Primary Progressive Aphasia as a model to study the neurobiology of language

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Primary Progressive Aphasia (PPA) is a clinical syndrome characterized by progressive loss of verbal communication abilities resulting from degeneration of the language networks in the brain. The first cases of a disorder similar to PPA were described by Pick in Pick (1892). In their seminal paper of 1982, Mesulam and colleagues produced the modern definition of PPA (Mesulam, 1982). Research conducted in the past decade has shown that PPA is an heterogeneous clinical and pathological entity. Three main clinical variants have been described (Gorno-Tempini et al., 2011), each associated with a specific pattern of speech and language deficits and anatomical changes, and a different probability of frontotemporal lobar degeneration-type (FTLD) or Alzheimer's pathology. Therefore, PPA offers a valuable model for the study, not only of cognitive and behavioral aspects of language, but also of the underlying molecular biology of the brain networks sustaining language.

This special issue of Brian and Language includes eight papers by prominent PPA investigators reporting on current clinical and research topics, ranging from pathological features to novel rehabilitative approaches. Rogalsky et al. discuss susceptibility factors and identify learning disabilities as the most likely determinants of the selective vulnerability of the language network to degeneration in PPA. Josephs et al., Machulda et al. and Rohrer et al., concentrate on lvPPA, the least studied presentation characterized by phonological impairment, left temporo-parietal damage and most often AD pathology. Machulda and colleagues describe a possible clinical variant of lvPPA with milder aphasia and slower longitudinal course. The same research group reports a quantitative study of imaging and pathological changes showing a greater concentration of neurofibrillary tangles in temporoparietal cortex in lvPPA than that found in classic Alzheimer's disease. Rohrer et al. report the first longitudinal neuroimaging and cognitive study of lvPPA showing spreading of disease in the left hemisphere and less severely in the corresponding network in the right.

Agosta et al. report on relatively selective dorsal and ventral white matter changes in the PPA variants, emphasizing the usefulness of the DTI MRI technique in PPA. Grossman et al. instead concentrate on nfvPPA, the variant characterized by speech and grammar deficits, left inferior frontal atrophy and most often tau pathology. They combine multimodal neuroimaging and neuropsychological data and identify three large-scale frontal networks responsible for different aspects of fluency. Race et al. focus on anomia in the whole PPA

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spectrum and show that volume in left posterior inferior temporal cortex correlates with word-retrieval deficits across tasks, providing further evidence for the role of this region in multimodal language processing. Finally, Henry and colleagues report two cases that support the efficacy of rehabilitation of lexical-retrieval deficits in PPA. Their successful approach exploits specific spared cognitive functions in different PPA variant to preserve targeted skills in the face of disease progression.

The papers included in this special issue attest to the remarkable progress made in the field of PPA research in the past three decades, and further establish this disorder as a viable model to study the neurobiology of language. The spirit of cooperation that inspired this collective effort highlights how the integration of different approaches is central to scientific progress.

References

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