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To split or not to split: data-driven components along the PPAOS-PAA spectrum

It is unclear whether primary progressive apraxia of speech (PPAOS) and progressive agrammatic aphasia (PAA) represent the two ends of a clinical continuum or exist as distinct syndromic entities with specific pathological/ prognostic correlates. We aimed to characterize motor speech and grammar changes along the PPAOS-PAA spectrum and explore the existence of data-driven clinical clusters with etiological/prognostic value.

We included 98 participants presenting with a progressive motor speech impairment and/or agrammatism, of which 43 had a neuropathological diagnosis. Speech pathologists rated motor speech features indicative of dysarthria and AOS. Quantitative measures of expressive/receptive agrammatism were obtained and compared with healthy controls. Baseline and longitudinal disease severity was assessed with the Clinical Dementia Rating sum-of-boxes (CDR-SB). We explored the clustering tendency and used principal component analysis to extract data-driven components. The longitudinal CDR-SB change was estimated with linear mixed-effects models.

Ninety-one participants fitted previously-reported clinical profiles (18 PPAOS, 4 PAA, and 69 AOS+agrammatism), while 7 remained unclassifiable. None of the baseline clinical features discriminated between FTLD subgroups. The Hopkins statistic ruled out the existence of syndromic clusters in the whole sample. Three data-driven components explained 71% of the variance ([i]severity-agrammatism, [ii]AOS, and [iii]dysarthria). The component characterized by prominent dysarthria was more specific to patients with Progressive Supranuclear Palsy. Baseline CDR-SB, expressive agrammatism, and executive dysfunction predicted a faster CDR-SB increase.

Our results suggest that the PPAOS-PAA spectrum represents a clinical continuum. The term "progressive nonfluent motor speech and language disorders" could be used to lump these speech/language phenotypes strongly associated with FTLD.