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Research report

Executive dysfunction contributes to verbal encoding and retrieval deficits in posterior cortical atrophy

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ABSTRACT

Posterior Cortical Atrophy (PCA) is a neurodegenerative syndrome that typically presents with predominant visual and spatial impairments. The early diagnostic criteria specify a relative sparing of functioning in other cognitive domains, including executive functions, language, and episodic memory, yet little is known of the cognitive profile of PCA as the disease progresses. Studies of healthy adults and other posterior cortical lesion patients implicate posterior parietal and temporal regions in executive functions of working memory and verbal fluency, both of which may impact episodic memory. Relatively little has been reported about these cognitive functions in PCA, and to our knowledge there has not yet been a study of the impact of such deficits on memory function in PCA. We sought to examine PCA patients' performance on tests of executive function and the associations to verbal episodic memory encoding, storage, and delayed recall. Nineteen individuals with PCA underwent neuropsychological and neuroimaging evaluations as part of a comprehensive clinical assessment. We developed a novel consensus rating method—the Neuropsychological Assessment Rating (NAR) scale—to grade the severity of test performance impairments in selected cognitive domains and subdomains. Hypothesis-driven analyses demonstrated relative deficits in working memory and lexical-semantic retrieval. Preliminary analyses suggested associations between both deficits and atrophy in the left-hemisphere inferior parietal lobule. These executive deficits were also associated with impairments in verbal encoding and delayed recall, but not with recognition discriminability. We conclude that deficits in verbal executive functions impact verbal episodic memory in PCA. Our findings also support theories emphasizing the role of the posterior parietal cortex in supporting executive and lexical-semantic contributions to verbal episodic memory.

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1. Introduction

Posterior cortical atrophy (PCA) is a focal neurodegenerative syndrome that primarily affects the parietal cortex, with or without involvement of occipital or posterior temporal cortex. Although PCA may infrequently arise due to non-Alzheimer's disease (AD) pathologies (Mitchell et al., 2016), it is more commonly thought of as an atypical or "visual variant" of AD (Borruat, 2013; Kaeser, Ghika, & Borruat, 2015; Levine, Lee, & Fisher, 1993). Patients with PCA typically present with early visual/spatial dysfunction due to neurodegeneration in these posterior cortical regions, and exhibit a variety of visual and non-visual signs referable to posterior cortices including diminished ability to identify or reach for objects, deficits in numeracy, literacy, and praxis, and other elements of Balint's and Gerstmann's syndromes as initially described by Benson and colleagues (Benson, Davis, & Snyder, 1988). Current diagnostic criteria propose that executive functions, language, episodic memory, and comportment/insight are relatively preserved in the earlier stages of illness, although PCA usually evolves toward a multi-domain cognitive-behavioral-motor dementia syndrome (Crutch et al., 2017). We are just beginning to develop a framework for understanding cognitive dysfunction outside of the visuospatial domain as PCA progresses.

In clinical neuropsychological or neurological assessment, executive dysfunction is commonly attributed to frontal lobes or frontostriatal circuit damage. Yet a growing body of cognitive and imaging neuroscience literature has built a compelling case for the existence of large-scale distributed brain networks that subserve executive functions, including not only frontal cortical and striatal regions but also lateral and medial parietal cortical regions (Corbetta & Shulman, 2002; Daffner & Willment, 2014; Dosenbach et al., 2006; Margulies et al., 2009; Vincent, Kahn, Snyder, Raichle, & Buckner, 2008). Specifically, key nodes of the dorsal attention network (DAN) and frontoparietal network (FPN) include regions of the superior and inferior parietal lobules (SPL and IPL), and intraparietal sulcus (IPS). The SPL and IPL have been implicated in directing responses to goal-appropriate stimuli via top-down control of attention (Corbetta & Shulman, 2002; Fox et al., 2005; Vincent et al., 2008), and strategic memory retrieval efforts (Cabeza, 2008), while regions of the IPL/IPS have also been specifically associated with supporting working memory tasks of "mental manipulation" (Champod & Petrides, 2007, 2010), a cognitive ability that plays a critical role in episodic memory encoding (Buchsbaum & D'Esposito, 2008; Wolk, Dickerson, & Alzheimer's Disease Neuroimaging, 2011). Activity within the IPL has been associated more directly with successful learning when encoding tasks involve memory search and retrieval as an opportunity for deeper encoding (Karpicke & Roediger, 2008), as is the case with many verbal list learning tests. In addition, the central dorsal precuneus is viewed by some investigators as a key node in the frontoparietal executive control network based on its connectivity pattern (Margulies et al., 2009). These observations raise the possibility that, when lateral and medial parietal cortical regions undergo neurodegeneration in PCA, critical components of the large-scale networks subserving complex attention and executive function are likely to be affected, leading to deficits in these functions that, in turn, impact memory encoding and retrieval. In contrast, memory storage loss seen in temporolimbic amnesias, such as typical AD, would not be expected.

Circumscribed cognitive impairment outside of the visuospatial domain has been described previously in a few studies of patients with PCA. Recent work has called attention to the frequency of impairment on memory tests in patients who otherwise meet diagnostic criteria for PCA (Ahmed et al., 2016). In a single case study of a PCA patient, deficits in autobiographical memory were reported, and thought to be associated with hypoperfusion in the precuneus and parahippocampal gyrus (Gardini et al., 2011). Deficits in episodic memory were recently linked with atrophy and tau deposition in the lateral parietal cortex in some PCA patients (Bejanin et al., 2017), while executive function deficits specific to controlled lexical retrieval processes (e.g., verbal fluency tasks) and/or length-dependent auditory-verbal working memory (e.g., reverse digit span tasks) have also been described in the literature (Crutch, Lehmann, Warren, & Rohrer, 2013; Magnin et al., 2013; Mitchell et al., 2016). Consistent with these findings in PCA, studies of other posterior cortical lesion patients have also suggested involvement of posterior parietal and temporal regions in executive functions of working memory (Berryhill & Olson, 2008; Koenigs, Barbey, Postle, & Grafman, 2009) and verbal fluency (Abraham, Beudt, Ott, & Yves von Cramon, 2012).

To our knowledge there are no studies directly examining the association between executive dysfunction in PCA and episodic memory test performance. We believe this is a particularly important topic to clarify, since episodic memory in PCA is currently conceptualized as a relatively spared domain. Our clinical observations of patients reinforce this idea, since many PCA patients are capable of discussing richly detailed memories of their own recent life or of current events, in contrast to patients with amnesic syndromes. Yet many PCA patients struggle to perform formal verbal memory tasks in the clinic (e.g., list learning). We undertook the present study of patients in our PCA cohort to test the hypotheses that (1) verbal executive function deficits are a common feature of PCA and have a neuroanatomical basis in the lateral parietal cortex, and (2) these executive deficits impact performance on verbal encoding and delayed recall in episodic memory tasks, but do not impact the recognition discriminability of previously learned information. We tested these hypotheses by examining neuropsychological performance in subdomains of attention/executive function and language, relating this performance to cortical thickness, and finally, examining the relationship of executive functions to verbal memory stages of encoding, delayed recall, and recognition discriminability.

2. Methods

2.1. Participant characteristics

Nineteen individuals (16 females; mean age of 63 years, age range of 52–81 years, all were Caucasian) were included in