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Title: Prosodic and Phonetic Subtypes of Primary Progressive Apraxia of Speech

Abstract (200 words): Primary progressive apraxia of speech (PPAOS) is a recently described neurodegenerative syndrome in which apraxia of speech is the sole and initial manifestation. Prior studies have identified hypometabolism, grey matter atrophy, and white matter tract degeneration in the frontal gyri, precentral cortex, and supplementary motor area (SMAs). In autopsy data, PPAOS is consistently associated with tau biochemistry. Recent clinical observations suggest that two clinically distinct types of PPAOS may exist. Phonetic PPAOS is characterized predominantly by sound distortions or distorted sound substitutions; Prosodic PPAOS is characterized predominantly by slow, segmented speech. In this study, demographic, clinical, and neuroimaging data (MRI, DTI, FDG-PET) of patients clinically classified as Phonetic or Prosodic PPAOS were analyzed to validate the subtypes and their anatomic correlates. The Phonetic type was dominated by a widespread process, with involvement of the SMAs, precentral gyrus, and insula. In contrast, the Prosodic type demonstrated more focal atrophy, hypometabolism, and reduced white matter tract integrity, with involvement of the SMA and right cerebellar peduncle. The findings provide converging evidence that differences in the reliably determined predominant clinical characteristics of AOS (predominant articulatory versus prosodic abnormalities) are associated with distinct patterns of cortical and subcortical involvement, independent of severity.