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The relationship between executive function and verbal memory in Parkinson's disease

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Abstract

A growing body of evidence suggests that the various cognitive symptoms found in Parkinson's disease (PD) are secondary to executive dysfunction. Studies addressing this possibility for memory impairment specifically have not included measures of working memory nor have they ruled-out potential mediating variables such as overall level of cognitive impairment or depression. The purpose of this study was to include measures of these variables in determining the relationship between multiple aspects of executive function and delayed verbal recall in 32 idiopathic PD patients. Results were consistent with the original hypothesis and further suggest that working memory is a key factor in recall memory and may mediate the relationship between other executive measures and recall in PD.

Keywords: Parkinson's disease; Working memory; Executive function; Verbal memory

1. Introduction

In addition to prominent motor symptoms, Parkinson's disease (PD) patients often exhibit cognitive difficulties involving executive function, complex attention, verbal fluency, visuospatial function, and memory (Lezak, 1995). The memory dysfunction of PD has received attention because of its utility in differential diagnosis (Benson, 1983a, 1983b; Bondi, Salmon, & Kaszniak, 1996). That is, PD patients' poor performance on free recall tasks but near normal performance on recognition and cued recall tasks is in contrast to the poor performance of Alzheimer's Disease patients on both types of tasks (Lezak, 1995). Based on this pattern of performance, the memory impairment associated with PD has been attributed to retrieval difficulty rather than encoding problems; ability to remember after the provision of cues suggests that material was successfully encoded into memory to some degree. Other pathological cognitive processes have been implicated, however. Because PD patients exhibit better performance on delayed memory tasks than immediate memory tasks, both slowed processing speed (i.e., bradyphrenia) or "cognitive akinesia" may also contribute to PD-related memory problems (Sagar, Sullivan, Gabrieli, Corkin, & Growdon, 1988; Taylor, Saint-Cyr, & Lang, 1986, 1990). In the case of bradyphrenia, PD patients benefit from the extra time provided in the delay period because they take longer to consolidate information. In the case of cognitive akinesia, patients benefit from additional time due to difficulty initiating the encoding process. In either case, the apparent recovery of memory following a delay argues against an independent memory problem in PD (Taylor & Saint-Cyr, 1992, 1995) and suggests that memory disturbance is secondary to some other cognitive dysfunction.

One possibility is that executive dysfunction is the cause of PD patients' memory problems (Cooper, Sagar, & Sullivan, 1993; Taylor et al., 1990). Executive function

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is a broad category of cognition associated with the frontal lobes. It encompasses the "highest order of cognitive abilities" (D'Esposito & Grossman, 1996), including: inhibition, abstraction, aspects of attention, cognitive flexibility, reasoning, problem solving, planning, sequencing, working memory, modulation of ongoing activity, and simultaneous operation of multiple cognitive processes, among other things (Baddeley, 1986; Owen, Sahakian, & Robbins, 1998; Smith & Jonides, 1999; Stern, 1987).

Executive dysfunction has long been implicated in PD (Dalrymple-Alford, Kalders, Jones, & Watson, 1994). Early in the course of the illness, prior to medical management, cognitive symptoms are predominantly "frontal like," (Owen et al., 1998) and involve set shifting (Owen et al., 1992; Richards, Cote, & Stern, 1993; Tamaru, 1997), planning, problem solving (Brown, Schneider, & Lidsky, 1997), organization, source memory, and sensitivity to interference (Taylor et al., 1990). After the initiation of levodopa (L-dopa) therapy, set-shifting deficits may resolve (Tamaru, 1997). Similarly, L-dopa withdrawal in chronically treated patients selectively decreases performance on executive tasks (Taylor & Saint-Cyr, 1995). Furthermore, surgical interventions that target the pallidum to treat PD motor symptomatology can create significant executive dysfunction (e.g., Dujardin, Krystkowiak, Defebvre, Blond, & Destee, 2000). Also, PD patients experience difficulty with specific aspects of memory associated with frontal lobe pathology, such as recency discrimination (Cooper et al., 1993; Fischer et al., 1990; Sagar et al., 1988; Sullivan & Sagar, 1989) and source memory (Taylor et al., 1990) further strengthening the link between executive function and memory in PD.

The neuropathology of PD, involving a loss of dopaminergic innervation and changes in neuronal activity in the basal ganglia circuitry, supports a primary role for executive dysfunction in memory. There is an intimate relationship between the basal ganglia and the frontal lobes. In fact, basal ganglia output selectively targets the frontal cortex (Owen et al., 1998; Taylor & Saint-Cyr, 1992) and dopamine levels decline in the frontal lobes as well as the striatum in PD (Scatton, Javoy-Agid, Rouquier, Dubois, & Agid, 1983). Plus, the greatest loss of dopamine in the caudate nucleus occurs in that area heavily connected to the dorsolateral prefrontal cortex (DLPFC; Owen et al., 1998). The caudate is a component of the basal ganglia implicated in cognitive function.

There is evidence for a significant relationship between executive function and memory in PD (Bondi, Kaszniak, Bayles, & Vance, 1993; Cooper et al., 1993; Pillon, Deweer, Agid, & Dubois, 1993). The clearest is provided by Bondi et al. (1993) who found that only after executive function was held constant statistically (i.e., through analysis of covariance) was the memory of non-demented PD patients similar to that of controls. Patients' performance on executive tasks remained worse than controls even after memory and visuoperceptual function were covaried. There are reasons to suspect the apparent association is spurious, however, such as evidence that memory and executive dysfunction are dissociable (Mohr et al., 1990; Owen et al., 1992) and load on different factors (Paolo, Tröster, Axelrod, & Koller, 1995), PD medications differentially affect memory and executive task performance, little variance in memory performance is accounted for by executive function, and significant correlations between memory and executive function may be mediated by a third variable such as severity of overall cognitive impairment (Tröster & Fields, 1995).

Working memory is an aspect of executive function (D'Esposito & Grossman, 1996; Owen et al., 1998) not included in previous studies addressing the relationship between executive function and memory. Working memory involves the active manipulation of information in a temporary store, thus including processes necessary for other cognitive tasks (Baddeley, 1986, 1992, 1998; Dalrymple-Alford et al., 1994; Smith & Jonides, 1999). Deficits on working memory tasks are common in PD (Brown et al., 1997; Dalrymple-Alford et al., 1994; Fournet, Moreaud, Roulin, Naegele, & Pellat, 2000; Owen et al., 1998). For example, Higginson et al. (2001) found that on the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III; Wechsler, 1997a) PD patients' performance on a working memory subtest was among the lowest and most variable. Thus, it appears reasonable to suspect that working memory processes may be a cause of PD patients' memory problems (Cooper, Sagar, Jordan, Harvey, & Sullivan, 1991).

The purpose of this study is to address the relationship between verbal working memory and verbal memory (i.e., recall) in PD. To avoid confusion between "working memory" and "memory," we will refer to the specific aspect of memory addressed here, delayed free recall. It is hypothesized that working memory will be predictive of recall, supporting the contention that memory difficulties in PD are secondary to components of executive dysfunction.

2. Method

2.1. Participants

Thirty-two (21 male and 11 female) idiopathic PD patients who were potential candidates for surgical intervention due to medically-refractory symptomatology (i.e., significant on/off fluctuations and dyskinesia) underwent neuropsychological assessment as part of their presurgical evaluation. Patients were diagnosed by a board-certified neurologist (V.L.W.) and excluded from