

Shalom K Henderson, Siddharth Ramanan, Matthew A Rouse, Thomas E Cope, Ajay D Halai, Karalyn E Patterson, James B Rowe, Matthew A Lambon Ralph, Impaired semantic control in the logopenic variant of primary progressive aphasia, *Brain Communications*, Volume 7, Issue 1, 2025,

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Abstract

We investigated semantic cognition in the logopenic variant of primary progressive aphasia, including (i) the status of verbal and non-verbal semantic performance; and (ii) whether the semantic deficit reflects impaired semantic control. Our *a priori* hypothesis that individuals with logopenic variant of primary progressive aphasia would exhibit semantic control impairments was motivated by the anatomical overlap between the temporoparietal atrophy typically associated with logopenic variant of primary progressive aphasia and lesions associated with post-stroke semantic aphasia and Wernicke's aphasia, which cause heteromodal semantic control impairments. We addressed the presence, type (semantic representation and semantic control; verbal and non-verbal), and progression of semantic deficits in logopenic variant of primary progressive aphasia. Since most people with logopenic variant of primary progressive aphasia have Alzheimer's disease pathology and are part of a broader multi-dimensional phenotype space encompassing Alzheimer's disease sub-types, we compared semantic performance in logopenic variant of primary progressive aphasia and typical amnesic Alzheimer's disease. Given the differences in lesion and atrophy patterns in semantic aphasia and Wernicke's aphasia versus semantic-dementia/semantic-variant primary progressive aphasia patients, our second aim was to examine atrophy patterns in people with logopenic variant of primary progressive aphasia and typical Alzheimer's disease compared to age-matched controls. Twenty-seven patients participated in the study. People were grouped into those meeting consensus criteria for logopenic variant of primary progressive aphasia ($N = 10$) and others who may have previously satisfied definitions of logopenic variant of primary progressive aphasia but had progressed with multi-domain cognitive impairments (herein referred to as 'logopenic variant of primary progressive aphasia+'; $N = 8$). People with typical amnesic Alzheimer's disease ($N = 9$) were relatively preserved across verbal and non-verbal semantic assessments. Logopenic variant of primary progressive aphasia patients were impaired on both verbal and non-verbal semantic tasks and their impairments showed the hallmark characteristics of a semantic control deficit. Logopenic variant of primary progressive aphasia and logopenic variant of primary progressive aphasia + patients showed effects of varying semantic control demands, positive cueing effects, and correlated performance between semantic and executive

tasks. Whole-brain voxel-based morphometry, comparing each of the patient groups to age-matched controls, revealed significantly reduced grey and white matter in the bilateral hippocampi and lateral temporal regions in typical Alzheimer's disease patients. The logopenic variant of primary progressive aphasia group exhibited an asymmetric pattern of reduced grey and white matter intensity in the language-dominant left hemisphere, including a significant portion of the lateral and medial temporal lobe. Logopenic variant of primary progressive aphasia + patients demonstrated reduced grey and white matter in the left temporal lobe extending sub-cortically, anteriorly and posteriorly, as well as right temporal involvement. Our findings could aid diagnostic sub-typing of primary progressive aphasia by adopting semantic control features and offer improved clinical characterization of logopenic variant of primary progressive aphasia in the trajectory of semantic decline.