010; Rapcsak et al., 2009), including phoneme deletion, phoneme substitution, and sound blending in both words and pseudowords (Table 1). Additional assessments included a motor speech evaluation, designed to detect characteristics of apraxia of speech (AOS; Wertz et al., 1984), as well as forward digit span, as a measure of phonological working memory. A composite score representing phonological performance was examined across anatomical subgroups using analysis of variance (ANOVA) and analysis of covariance (ANCOVA). Initially, performance was analyzed with participants divided into those with damage to dorsal (nonfluent and logopenic variants of PPA) versus ventral (semantic variant) language pathways. Subsequently, the dorsal pathway group was subdivided into those with anterior (nonfluent) versus posterior (logopenic) perisylvian damage in order to explore the respective contributions of these neuroanatomical regions to phonological processing.

## Results

All participants were determined to be 100% correct on repetition of words up to three syllables in length, which confirmed sufficient speech production ability for the motor output demands of the phonological battery. Phonological battery performance in the PPA variants and normal controls is presented in Figure 1. Results of the ANOVA examining phonological composite scores across participants in dorsal versus ventral subgroups (and healthy controls) revealed a significant effect of group ( $F(2,44)=27.80, p<0.001$ ). Planned pairwise comparisons revealed no difference between patients with ventral damage and controls ( $p=0.09$ ). A significant difference was observed between dorsal pathway patients (logopenic and nonfluent variants combined) and controls ( $t(31)=-6.52, p<0.001$ ) and dorsal and ventral patients ( $t(30)=4.69, p<0.001$ ). These analyses were repeated with speech apraxia rating included as a covariate, revealing the same pattern of results.

In order to explore phonological performance of the two subgroups of patients with damage to the dorsal pathway, this group was further divided into nonfluent (with anterior damage) and logopenic (with posterior damage) patient groups and the above analyses repeated. The ANOVA again revealed a significant effect of group ( $F(3,43)=20.10, p<0.001$ ). Planned pairwise comparisons showed significant differences between nonfluent patients and controls ( $t(20)=-5.11, p<0.001$ ) and semantic variant patients ( $t(19)=-3.06, p<0.01$ ) as well as between logopenic patients and controls ( $t(24)=-7.62, p<0.001$ ) and semantic variant patients ( $t(23)=-5.21, p<0.001$ ). Nonfluent and logopenic patients were not significantly different ( $p=0.27$ ). When AOS rating was included in the analyses as a covariate, results were similar, with one notable exception: nonfluent patients were no longer significantly different from normal controls ( $p=0.06$ ) or semantic patients ( $p=0.38$ ).

Finally, a significant correlation was observed between phonological battery scores and digit span ( $r=.73, p<0.001$ ). Nonetheless, the difference between dorsal and ventral patient groups remained marginally significant when controlling for span ( $F(2,29)=20.52, p=0.05$ ), as did the difference between logopenic and semantic variant patients ( $F(2,22)=23.10, p=0.05$ ).

## Discussion

Imaging studies in PPA indicate that the three variants show selective breakdown of regions within the proposed dorsal (nonfluent and logopenic variants) and ventral (semantic variant) pathways involved in processing spoken language. Findings from our phonological battery confirm the dorsal (articulatory-phonological) versus ventral (lexical-semantic) stream distinction in a relatively large cohort of individuals with PPA. Patients with damage to the dorsal pathway showed phonological impairment relative to controls and patients with ventral pathway damage. In contrast, there was no observed difference between ventral pathway patients (i.e., those with semantic variant) and healthy controls. Despite a significant correlation between digit span and phonological battery scores in the patient group as a whole, there was a dorsal versus ventral group effect independent of span, suggesting that the phonological battery may capture some aspect of phonological processing above and beyond phonological working memory. Examination of performance by PPA variant revealed that, amongst dorsal pathway patients, the logopenic subgroup, with posterior perisylvian atrophy, demonstrated more profound impairment of phonological processing than the nonfluent subgroup, whose atrophy involves anterior perisylvian regions critical for converting phonological representations into motor output.

In summary, our results confirm a striking impairment of phonological processing in individuals with the logopenic variant of PPA, and thus the appropriateness of the term “phonological PPA” for this cohort. The contrast between the core phonological deficit in logopenic PPA and the sparing of phonological processing in semantic variant patients has implications for treatment in these groups. Whereas both groups exhibit anomia as a primary characteristic, the underlying cause (semantic versus phonological) likely differs in each. Future studies should address this issue by directly examining the relation between phonological task performance and other language measures, including naming and repetition skills, in semantic and logopenic variants of PPA.

## References

Beeson, P. M., Rising, K., Kim, E. S., & Rapcsak, S. Z. (2010). A treatment sequence for phonological alexia/agraphia. *Journal of Speech, Language and Hearing Research, 53*(2), 450-468.

Gorno-Tempini, M. L., Brambati, S. M., Ginex, V., Ogar, J., Dronkers, N. F., Marcone, A., ... & Miller, B. L. (2008). The logopenic/phonological variant of primary progressive aphasia. *Neurology, 71*(16), 1227-1234.

Gorno-Tempini, M. L., Hillis, A. E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S. F., ... & Grossman, M. (2011). Classification of primary progressive aphasia and its variants. *Neurology, 76*(11), 1006-1014.

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews Neuroscience, 8*(5), 393-402

Rapcsak, S. Z., Beeson, P. M., Henry, M. L., Leyden, A., Kim, E., Rising, K., ... & Cho,

H. (2009). Phonological dyslexia and dysgraphia: Cognitive mechanisms and neural substrates. *Cortex; a journal devoted to the study of the nervous system and behavior*, 45(5), 575-591.

Table 1. Sample tasks from the Arizona Phonological Battery

<i>Task</i>	<i>Example</i>
<b>Phoneme deletion</b> (n=10 words, 10 pseudowords)	Say “fat”...now take away “f” → “at” Say “zane”...now take away “z” → “ane”
<b>Phoneme substitution</b> (n=15 words, 15 pseudowords)	Say “mouth”...now change /th/ to /s/ → “mouse” Say “bazz”...now change /b/ to /d/ → “dazz”
<b>Phoneme blending</b> (n=10 words, 10 pseudowords)	Blend these sounds together /b/ /oi/ /l/ → “boil” /z/ /aI/ /p/ → “zipe”

Figure 1. Phonological battery performance by diagnostic group

