Consensus classification of posterior cortical atrophy

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http://dx.doi.org/10.1016/j.jalz.2017.01.014
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1. Introduction

The term posterior cortical atrophy (PCA) was coined by D. Frank Benson and colleagues to describe a series of patients with early visual dysfunction in the setting of neurodegeneration of posterior cortical regions [1] (Fig. 1). The PCA syndrome aligned with several other reports of patients with similar progressive loss of higher visual function (e.g., [2–12]). PCA typically presents in the mid-50s or early 60s with a variety of unusual visuoperceptual symptoms, such as diminished ability to interpret, locate, or reach for objects under visual guidance; deficits in numeracy, literacy, and praxis may also be apparent. Although episodic memory and insight are initially relatively preserved, progression of PCA ultimately leads to a more diffuse pattern of cognitive dysfunction.

Several single-center groups of researchers have proposed diagnostic criteria for the syndrome [13,14] or detailed inclusion criteria for individual studies (e.g., [15–17]). PCA has also been recognized and described in consensus criteria for typical and atypical Alzheimer’s disease [18,19]. These existing criteria have reasonable consistency and have proved useful in many clinical and research contexts.

However, the extant detailed descriptions of PCA are based on clinical experience at single centers and have not been deliberated or validated more widely. Present-day PCA criteria were also formulated before the development of Alzheimer’s disease (AD) pathophysiological biomarkers, and although recent AD criteria include PCA, the clinical phenotype is not described in detail and such criteria naturally do not encompass individuals with the PCA syndrome who are negative for AD pathophysiological biomarkers. Some inconsistencies exist among the core features described, with the Tang-Wai but not Mendez criteria excluding individuals with early Parkinsonism or hallucinations, while Mendez but not Tang-Wai stipulates the relative preservation of verbal fluency [13,14]. Such inconsistencies are mirrored explicitly or implicitly in the application of terminology, with the term PCA sometimes being used as a descriptive clinical (syndrome level) term and sometimes as a diagnostic (disease level) label. For example, some researchers consider PCA primarily or solely as an atypical form of AD (the “visual variant of AD,” e.g., [20]), whereas others cite neuropathological evidence demonstrating that multiple pathologies can underlie the PCA syndrome (e.g., [15]). Inconsistency of terminology and usage likely reflects in part the interests or requirements of different investigators or research contexts. For example, syndromic classification is likely to be entirely appropriate for studies exploring behavioral interventions, whereas clinical trials of disease-specific pharmacological agents may additionally require consideration of the underlying molecular pathology. In the absence of criteria that clearly reflect this potential diversity of use, it remains unclear whether individuals with PCA should be included or excluded from conventional clinical trials for AD (e.g., owing to the potential unsuitability of the associated interventions, biomarkers, and/or outcome measures). Consequently, individuals...
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