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Thursday

Identifying white matter signatures of cognitive heterogeneity in primary progressive aphasia: a data-driven transdiagnostic approach

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State of the art: Clinical variants of primary progressive aphasia (PPA) are diagnosed based on unique patterns of language deficits and corresponding grey-matter changes. Mounting evidence indicates overlapping profiles of language performance and multi-domain non-linguistic cognitive difficulties between variants, and concurrent white-matter changes. An understanding of the relationship between these three variables is important for improved PPA characterisation. Accordingly, we adopted a data-driven transdiagnostic approach to chart language, cognitive changes and their associations with white-matter degeneration across PPA variants, irrespective of diagnostic labels.
Methodology: Forty-seven PPA patients (13 semantic, 15 non-fluent and 19 logopenic variant) underwent assessment of general cognition, errors on language performance, and diffusion magnetic resonance imaging to index whole-brain white-matter changes. All data were independently entered into varimax principal component (PC) analyses (for language/cognition data) and its sparse counterpart (for diffusion data) to derive orthogonal factors of test performance and white-matter changes. Across variants, associations between cognition and white-matter PCs were examined using multiple regressions.
Results: Four cognitive PCs emerged: general cognition, semantics, working memory, and phonology/motor-speech. Performance patterns on the latter three PCs were in keeping with each variant's characteristic profile. General cognitive changes were most marked in logopenic PPA. Regardless of clinical diagnosis, white-matter disconnections between left temporal and fronto-parietal cortices, and between bilateral temporo-parietal and fronto-temporal regions explained linguistic and cognitive heterogeneity, respectively.
Conclusion: Pervasive cognitive heterogeneity in PPA closely relates to structural disconnections of regions within and beyond the language network, highlighting a new dimension of brain-behaviour dysfunction in these syndromes.

Conflicts of interest

None