Mapping characteristic speech-language features of the nonfluent/agrammatic variant primary progressive aphasia to their neural substrates

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The nonfluent/agrammatic variant of primary progressive aphasia (nfvPPA) is characterized by impaired motor speech (mainly apraxia of speech, AoS) and/or expressive agrammatism. However, many nfvPPA patients also exhibit dysarthria and/or receptive agrammatism, leading to substantial phenotypic variation within the speech-language domain across individuals and time.

By leveraging a large cohort of nfvPPA patients ($n = 104$), we sought to uncover where in the brain the degree of tissue loss is associated with variability in the presence and severity of AoS, dysarthria, expressive agrammatism, or receptive agrammatism.

First, we show that the neural correlates of AoS and expressive agrammatism lie side by side in the left posterior inferior frontal lobe. Second, we highlight (i) that dysarthria, but not AoS, is significantly influenced by tissue loss in right motor-speech regions and (ii) that dysarthria and AoS map onto dorsally versus ventrally located left motor-speech regions, respectively. Third, we confirm that, within the grammar network, left frontal tissue loss in preferentially involved in expressive agrammatism and left temporal tissue loss in receptive agrammatism.

This study isolated the neural substrates of these four characteristic clinical features within a single cohort of nfvPPA patients. Taken together, our findings not only help to define the nodes in large-scale neural networks that are likely to contribute to the selective breakdown of core speech-language functions following the onset and progression of neurodegeneration, but also encourage a unifying view where nfvPPA may be better conceptualized as a spectrum of speech-language phenotypes that are closely linked by the underlying neuroanatomy.

Conflicts of interest

N/A