Primary progressive aphasia (PPA), characterized by deterioration in language for at least 2 years before the onset of other cognitive deficits, has been widely recognized as a distinct clinical entity since Mesulam’s description in 1982.\(^1\) However, as well characterized in the article, ‘Primary Progressive Aphasia: A Comparative Study of Progressive Nonfluent Aphasia and Semantic Dementia’ in this issue, PPA exists in two forms. The first, progressive nonfluent aphasia (PNFA) is often compared to Broca’s aphasia, since patients often have effortful articulation, agrammatic sentence pro-
duction, and relatively intact comprehension. Patients with both PNFA and Broca’s aphasia due to stroke frequently have more difficulty naming verbs than nouns. Likewise, semantic dementia (SD) is often compared to Wernicke’s aphasia, since both are characterized by fluent, grammatical, and well-articulated speech with little content, impaired comprehension, and disproportionate difficulty naming nouns relative to verbs. As demonstrated with voxel-based morphometry, the brain regions affected in PNFA generally lie within the vascular territory typically damaged in Broca’s aphasia, the left inferior frontal gyrus and anterior insula. Semantic dementia, like Wernicke’s aphasia, often reflects atrophy in the left temporal lobe, although the abnormality is generally more anterior and inferior in SD.

However, there are important differences from the vascular syndromes of Broca’s and Wernicke’s aphasia. Individuals with PNFA often have relatively spared spelling of both verbs and nouns. Such a pattern is extraordinarily rare in Broca’s aphasia. The dissociation between written language (intact) and other aspects of communication – speech articulation, oral naming of verbs, and grammatical sentence production (which are impaired) may provide insights into brain/language relationships. For example, brain regions that are spared in PNFA but damaged in Broca’s aphasia after stroke, are good candidates for the neural regions subserving written naming.

In the same vein, there are crucial differences between SD and Wernicke’s aphasia. Most notably, patients with SD typically have associative agnosia – impaired access to the meanings of objects – not just the names of objects. They often use objects inappropriately, despite normal visual perception. This deficit has not been described in Wernicke’s aphasia caused by unilateral stroke. Identifying areas of the brain that are dysfunctional in SD but not in Wernicke’s aphasia would provide clues as to the areas responsible for object meaning. To illustrate, SD is generally associated with atrophy in temporal areas that are inferior and anterior to Wernicke’s area, and more bilateral. Thus, bilateral inferior and anterior temporal cortex may be crucially involved in accessing the meanings of objects and their associations.

Thus PPA and other focal dementias provide the opportunity to investigate the functions of brain regions that are not often damaged by stroke. However, progress in this domain has been limited, largely because criteria for classification are insufficiently objective and reliable to ensure that investigators worldwide classify patients the same way. For example, the classification of PNFA requires agrammatism and/or impaired articulation for some authors but not others. This dissonance is unsurprising, given that speech ‘fluency’ is a multidimensional characteristic that encompasses parameters of melody, phrase length, syntax, articulatory agility, and rate of speech. One patient might be fluent along one dimension and nonfluent along another. This problem of classification in nontrivial, since different types of PPA may have different etiologies, but such a clinicopathological relationship has been obscured by different criteria for classification across centers. Studies that carefully describe characteristics of aphasia underlying classification, such as the study in this issue, represent an important first step in forming a set of criteria for distinguishing various types of PPA with high interjudge reliability. Achieving this goal is essential for future multi-center clinical trials of treatment for PPA.

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