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**TEMPORAL MEMORY AND EXECUTIVE FUNCTIONS
IN HIGH-FUNCTIONING PARKINSONIAN PATIENTS**
by
BRIGITTE N. PATRY

A thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfillment of
the requirements for the degree of Master of Arts

Department of Psychology

Carleton University
Ottawa, Ontario
November, 1998
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acceptance of the thesis

**“TEMPORAL MEMORY AND EXECUTIVE FUNCTIONS
IN HIGH-FUNCTIONING PARKINSONIAN PATIENTS”**

submitted by **Brigitte N. Patry**
in partial fulfillment of the requirements for
the degree of Master of Arts

Chair

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Thesis Supervisor

CARLETON UNIVERSITY

November, 1998

Abstract

Considerable evidence suggests that nondemented patients with Parkinson's disease (PD) exhibit deficits in temporal memory and executive ability, reflective perhaps of compromise to the functional integrity of the frontal lobes. An investigation of temporal memory and executive skills in high-functioning PD patients, who are least likely to exhibit deficits in this arena, sought to clarify the issue. This study also investigated the relationship between deficits of temporal memory and cognitive sequencing. Twenty nondemented outpatients with PD and 20 healthy volunteers, 50 years or older, with a university degree and/or a professional work history were recruited. The tests administered assessed executive functions, temporal memory, episodic memory, and vocabulary. Adequate performance of patients on cognitive sequencing tests does not support the hypothesis that poor sequencing skills account for temporal memory deficits. Such deficits were observed on only one of three tests. Furthermore, the lack of group differences on most tests assumed to tap dorsolateral prefrontal cortex function suggests that the functional integrity of this region is relatively preserved in this subpopulation of PD patients. Alternatively, the tests may be relatively insensitive to subtle deficits in these patients.

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List of Text Abbreviations

CALT	Conditional Associative Learning Test
DA	dopamine
DLP	dorsolateral prefrontal
DLPFC	dorsolateral prefrontal cortex
GDS	Geriatric Depression Scale
LTM	long-term memory
MMSE	Mini-Mental State Examination
MQ	memory quotient
PFC	prefrontal cortex
STM	short-term memory
UPDRS	Unified Parkinson's Disease Rating Scale
VTA	ventral tegmental area
WAIS-R	Wechsler Adult Intelligence Scale-Revised
WCST	Wisconsin Card Sorting Test
WMS-R	Wechsler Memory Scale-Revised

Introduction

Motor and Cognitive Dysfunction in Parkinson's Disease

Parkinson's disease (PD) was originally conceived as a disorder of only the motor system. It was first identified in 1817 by James Parkinson, who attested to the sole motor dysfunction observed in patients with this illness in the absence of intellectual and cognitive decrements (p. B).

However, in the second half of the twentieth century, several studies began to report alterations in the cognitive functions of patients with idiopathic PD (e.g. Loranger, Goodell, McDowell, Lee, & Sweet, 1972; Reitan & Boll, 1971; Warbuton, 1967) and such changes are now accepted as an integral part of the clinical presentation of the illness. Nevertheless, the prevalence, nature, and neuropathological bases of these cognitive deficits remain the target of debate even today (Levin & Katzen, 1995; Mohr, Mendis, & Grimes, 1995).

The degree of cognitive decline in PD can range from mild dysfunction to global dementia as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, 1994). It is as yet unclear whether a common mechanism or distinct ones underlie the mild cognitive changes and dementia. The latter explanation is currently favored by most investigators given that mild cognitive dysfunction does not progress to dementia in all afflicted patients (McFadden, Mohr, Sampson, Mendis, & Grimes, 1996). Dementia is rare in the early stages of PD (Hoehn & Yahr stages I and II or disease duration of less than five years), with a higher prevalence of mild deficits within relatively circumscribed cognitive domains. However, these remain controversial issues (Levin & Katzen, 1995). A recent study by Mohr, Hildebrand, Mendis, Barclay, and Grimes (1996) suggests that the nature and extent of cognitive deficits cannot be solely predicted by the motor disability stage of Parkinsonian patients. The authors found that the motor and cognitive deterioration associated with the illness do not necessarily progress in parallel. Although

the degree of motor disability seems to be linked to a subcortical dementia profile, no such correspondence was found for a cortical dementia profile.

Disease stage may thus not be an accurate dimension along which to classify Parkinsonian patients to study their cognitive functions. A neuroanatomical framework of subcortical-frontal circuits, developed by Alexander, DeLong, and Strick (1986), is compatible with this idea by postulating the presence of five largely segregated pathways, including one involved in cognition and another in motor function. Based on this model, patients with PD may experience independent and selective disturbances of cognitive and motor function resulting from lesions to the caudate nucleus and to the putamen, respectively. The lack of a significant correlation between neuropsychological test performance and clinical variables, such as disease duration, clinical disability stage, and severity of motor symptoms in nondemented Parkinsonian patients supports this contention (e.g. Beatty & Monson, 1990; Beatty, Staton, Weir, Monson, & Whitaker, 1989; Bondi, Kaszniak, Bayles, & Vance, 1993; Cooper, Sagar, Jordan, Harvey, & Sullivan, 1991; Cooper, Sagar, & Sullivan, 1993; Mohr et al., 1990; Morris et al., 1988; Ogden, Growdon, & Corkin, 1990; Taylor, Saint-Cyr, & Lang, 1986). A PET study conducted by Holthoff-Detto et al. (1997) on nondemented Parkinsonian patients also supports the functional model proposed by Alexander et al. Indeed, this study revealed a correlation between the degree of motor disability and the reduction of fluorodopa F18 uptake by the putamen. Conversely, they found that a similar decrease in uptake by the caudate was related to impairment on a delayed recall task.

Studies on PD have largely focused on the selective cognitive changes experienced by nondemented patients rather than on the pervasive cognitive deficits afflicting those with dementia. In nondemented Parkinsonians, there is considerable evidence of selective impairments of visuospatial skills, executive ability, and specific domains of memory function. Depression and bradyphrenia have also been described in these patients (see Levin & Katzen, 1995 for a review). On the other hand, priming,

recognition ability, long-term memory, attention span, and naming are usually reported to be spared (Taylor & Saint-Cyr, 1995). The advantage of working with this subpopulation of patients lies in the hypothetically limited extent of the neurochemical dysfunction to the basal ganglia (Bondi et al., 1993) with relative sparing of cortical and limbic structures, thus providing a clearer picture of the basal ganglia's role and that of its connections in cognition.

The involvement of the basal ganglia in the motor disturbances characteristic of PD is currently better understood than their role in cognitive functions. Indeed, the principal neuropathology of PD is characterized by dopaminergic cell loss occurring in the substantia nigra. Within the substantia nigra compacta, damage is more prominent in the lateral (caudal) portions projecting preferentially to the putamen than in the medial (ventral) portions, which project to the caudate. It is thought that only those specific neurons are affected in the early stages of the disease and that dopamine (DA) depletion levels in the nigrostriatal pathways must reach approximately 80% prior to symptomatic expression of PD (FitzGerald, 1985, p. 130). The deficient striatal dopaminergic transmission is suspected of inducing a disturbance of basal ganglia function, particularly in the putamen. Dopamine depletion in the putamen (FitzGerald, 1985, p. 130) has been implicated in the motor symptoms of PD. This striatal structure is part of the motor loop terminating in the supplementary motor area (SMA) and mediating the programming, initiation, and execution of movement (Alexander et al., 1986).

A number of recent studies on PD have dealt largely with the cognitive, rather than with the motor, dysfunction associated with the illness. Considerable research has focused on memory deficits, which remain among the most commonly observed cognitive symptoms in nondemented PD patients (Beatty, 1992). Nevertheless, conflicting results have been obtained regarding the presence of functional decrements (see Beatty, 1992 and Brown & Marsden, 1987 for reviews). This lack of consensus has been attributed, on one hand, to the heterogeneity of the Parkinsonian population, with

most studies collapsing across such variables as age, disease duration, severity of motor symptoms, and medication regimen. On the other hand, a wide range of task conditions have been employed, contributing to variability among study results.

Furthermore, an important consideration in the investigation of memory concerns the multifaceted nature of this cognitive sphere. Its multiple components have been postulated to have distinct underlying mechanisms and to be dissociable in many neurological diseases. Consequently, Parkinsonian patients may experience selective memory deficits, possibly following differential rates of decline (Levin & Katzen, 1995) and/or depending on the severity of clinical symptoms (Owen et al., 1993). Therefore, each specific domain of memory should be independently assessed for a more accurate description of memory function in individuals with PD.

Most aspects of memory function that appear to be deficient in nondemented Parkinsonian patients are thought to involve the frontal lobes, raising the possibility of frontal lobe dysfunction. Besides these “frontal-type” memory deficits, impairment of executive ability in general has often been reported in both treated and untreated patients who were not demented and/or who were in the early stages of PD (Bondi et al., 1993; Canavan et al., 1989a; Cooper et al., 1991; Lees & Smith, 1983; Ogden et al., 1990; Owen et al., 1992; Paolo, Axelrod, Tröster, Blackwell, & Koller, 1996; Sullivan, Sagar, Gabrieli, Corkin, & Growdon, 1989; Taylor et al., 1986; Venneri et al., 1997). Executive functions, namely the ability to plan, track, sequence, form abstractions, and profit from feedback, are presumably subserved by the frontal lobes, particularly by the prefrontal cortex (PFC). Therefore, although the precise neuropathological basis of the cognitive disturbance observed in many nondemented Parkinsonian patients remains subject to speculation, most investigators suggest that disruption of subcortical-frontal circuits may compromise the functional integrity of the frontal lobes, particularly the dorsolateral prefrontal cortex (DLPFC), and thus play a role in the etiology of the cognitive deficits experienced by these patients (Beatty & Monson, 1990; Bondi et al., 1993; Cooper et al.,

1991, 1993; Fisher, Kendler, & Goldenberg, 1990; Ogden et al., 1990; Owen et al., 1992; Pillon et al., 1997; Sullivan & Sagar, 1989, 1991; Taylor et al., 1986; Taylor, Saint-Cyr, & Lang, 1990; Venneri et al., 1997; Vriezen & Moscovitch, 1990).

Neuropathology of Parkinson's Disease: Possible Compromise to the Frontal Lobes

The neuroanatomical framework of subcortical-frontal circuits developed by Alexander et al. (1986) provides additional support for this hypothesis. In this model, five or more partially closed, parallel, and both structurally and functionally independent pathways form the basal ganglia-thalamocortical circuits, which include a dorsolateral prefrontal (DLP) loop involved in cognitive functions. Within this particular circuit, the DLPFC constitutes one of several cortical inputs to the rostral head of the caudate nucleus. This striatal structure then sends projections to the globus pallidus/substantia nigra complex, which relays the signals to the ventral anterior and medial dorsal thalamic nuclei. The DLPFC, located within and around the principal sulcus on the dorsal prefrontal convexity, is the exclusive cortical target of efferent projections from these thalamic regions.

In postmortem studies of Parkinsonian patients, reduced levels of DA metabolites reveal a marked DA deficiency in the caudate nucleus (Scatton, Rouquier, Javoy-Agid, & Agid, 1982). The DA levels in its caudal regions may become reduced by approximately 60% whereas in the rostral head of the caudate, the depletion may reach 90% (Kish, Shannak, & Hornykiewicz, 1988). Damage to the rostral regions of the caudate nucleus may not only be greater than that to more caudal caudate areas, it may also precede it (Owen et al., 1993). Afferents originating within the PFC project most rostrally within the head of the caudate (Levy, Friedman, Davachi, & Goldman-Rakic, 1997), followed by inputs from the inferotemporal cortex, and then by afferents from other regions of the temporal lobes.

These neuropathological changes have been postulated to be implicated in the cognitive symptoms of the disease (Brown & Marsden, 1990) by ultimately disrupting the ascending central dopaminergic pathways linking the striatum and the frontal lobes (Vriezen & Moscovitch, 1990). Consequently, the PFC may be deprived of subcortical dopaminergic input (Scatton et al., 1982), leading to its functional compromise. Given the anatomical link between the caudate nucleus and the PFC and the selective biochemical changes occurring in either or both of these structures, the neuropsychological profile of PD patients should resemble that of patients with dysfunction in the PFC. Additionally, dopaminergic cell loss occurring in the ventral tegmental area (VTA) reportedly results in a 19% loss of DA in the lateral convexity of the PFC (Scatton et al., 1982). It has also been proposed that “the combination of disturbed caudate outflow and reduced availability of dopamine places functions which depend upon the prefrontal component of the ‘complex loop’ in double jeopardy” (Taylor et al., 1986, p. 852). Similarly, Brown and Marsden (1990) have raised the possibility of additive effects of “subthreshold” DA depletion in the caudate nucleus and the PFC on cognitive functions.

Within the frontal lobes, it has generally been agreed that the prefrontal cortex subserves higher-order cognitive abilities. The PFC is commonly subdivided into three main areas: the orbitofrontal, mesial, and dorsolateral regions (Stuss & Benson, 1986, chap. 15), which mediate different cognitive domains. Evidence for functional differences among these prefrontal areas is provided by studies of animals or individuals with frontal pathology. The association between lesion localization and behavioral patterns is fairly consistent. However, the functional subdivision of the PFC remains at a conceptual level.

The orbitofrontal cortex may mostly be involved in set-maintenance, perceptual set-shifting, and inhibition of interference (Stuss & Benson, 1984, 1986, chap. 15). Lesions to this area are often associated with personality and/or affective disorders (Stuss

& Benson, 1984; see also Cummings, 1995 for a brief review). The mesial region is thought to subserve impulse control. Most executive skills, however, are hypothesized to be mediated by the DLPFC. Its functions would include the monitoring of one's behavior through use of feedback, set-shifting and maintenance (Stuss & Benson, 1984), planning, and the temporal or sequential organization and integration of events, items, and/or behavior (Cabeza et al., 1997; Fuster, 1990; Milner, 1963; Milner, Petrides, & Smith, 1985; Moscovitch, 1992; Stuss & Benson, 1984).

There is also strong evidence that the DLPFC plays a critical role in working memory, at least in nonhuman primates. Research conducted by Goldman-Rakic (1996) led her to hypothesize that each of several subdivisions of the DLPFC would be part of a network connecting it with relevant sensory, motor, and limbic areas. Each DLPFC subdivision would control the "on-line" processing of a specific type of information and belong to a particular network based on the informational domain. At a cellular level, Goldman-Rakic (1995) has described what she hypothesizes to be the cellular basis of memory. The administration of a selective D1 antagonist was reported to change the pattern of activation of some PFC neurons during the delay period of a delayed-response task (Williams & Goldman-Rakic, 1995). Without the antagonist, some neurons in the PFC will fire maximally during the delay period of a spatial delayed-response task.

However, the firing of a particular neuron seems to depend on the location of the stimulus. Neuronal firing while the primate must remember the location of a stimulus is directly associated with the accuracy of subsequent recall. The involvement of neurons in the PFC in working memory tasks can also be distinguished by their location within the PFC. Whereas the inferior convexity of the PFC contains neurons that are generally responsive during the processing of non-spatial (e.g. form, color) information, neurons in the dorsolateral region are typically activated by the spatial aspects of stimuli (Goldman-Rakic, 1995).

Goldman-Rakic's research with nonhuman primates thus suggests a crucial role of the DLPFC in working memory. However, it is difficult to draw firm neuroanatomical comparisons to humans. Generalizability of the results to the human population, although likely, at least to an extent, remains limited.

"Frontal" Profile of Cognitive Deficits

The neuroanatomical evidence of a "frontal-lobe" profile of cognitive deficits in nondemented Parkinsonian patients (Bondi et al., 1993; Taylor et al., 1986, 1990) is supported by indications of a greater susceptibility to deficient performance on tasks sensitive to frontal lobe pathology than on those affected primarily by temporal lobe damage (Owen et al., 1992). Indeed, many of the cognitive changes incurred by patients with PD resemble those associated with frontal lobe damage (Bondi et al., 1993; Lees & Smith, 1983; Sagar, Sullivan, Gabrieli, Corkin, & Growdon, 1988b; Taylor et al., 1986).

Like the majority of patients with frontal lobe pathology, nondemented Parkinsonian patients may evidence problems in self-directed planning (Bondi et al., 1993). Planning is a complex task which likely involves a number of processes including, but not limited to, working memory, set-formation, set-shifting, and sequencing (Owen et al., 1992). For planning to be successful, affected Parkinsonian patients depend heavily on external feedback and guidelines (Taylor et al., 1990).

The Tower of Toronto test (Saint-Cyr, Taylor, & Lang, 1988) is an executive task which assesses planning and sequencing abilities, as well as working memory. Nondemented Parkinsonian patients in the early stages of the disease seem to be impaired only during the delayed portion of the task (Saint-Cyr et al., 1988). The authors interpreted these findings as reflecting a reduced ability to profit from practice. Given their intact performance on the 3-disk stage, patients with PD may have difficulty solely when the number of moves to be executed exceeds their attention span.

The Tower of London (Shallice, 1982) is a similar, although somewhat less complex task than the Tower of Toronto. Instead of four colored discs, subjects must rearrange three discs from their initial peg positions to a new set of predetermined positions. Contrary to the Tower of Toronto task, discs are initially placed on two pegs and sometimes must be moved onto more than one peg. Patients with frontal lobe involvement are reportedly impaired on the Tower of London test (Owen et al., 1990). Similarly, the performance of Parkinsonian patients is deficient. Slowed initial thinking time was reported on a computerized version of the task in groups of medicated and nondemented Parkinsonian patients with mild, moderate, or severe clinical motor disability (Morris et al., 1988; Owen et al., 1992). This selective task-related impairment may be accounted for by a planning deficit. Similarly, Lange et al. (1992) reported that withdrawal from L-dopa therapy slowed the initial thinking time and decreased the number of perfect solutions obtained by nondemented patients. However, patients who were both unmedicated and nondemented did not evidence any deficits on the Tower of London test (Owen et al., 1992).

The Wisconsin Card Sorting Test (WCST, Heaton, 1981) is a well-established measure of executive ability. It is described as a classic test of dorsolateral function since test performance is maximally impaired with lesions to this prefrontal area (Milner, 1963, 1964, 1971). Within the WCST, an increased number of perseverative errors and a reduced number of categories completed have especially been associated with such lesions (Milner, 1963) whereas a failure to maintain set may arise from orbitofrontal dysfunction (Stuss & Benson, 1986, chap. 15). In his studies of patients with brain injury, Heaton (1981) found that perseverative errors and trials to the first category can distinguish those with frontal vs. non-frontal damage in the absence of diffuse disease. Indeed, both Canavan et al. (1989a) and Shimamura et al. (1991) reported a high number of perseverative errors in patients with frontal damage. In the latter study, patients additionally completed fewer categories. No such impairment was observed when

combined lesions to the orbital-frontal and temporal cortices were present (Milner, 1964).

Since the WCST (Heaton, 1981) elicits deficits in nondemented Parkinsonian patients, even those in the early, untreated stages of the disease, it provides further support to the notion of frontal lobe dysfunction in PD (Cooper et al., 1991; Lees & Smith, 1983). However, this test provides an assessment of many executive abilities and there is a lack of agreement regarding the specific task demands underlying the deficits. Moreover, several studies have utilized modified versions of the standard WCST (e.g. Bondi et al., 1993; Canavan et al., 1989a; Lees & Smith, 1983; Paolo et al., 1996; Venneri et al., 1997). Nevertheless, relatively reduced efficiency in performance of PD patients on specific WCST measures has been reported by many investigators. Notably, patients show an increase in perseverative errors (Canavan et al., 1989a; Lees & Smith, 1983; Levin, Llabre, & Weiner, 1989; Paolo et al., 1996; Venneri et al., 1997), a failure to maintain set (Beatty et al., 1989), impaired set-formation revealed by the high number of trials needed to achieve the first category (Cooper et al., 1991; Taylor et al., 1986), and/or set-shifting difficulty indicated by the fewer categories completed (Beatty et al., 1989; Lees & Smith, 1983). In addition, an overall impairment was noted on this test by Bondi et al. (1993), who obtained a composite score for the number of categories achieved, perseverative errors, and total number of errors. However, Beatty and Monson (1990) noted that only PD patients with lower mental status evidenced deficits on the WCST, measured by an increase in perseverative errors and trials to the first category as well as a reduced number of categories completed.

Executive skills can also be assessed with Picture Arrangement, a subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R, Wechsler, 1981). Picture Arrangement evaluates cognitive sequencing ability independently of memory components and has been shown to elicit impairments in patients with frontal lobe pathology who were matched on IQ with normal controls (Janowsky, Shimamura,

Kritchevsky, & Squire, 1989). All other WAIS-R subtests were adequately performed by these patients with the exception of Digit Span Forward and Backward.

Several studies have reported deficits in the performance of many nondemented Parkinsonian patients on Picture Arrangement (Wechsler, 1981) under both timed and untimed conditions (Bondi et al., 1993; Cooper et al., 1991; Ogden et al., 1990; Sullivan, Sagar, Gabrieli, Corkin, & Growdon, 1985) and irrespective of the use of age-corrected scaled scores (Sullivan et al., 1989). Even nondemented patients who were in the early stages of the disease and were yet to receive antiparkinsonian medications exhibited a selective Picture Arrangement deficit relative to normal controls (Cooper et al., 1991). A group of nondepressed Parkinsonians, many of whom were high-functioning, were also reportedly impaired on this task (Ogden et al., 1990). Impairment on Picture Arrangement has been attributed to a general inability to mentally manipulate multiple items, of which cognitive sequencing is an example (Sullivan et al., 1989). Furthermore, some PD patients' failure to rearrange the cards reflects a difficulty in set-formation (Cooper et al., 1991) but such an impairment was not reported by Sullivan et al. (1989). Another sequencing test, in which four cards depicting familiar everyday scenes have to be arranged to form a logical "story" (Picture Sequencing), was administered to nondemented Parkinsonian patients by Beatty and Monson (1990). The patient group was impaired on this test despite being allowed unlimited time to complete it..

Poor cognitive sequencing has also been observed on tests requiring mental manipulation and reorganization of digits in a predetermined order not previously presented. The Backward Digit Span subtest of the WAIS-R (Wechsler, 1981) and Digit Ordering are two tasks conducive to such an impairment in many nondemented patients with PD (Cooper et al., 1991; Sullivan et al., 1989). Contrary to Forward Digit Span (Wechsler, 1981), which solely involves the retention and repetition of digits, Backward Digit Span and Digit Ordering also require the ordering of digits according to a specified sequence. This processing component may account for the generally greater impairment

noted on the latter tests in nondemented patients with PD. These deficits parallel those experienced by patients with frontal involvement on Backward Digit Span (Canavan et al., 1989b). However, these authors failed to find an impairment on this task by Parkinsonian patients with a short disease duration. Finally, some Parkinsonian patients' inability to recite the months backward suggests a sequencing deficit (Levin et al., 1989).

Verbal fluency is another frontally-associated task which reportedly elicits deficits in many nondemented patients with PD. It has been shown to be mostly dependent upon the dorsolateral and possibly the mesial frontal cortical regions (Milner, 1963, 1964), although Stuss and Benson (1986, chap. 15) state that either or both the dorsolateral and/or the medial regions of the PFC may mediate verbal fluency. Tests of semantic (or category) fluency have often been found to yield impairment in nondemented Parkinsonian patients (Beatty et al., 1989; Bondi et al., 1993; Cooper et al., 1991; Levin et al., 1989) and therefore may be more affected than letter fluency (Beatty et al., 1989), which was reportedly intact in studies by Beatty et al. (1989) and by Beatty and Monson (1990). On the other hand, Lees and Smith (1983), who do report impaired letter fluency in Parkinsonian patients, have attributed the deficits to increased perseverative intrusions rather than to reduced verbal output. The more frequently observed deficit in semantic fluency has been attributed to the greater organizational demand associated with this fluency task (Brown & Marsden, 1987).

Nondemented Parkinsonian patients are not impaired on all executive tasks. They appear to experience particular difficulty on tasks requiring the management of novel input (Taylor & Saint-Cyr, 1995). They are markedly impaired when a task requires them to spontaneously generate context-dependent associations or efficient strategies and to use internal cues to guide behavior (Taylor et al., 1986, 1990). Tasks requiring subjectively organized task-specific strategies have been noted to best distinguish nondemented Parkinsonian patients from normal controls (Taylor et al., 1986). The decreased efficiency of strategic processes is consistent with the fronto-striatal

dysfunction associated with PD since these processes are dependent upon the integrity of the frontal lobes (Moscovitch, 1992; see Poldrack & Gabrieli, 1997 for a review). In sum, only those executive function tasks without explicit guidelines, for which no prior experience exists, which are effort demanding and require the development of a strategy, may be performed more poorly by nondemented patients with PD than by normal controls (Taylor & Saint-Cyr, 1995).

Although most studies report such frontal-lobe type deficits in nondemented Parkinsonian patients, performance on “frontal” tasks has also occasionally been described as comparable to that of normal controls. Variability among study results may be due to sampling (e.g. disease duration, IQ level) and/or to methodological differences in the tasks used (e.g. task modifications, use of different stimuli). Furthermore, manifestation of cognitive deficits may depend on the degree of DA depletion in the caudate nucleus (Canavan et al., 1989a).

Despite a few contradictory results, evidence overwhelmingly suggests that nondemented patients with PD experience relatively circumscribed deficits on frontal system tasks. In a study by Bondi et al. (1993), patients were impaired on all tasks sensitive to frontal lobe dysfunction, including the WCST (Heaton, 1981), verbal fluency, and temporal ordering. Frontal system dysfunction in these patients appeared to account for their selective failures in visuoceptive, visuoconstructive, learning, and memory tasks. When performance on frontal system tasks was used as a covariate, performance on the visuoceptive, visuoconstructive, learning, and memory tasks was comparable to that of normal controls. This did not hold true when these tasks served as covariate for performance on frontal system tasks. The view that visuospatial deficits may reflect an underlying executive impairment such as a difficulty generating, maintaining, or shifting sets has also been held by Ogden, Growdon, and Corkin, 1990 as well as by Pillon et al., 1997.

Selective Memory Impairments Associated with Frontal-Lobe Disruption

Consistent with the hypothesis of frontal lobe dysfunction in PD, specific and similar patterns of memory impairment are reported in both nondemented patients with PD and patients with frontal lobe damage. Frontal lesions appear to induce “prospective” memory deficits, whose deficient underlying processes may involve planning, organization, and other strategies that facilitate encoding and/or retrieval (Shimamura et al., 1991). The same type of deficits may thus underlie Parkinsonian patients’ poor performance on selective memory tasks.

A decrease in the number of dopaminergic projections reaching the frontal lobes has been suggested to be responsible for the memory deficits noted in Parkinsonian patients (Weingartner, Burns, Diebel, & LeWitt, 1984). Lesions to the DLPFC area have been associated with poor organizational strategies and impaired learning and retrieval of information (Stuss & Benson, 1986, chap. 15). Patients with frontal lobe pathology are occasionally impaired on free recall tasks despite adequate recognition of stimuli (Janowsky et al., 1989; Shimamura, Janowsky, & Squire, 1990). This differential compromise points to difficulties with the organization of material in memory and with internally generated search and retrieval strategies (Shimamura, 1990). Indeed, tests of free recall may require self-initiated executive processes (Shimamura et al., 1990). In patients with frontal lesions, recall is compromised when the material to be remembered requires organization, categorization, ordering, or monitoring (Shimamura et al., 1991). On the other hand, associative processes remain intact (Vriezen & Moscovitch, 1990). These processes are linked to the mesial temporal regions and become activated when retrieval is mediated by a cue which directly evokes the stimulus previously associated with it.

Executive deficits may also account for the selective memory impairments noted in nondemented patients with PD upon conditions of free recall (Mohr et al., 1995). Specifically, their mildly impaired recall of previously presented material has been

attributed to the lack of a spontaneous and efficient strategy to retrieve or organize information in memory (Bondi et al., 1993; Gabrieli, 1996; Taylor et al., 1986, 1990). Besides a lack of strategy development, impairments of several other executive skills have been proposed to underlie poor performance on recall measures. Deficits in planning and in the establishment of subjective models of reality have been evoked as sources of retrieval difficulties (e.g. Taylor et al., 1990). Consequently, nondemented Parkinsonian patients evidence the greatest impairment on tasks requiring spontaneous self-organization of the material-to-be-remembered and they appear to rely excessively on external feedback or guidelines (Taylor et al., 1986, 1990). This pattern of impairment is suggestive of frontal lobe dysfunction since the integrity of this cortical region is thought to be crucial for the strategic organization of material in memory in the absence of external cues (Moscovitch, 1992).

Based on the theory of Hasher and Zacks (1979), Weingartner et al. (1984) have argued that the amount of effort required to accomplish a task is a good predictor of impairment in episodic memory. This type of memory contains information associated with a unique spatiotemporal context and often includes a representation of oneself as a participant or an observer. In nondemented PD patients, automatic processes requiring little effort and attention, such as the retrieval of stimulus properties incidentally encoded, generally remain intact. Conversely, effortful cognitive processes such as explicit search and strategy procedures are impaired.

Findings of decrements in free recall (e.g. Beatty et al., 1989; Bondi & Kaszniak, 1991; Cooper et al., 1991; Gabrieli, 1996; Levin et al., 1989; Mohr et al., 1990; Taylor et al., 1986, 1990; Weingartner et al., 1984) compared to relatively intact recognition performance (Beatty & Monson, 1990; Beatty et al., 1989; Bondi & Kaszniak, 1991; Flowers, Pearce, & Pearce, 1984; Gabrieli et al., 1996; Lees & Smith, 1983; Mohr et al., 1990; Taylor et al., 1986, 1990; Venneri et al., 1997; Vriezen & Moscovitch, 1990; Weingartner et al., 1984) are consistent with this hypothesis. Given the selective sparing

of recognition memory in nondemented Parkinsonian patients, episodic memory deficits appear to be linked to a retrieval problem rather than to difficulties in the encoding or storage of information (Beatty, 1992; Brown & Marsden, 1987; Flowers et al., 1984). When provided with explicit guidelines, as in cued recall tasks, patients' performance is comparable to that of normal controls (Bondi & Kaszniak, 1991; Venneri et al., 1997). However, the differential impairment of recall and recognition memory in the absence of dementia in PD is by no means a universal finding. Short-term memory recognition deficits have occasionally been reported in nondemented Parkinsonian patients (Sahakian et al., 1988; Sullivan & Sagar, 1989, 1991).

Short-term memory (STM) and long-term memory (LTM) stores have been dissociated. Short-term memory processes are usually linked to the frontal lobes whereas LTM has traditionally been associated with the temporal lobes (Sullivan & Sagar, 1991; Winocur, 1992). In nondemented patients with PD, STM is generally found to be more impaired than LTM (Cooper et al., 1993; Sagar, Cohen, Sullivan, Corkin, & Growdon, 1988a; Sagar et al., 1988b; Sahakian et al., 1988; Sullivan & Sagar, 1989, 1991; Taylor et al., 1986, 1990). Therefore, disruption of the frontostriate system in PD may account for the selective impairment of STM processes found in nondemented patients (Cooper et al., 1991). In terms of the deficient cognitive processes underlying the selective STM deficit, bradyphrenia has been proposed by Sullivan and Sagar (1989). Bradyphrenia refers to a slowing of thought processes. However, Parkinsonian patients' intact performance on a task requiring rapid processing of novel information argues against such a deficit (Beatty et al., 1989), as does their adequate performance on the Stroop test (Pillon et al., 1997; Venneri et al., 1997).

Working memory is a limited capacity memory system which overlaps with STM to an extent. Its defining feature is its ability to hold information "online" transiently for its use in cognitive tasks. Working memory allows the maintenance, manipulation, and transformation in memory of stimuli that are no longer present. Animal lesion studies

(Goldman-Rakic, 1995), neuropsychological investigations (Owen et al., 1996), as well as neuroimaging data (Fiez et al., 1996) have linked this type of memory to the DLPFC. Deficits in working memory have been confirmed in patients with frontal lobe pathology (Owen et al., 1993, 1996). For example, Shimamura (1990) noted this selective impairment with the Digit Span subtest of the Wechsler Memory Scale-Revised (WMS-R, Wechsler, 1987) despite a relatively preserved ability to learn new material. Similarly, working memory tasks have revealed deficits in nondemented Parkinsonian patients (Cooper et al., 1991; Owen et al., 1992, 1993). For example, Cooper et al. (1991) have reported that the performance of newly diagnosed and untreated patients is particularly impaired on such tests as Picture Arrangement (Wechsler, 1981), Digit Ordering, and the Brown-Peterson technique (Petersen & Petersen, 1959).

Working memory is traditionally ascribed to the frontal lobes, particularly the PFC (Tranel, 1994, p. 162). A selective impairment of spatial working memory in nondemented patients with PD contrasts with the relative sparing of pattern and spatial recognition associated with intact temporal lobe structures (Owen et al., 1993). Working memory for the spatial location of stimuli has been shown to be mediated by the principal sulcus area of the PFC. Tasks which place demands on spatial working memory have also been reported to activate the dorsal and central regions of the head of the caudate nucleus (Levy et al., 1997). According to Owen, Sahakian, Semple, Polkey, and Robbins (1995), this dissociation suggests that, early in the course of the disease, “frontal-type” deficits emerge and only later do more posterior cortical functions become impaired.

In neuropsychological studies, assessment of working memory is sometimes based on patients’ ability to perform conditional associative learning tasks (CALTs). Such tasks require subjects to learn a set of stimulus-response pairs, such as associations between various pairs of visual stimuli or between different visual stimuli and spatial locations. One of two types of conditional associative learning tasks can be administered.

On the trial-and-error version, subjects must first guess which number or spatial location is associated with each one of a series of stimuli. Guessing continues until the correct pair has been given. Subjects are then required to reproduce the correct associations. On the second version, the correct stimulus-response associations are initially revealed to the subjects, who are then provided with correction feedback as they attempt to reproduce the associations. The poor performance of nondemented patients with PD on the first version suggests a difficulty in the maintenance of highly arbitrary and competitive associations in working memory (Taylor et al., 1990). The differential impairment on the two versions of the CALT reflects the greater demand of the trial-and-error version on strategic processes such as the organization and monitoring of responses (Vriezen & Moscovitch, 1990). Trial-and-error learning on the CALT is also compromised in patients with frontal lobe lesions (Canavan et al., 1989a).

The procedural memory system contains memories for rules and procedures governing certain behavioral (e.g. sensorimotor) and cognitive skills. Information stored in this memory system often cannot be verbalized. The procedures may be automatically activated without conscious awareness of their features. Their acquisition is manifested by an improvement in performance with practice. Indeed, procedural memory is characterized by gradual, incremental learning. Findings surrounding procedural memory remain equivocal, with deficits being only occasionally observed, possibly as a result of the wide variety of tasks employed to assess this memory component (e.g. fragmented pictures test, Tower of Toronto). Task performance by nondemented patients with PD remains relatively intact when highly constrained, rule-bound motor or perceptual skill learning is required (e.g. mirror-reading, pursuit rotor tracking). On the other hand, particular difficulty has been noted on skill learning tasks requiring self-directed cognitive/perceptual processes and/or having a strong sensorimotor component (Bondi & Kaszniak, 1991; Moscovitch, 1992; Saint-Cyr et al., 1988). The latter subset of procedural memory tasks has been associated with basal ganglia function, which could

conceivably link inefficiencies in this type of memory with the primary pathophysiology of PD. The differential impairment exhibited by nondemented Parkinsonian patients on various procedural learning tasks may also be partly ascribed to frontal lobe dysfunction. Supporting this view is the finding that only certain procedural tasks require the skill learning subserved by the neostriatum via the “complex” loop (Bondi & Kaszniak, 1991). It has been suggested that procedural tasks requiring nonmotor skills may depend on the integrity of the caudate nucleus (Moscovitch, 1992).

Temporal Memory vs. Content Memory

An area of memory which has received considerably less attention in the study of cognitive function in Parkinsonian patients is temporal memory. Studies concerned with temporal memory function in nondemented patients with PD have unanimously found it to be impaired (e.g. Bondi et al., 1993; Sagar et al., 1988; Vriezen & Moscovitch, 1990). This type of memory is concerned with the temporal organization of information. It involves the ability to recall and recognize the order in which a series of events occurred or a series of items appeared. Nondemented Parkinsonian patients reportedly have difficulty remembering the order in which both words (Bondi et al., 1993; Vriezen & Moscovitch, 1990) and drawings (Vriezen & Moscovitch, 1990) were presented.

Several experimental tasks have been developed to assess temporal memory. In the temporal ordering task, patients are required to rearrange a series of stimuli in order to form a sequence identical to one previously presented with the same stimuli. Impaired judgment of the relative recency of two previously seen items has also been observed on recency discrimination tasks (Fisher et al., 1990; Gabrieli, 1996; Sagar et al., 1988b; Sullivan et al., 1985; Sullivan & Sagar, 1989). Finally, both demented and nondemented patients with PD reportedly experience difficulty in dating past public and personal events (Sagar et al., 1988a).

Dating ability likely involves both temporal ordering and recency discrimination since the event to be dated must be placed in context relative to other events for which the date is known (Brown & Marsden, 1990). Similarly, a difficulty in making temporal discriminations has been proposed to partly account for patients' impaired performance on memory tasks involving temporal ordering (Vriezen & Moscovitch, 1990) or dating of events (Sagar et al., 1988b). Temporal discrimination entails the reconstruction of the sequential order of occurrence of items or events in memory and their relative position along a temporal framework.

A role for temporal memory in the Brown-Petersen task (Petersen & Petersen, 1959) has been raised by Schacter (1987). In order to provide the correct response for a particular trial, subjects must perform accurate temporal discriminations between the various trials. Nondemented Parkinsonian patients are impaired on this task (Cooper et al., 1991).

Serial learning constitutes another task which provides an assessment of temporal memory. Patients with PD reportedly perform poorly on this task compared to normal controls (Weingartner et al., 1984). Deficient serial learning may indicate difficulties in forming relationships among the items to be remembered (Breen, 1993).

Several investigators have argued for the critical role of the frontal lobes in temporal memory, which is usually adversely affected by frontal lesions (Milner, 1971; Milner et al., 1985; Schacter, 1987; Shimamura et al., 1990). Specifically, the ability to make recency judgments has been associated with the dorsolateral region of the frontal lobes (Milner & Petrides, 1984; Milner et al., 1985). A study by Milner et al. (1991) further suggests a degree of hemispheric specificity for such recency discrimination tasks. Patients with mid-lateral frontal cortex excisions are reportedly impaired on the verbal version of the task whereas the right frontal lobe appears to be highly implicated when the stimuli consist of abstract paintings. In other neurological populations with damage to the frontal lobes (e.g. Korsakoff's syndrome), performance on temporal

memory tasks has been selectively correlated with performance on tasks sensitive to frontal lobe disruption (e.g. Squire, 1982).

A dissociation has been drawn between memory for the context vs. content of information (see Moscovitch, 1992 for a review). Context memory refers to memory for the temporal and spatial characteristics of an item or event (when/where/how) independently of the nature of that item or event (Schacter, 1987). In contrast, content memory refers to memory for items or events independently of the temporal or spatial context in which they were introduced (Moscovitch, 1992).

Retention of context and content information is differentially impaired in patients with frontal lesions, as evidenced by poor performance on tasks of temporal order recall and recency discrimination despite accurate item recall and recognition (e.g. Milner, 1971; Milner & Petrides, 1984; Milner et al., 1985; Milner et al., 1991; Shimamura et al., 1990). Context memory is characterized by disproportionately severe impairments of the ability to remember the spatiotemporal context in which items were presented. Impaired context memory relative to a relatively preserved ability to remember item content (e.g. verbal or visual stimuli) is associated with signs of frontal lobe dysfunction. The performance of amnesic patients on tasks requiring access to spatiotemporal information is only deficient if signs of frontal pathology are evident (Schacter, 1987).

With pathology to the temporal lobes, the reverse pattern of impairment is observed (Milner et al., 1991). Lesions restricted to the medial temporal areas are associated with an impairment of content memory despite a preserved ability to place the retained memories in their proper spatiotemporal context such as is required in the recency discrimination task (Milner et al., 1985; Shimamura et al., 1990). The double dissociation between the effects of right-frontal and right-temporal lobe excisions on the recognition of stimuli and the judgement of their temporal order suggests the existence of separate neuroanatomical substrates (Moscovitch, 1992) and independent underlying cognitive processes (Milner et al., 1991; Sagar et al., 1988b). Supporting this contention

is the lack of a correlation between recognition and temporal ordering performance in nondemented patients with PD (Vriezen & Moscovitch, 1990).

In these patients, impairment of content memory has rarely been observed, if at all (e.g. Sagar et al., 1988a, 1988b; Taylor et al., 1986; Vriezen & Moscovitch, 1990) whereas their memory for context appears to be deficient. Specifically, recall and recognition of the context or temporal order of items or events are impaired while recognition of stimulus content remains relatively unaffected (Fisher et al., 1990; Gabrieli, 1996; Sagar et al., 1988a, 1988b; Taylor et al., 1986, 1990). Thus, nondemented patients with PD are often able to distinguish an item that has previously been shown from one that is new, although they have much more difficulty identifying which of two previously seen items appeared more recently or recall the order of presentation of a series of items. Dissociation of nondemented Parkinsonian patients' performance on context-versus-content memory tasks thus suggests that there may be a selective compromise to the integrity of the frontal lobes, with relative sparing of the temporal lobe structures. The differential impairment has even been noted on tasks assessing remote memory function (Sagar et al., 1988a).

Deficient Cognitive Processes Hypothesized to Underlie Temporal Memory Deficits

Given the similarity between the executive and memory deficits experienced by nondemented Parkinsonian patients and by those with frontal lobe pathology, the memory problems noted in the former may stem from impairments in frontal lobe function, rather than from compromise of posterior cortical function. The notion of a primary memory deficit of frontal lobe origin is subject to controversy, as such an impairment has also been described as a by-product of disordered attention and motivation (Stuss & Benson, 1986). However, it is unlikely that such disorders are predominantly responsible for memory deficits in this case, since no attentional deficits were detected upon the administration of several tests of attention by Levin et al. (1989).

Nondemented Parkinsonian patients generally perform normally on tests of forward digit and spatial span (Canavan et al., 1989b; Cooper et al., 1991; Fisher et al., 1990; Huber et al., 1986; Morris et al., 1988; Owen et al., 1992), a finding also reported in patients with frontal lobe injury (Canavan et al., 1989b; Owen et al., 1990). Thus, nondemented patients with PD appear able to reproduce a series of items in their correct temporal order when a limited number of items are presented (Brown & Marsden, 1990). They also have relatively intact LTM recall and recognition abilities, again suggesting adequate attentional resources.

It remains unclear whether the temporal memory deficits evidenced by nondemented Parkinsonian patients represent a specific and primary memory dysfunction or whether such impairments are instead nonspecific to memory and secondary to cognitive and executive difficulties associated with frontal lobe dysfunction. The latter explanation has been proposed by several studies (e.g. Bondi et al., 1993; Sagar et al., 1988b; Vriezen & Moscovitch, 1990). Temporal memory tasks rely heavily upon retrieval strategies since subjects must search through memory for the temporal context in which items to be compared or ordered appeared (Milner et al., 1985, 1991). Strategic processes are needed not only to retrieve the items but also to organize them in a proper spatiotemporal context relative to other items in memory (Moscovitch, 1992). Therefore, inadequate use of strategies by patients with PD may explain their poor performance on temporal ordering tasks. The role of strategic processes in the reconstruction of temporal order has been highlighted by Vriezen and Moscovitch (1990). These authors described temporal ordering as being largely self-initiated and involving organization, estimation, and formation of relational judgments.

Deficits in the temporal processing of information may also be part of a broader deficit termed “dysexecutive syndrome”, which refers to impairments in the coordination, monitoring, and organization of information in working memory that may also be the source of other deficits, including those in planning, initiating, and executing

search and retrieval strategies (Baddeley, 1986, chap. 10; Shimamura et al., 1990). The possibility of an association between temporal memory and working memory is suggested by a correlation between performance on temporal ordering and the trial-and-error version of the conditional-associative-learning tasks (Vriezen & Moscovitch, 1990). Supporting this view, impaired temporal judgments have so far only been demonstrated at short stimulus-test intervals (Cooper et al., 1993). However, performance was not assessed at longer intervals. Furthermore, at the shortest intervals, recency discrimination performance was related to scores on measures of attention, executive functions, and STM (e.g. Brown-Petersen task, Digit Ordering, number of categories completed on the WCST). A deficit affecting STM, reconstructive ability, and sequencing may also account for impaired temporal judgments (Cooper et al., 1993). Alternatively, disruption of a higher-order memory system involved in the manipulation, discrimination, and comparison of independent memoranda (Baddeley & Wilson, 1986, p. 249) or several non-mnemonic items may account for the selective impairment experienced by both demented and nondemented Parkinsonian patients on dating, recency discrimination, and cognitive sequencing tasks (Sagar et al., 1988b).

Although a number of hypotheses have been formulated with respect to the cognitive processes whose compromise underlies impaired temporal judgments, the relationship between impairments of temporal memory and that of other cognitive functions in PD has not been systematically studied. The notion of a specific involvement of the frontal lobes in the temporal processing and retention of information is, as yet, unresolved.

Successful performance on public event dating, temporal ordering, and recency discrimination memory tasks is thought to depend heavily upon the ability to order or sequence a series of items or events along a temporal dimension in memory (Sullivan et al., 1985). For example, recency discrimination involves remembering the sequence in which a series of items were presented in order to state which of two stimuli appeared

most recently. Similarly, dating capacity depends upon the ability to sequence remote events in memory in order to make recency judgments between events to be dated and highly memorable public or personal events for which the dates are well-known (Loftus & Marburger, 1983).

The impairments of temporal memory repeatedly observed in both demented and nondemented patients with PD may therefore be secondary to a broader deficit of executive skills, particularly of sequencing ability, resulting from abnormalities in frontal lobe function (Beatty, 1992; Sagar et al., 1988b) rather than reflecting a true memory disorder (Stuss & Benson, 1984). Several cognitive deficits present in Parkinsonian patients may originate from sequencing impairments. First, this patient population exhibits difficulty in ordering items or events along a temporal dimension. Second, they seem to “lose their place” when a task requires mental tracking of a series of steps in a specific sequence. Finally, when patients are engaged in temporal memory tasks such as recency discrimination, dating of events, or temporal ordering, they must not only retrieve the temporal information specific to each item but also organize the memories in their correct temporal sequence (Vriezen & Moscovitch, 1990).

The parallel impairment of temporal memory and cognitive sequencing in Parkinsonian patients was interpreted by Sagar et al. (1988a) as possibly reflecting an association between these processes. Both temporal memory and sequencing are cognitive processes which have been ascribed to the frontal lobes, particularly the PFC. Damage to this area, particularly to the lateral regions (Stuss & Benson, 1986, chap. 15), produces deficits in the ordering or handling of sequential information and/or behavior. The cognitive domains of language, motor function, and memory all seem to be affected. Patients with frontal lobe pathology experience difficulties in organizing words in a logical sequence, in sequencing motor acts, and in judging the relative recency of items (Stuss & Benson, 1984). These authors concluded that the PFC must play a critical role in the ordering or handling of sequential behaviors/items. The temporal organization of

items or behaviors includes both the judgment of the order of preceding events and the organization and sequencing of responses to carry out (Milner et al., 1985).

Deficient temporal memory and sequencing performance in groups of nondemented patients with PD is consistent with the hypothesized fronto-striatal disruption occurring in this illness. This contention is supported by findings of an association between poor motor and cognitive sequencing and an increased number of perseverative errors and trials to the first category on the WCST (Heaton, 1981) (Beatty & Monson, 1990). These authors interpreted the correlations as reflecting the role of frontostriate disruption in the sequencing deficits observed in nondemented Parkinsonian patients. The performance of nondemented patients with PD on temporal memory tasks was also found to be related to WCST measures (trials to the first category, number of categories achieved) as well as to scores on a sequencing task, notably Digit Ordering (Cooper et al., 1993). On the other hand, performance on both temporal memory and sequencing tasks has generally been found to be unrelated to disease stage and duration (Beatty & Monson, 1990; Cooper et al., 1993) although temporal ordering has been found to be slightly related to disease duration (Fisher et al., 1990). Performance on other tasks sensitive to frontal lobe injury (e.g. WCST, Tower of London) also appears to be unrelated to degree of motor impairment (Morris et al., 1988; Taylor et al., 1986). This weak or absent association between the cognitive and motor deficits suggests different underlying pathologies.

Neuropsychological Performance of High-Functioning Parkinsonians

Most studies addressing cognitive function in PD have been conducted on an otherwise unselected Parkinsonian population, collapsing across a number of variables which possibly contribute to the cognitive deficits of the patients. These factors include motor disturbance, poorly sustained attention due to pain, dyskinesia, and easy fatigability, age-related cognitive decline, medication side effects, and concomitant

disease processes. Consequently, it may be difficult to attribute deficiencies in temporal memory and executive function in an otherwise unselected Parkinsonian population solely to the pathophysiology of the illness.

In an attempt to address this question, high-functioning Parkinsonian patients were selected from a group who sought medical assistance principally for the management of their motor dysfunction. It was thought that the study of frontally-associated cognitive skills in high-functioning patients would likely provide a clearer picture of frontal lobe function in the absence of dementia in PD. Indeed, within the Parkinsonian patient population, those qualified as high-functioning are thought to be least likely to exhibit neuropsychological deficits, all other factors being equal (e.g. age, disease duration). Exceptional professional standing in a premorbid occupation or a university-level education, as well as an absence of global dementia, characterize high-functioning patients.

A study of cognitive status in high-functioning patients with PD was undertaken by Mohr et al. (1990). The authors reported selective deficits in their patients, suggesting that cognitive decline is a feature of PD, even in this sub-group of patients. Of interest is the fact that memory functions were differentially compromised in both verbal and visuospatial modalities, depending upon the amount of effort involved. Poor performance on the Logical Memory and Visual Reproduction subtests of the Wechsler Memory Scale (WMS, Wechsler, 1945) as well as on the 3-minute recall of the Rey-Osterrieth Figure (Osterrieth, 1944) attests to substantial deficits in high-functioning Parkinsonian patients on effort-demanding episodic memory tasks such as free recall. Conversely, patients performed within the normal range on simpler tasks such as the Benton Visual Retention Test (BVRT, Benton, 1974), which assesses immediate and delayed item recognition.

Recognition memory has traditionally been associated with the temporal and diencephalic regions of the brain (Nyberg et al., 1996; Shimamura et al., 1991) while retrieval processes involved in the free recall of information are thought to also involve

the frontal lobes (Poldrack & Gabrieli, 1997; Shimamura et al., 1991). Thus, the etiology of the selective recall impairment observed in high-functioning Parkinsonian patients may stem from particular compromise to the frontal lobes with relative sparing of the temporal lobes. Most studies on PD agree in implicating varying degrees of frontal lobe involvement in the cognitive deficits of Parkinsonian patients.

Tests of executive ability are often used in the assessment of frontal lobe function. However, patients in the study by Mohr et al. (1990) failed to evidence deficits in the executive realm. This finding is rather surprising given the consistent impairment found in most studies of nondemented patients with PD. While these results suggest preserved functional integrity of the frontal lobes in nondemented Parkinsonian patients, it could be argued that other factors accounted for the absence of executive deficits in this particular subpopulation.

According to Mohr et al. (1990), the selection criteria employed in their study may have contributed to the preservation of executive skills in their patients. High-functioning patients may thus form a subset of the Parkinsonian population without executive deficits. However, since executive functions encompass various components measured by different tasks (Taylor et al., 1986), it is possible that high-functioning Parkinsonian patients experience selective impairments in executive ability which may not have been ascertainable with the tasks employed by Mohr et al. (1990).

These authors administered the WCST (Heaton, 1981) as well as the Mental Control subtest of the WMS (Wechsler, 1945) and the Initiation and Conceptualization subtests of the Mattis Dementia Rating Scale (DRS, Mattis, 1976). Since performance on the WCST has often been reported to be impaired in nondemented patients with PD, the lack of such deficient performance in high-functioning patients may reflect a relative insensitivity of the WCST to this particular patient population. This insensitivity may be even more pronounced with high-functioning individuals since performance on the WCST has been reported to be strongly related to IQ (Taylor et al., 1986) and to the level

of education (Beatty et al., 1989). Nondemented Parkinsonian patients also frequently exhibit deficits of other executive skills, such as planning and sequencing. These executive components have not yet been assessed in high-functioning patients with PD.

Study Purpose and Hypotheses

Therefore, while the study by Mohr et al. (1990) supports the notion of a consistent impairment of cognitive function in PD, certain questions remain unanswered. Although it has been suggested that effortful episodic memory processes are impaired in high-functioning Parkinsonian patients, it is not known whether other memory functions are compromised. The physiological changes in PD, particularly at the level of the caudate nucleus, might have implications for memory functions associated with the PFC since this region constitutes the cortical destination of efferent pathways from the caudate. It also remains unclear whether high-functioning Parkinsonian patients do not sustain executive deficits in general, since many executive components were not assessed in the study by Mohr et al. (1990). To obtain a clearer picture of frontal lobe function in the absence of dementia in PD, this study examined executive skills, notably the ability to form, maintain, and shift sets, as well as cognitive sequencing, in nondemented, high-functioning patients with PD. High-functioning individuals were chosen because, among the PD population, they were deemed relatively least likely to evidence neuropsychological deficits. A secondary objective of this investigation was to explore the potential relationship between temporal memory function and sequencing ability in this illness, since a possible sequencing deficit could account for the decreased temporal memory function usually observed in nondemented Parkinsonian patients.

It was hypothesized that the functional integrity of the DLPFC may be compromised in high-functioning nondemented patients with PD. This hypothesis was based on the conceptual framework developed by Alexander et al. (1986, 1990), in which this area of the frontal lobes constitutes the cortical destination of efferent pathways from

the caudate nucleus, a subcortical structure shown to undergo physiological changes in PD (Holthoff-Detto et al., 1997; Kish et al., 1988). Furthermore, nondemented Parkinsonian patients frequently demonstrate neuropsychological deficits similar to those seen in patients with lesions to the DLPFC (e.g. Bondi et al., 1993; Cooper et al., 1991; Taylor et al., 1986), including impairment of executive functions and selective aspects of memory function. Given the pathophysiology of PD, the patient group was expected to perform significantly worse than the normal control group on the following tests: WCST (Heaton, 1981), Digit Ordering, Backward Digit Span (Wechsler, 1981), Picture Arrangement (Wechsler, 1981), word sequencing, temporal ordering, recency discrimination, and WMS-R (Wechsler, 1987) subtests assessing recall of stimuli (Logical Memory and Visual Reproduction). On the other hand, the patient group's performance on cued recall and recognition tests was expected to be comparable to that of the normal control group since performance on such tests is usually associated with temporal lobe function (Poldrack & Gabrieli, 1997; Shimamura et al., 1991). Therefore, no group differences were expected on the Figural Memory, Verbal Paired Associates, and Visual Paired Associates subtests of the WMS-R, nor on the recognition component of the recency discrimination and temporal ordering tasks.

It was hypothesized that the PD group would have temporal memory deficits. High-functioning Parkinsonian patients reportedly experience deficits on tests of free recall requiring search and retrieval strategies (Mohr et al., 1990) thought to be mediated by the DLPFC (Poldrack & Gabrieli, 1997; Shimamura et al., 1991); these processes and cortical region have been postulated to play a role in temporal memory (Milner & Petrides, 1984; Milner et al., 1985, 1991; Moscovitch, 1992). Performance on temporal memory tasks has been correlated with other measures of frontal lobe function (Cooper et al., 1993). It was also anticipated that this patient group evidences temporal memory deficits because several studies have reported deficient performance by nondemented Parkinsonian patients on temporal memory tasks (e.g. Bondi et al., 1993; Gabrieli, 1996;

Vriezen & Moscovitch, 1990). Specifically, this patient group was expected to perform more poorly than the normal control group on the word sequencing, temporal ordering, and recency discrimination tests.

It was hypothesized that the temporal memory deficits observed in the patient group are not solely due to an impairment of memory but also stem from a broader impairment of cognitive sequencing. These two types of deficits are thought to be related since both cognitive sequencing and temporal memory function require the organization/ordering of information (Vriezen & Moscovitch, 1990). Cognitive sequencing deficits have been reported in nondemented patients with PD (e.g. Sullivan et al., 1989), some of whom were high-functioning (Ogden et al., 1990) and such deficits have been correlated with deficient performance on a temporal memory task (Cooper et al., 1993). Thus, performance by the patient group on the word sequencing, temporal ordering, and recency discrimination tasks was expected to be significantly correlated with their performance on the Backward Digit Span (Wechsler, 1981), Digit Ordering, and Picture Arrangement (Wechsler, 1981) tests.

Method

Participants

Patients with Parkinson's Disease

Twenty consecutive outpatients (18 men, 2 women) from the Parkinson's Disease Clinic of the Ottawa Civic Hospital, diagnosed with idiopathic PD, were recruited. The diagnosis, made by a neurologist at the clinic, was based on the presence of at least two of the three cardinal motor signs, namely bradykinesia, resting tremor, and rigidity, and on the absence of any known cause of secondary Parkinsonism.

Patients were identified by a review of medical records. Only those who had sought medical assistance on the sole basis of the motor dysfunction associated with the illness were considered to be eligible. A history of cranial neurosurgery, the presence of pseudoparkinsonian features or clinically significant adverse effects of antiparkinsonian medications, and the intake of anticholinergic agents eliciting significant effects centrally served as exclusion criteria. Patients whose motor symptoms were insufficiently controlled to allow the execution of neuropsychological tests requiring manual manipulation were also excluded.

Patients had a mean age of 62.0 ($SD = 7.7$) and all but one were right-handed. They had an average of 18.2 years of education ($SD = 2.3$). Scores obtained from the Vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R, Wechsler, 1981) were commensurate with high premorbid intellectual resources ($M = 61.4$, $SD = 6.2$; see Table 1). Patients had a mean duration of illness of 8.9 years ($SD = 5.7$). Severity of motor symptoms ranged from 8.0 to 53.5 on the Unified Parkinson's Disease Rating Scale (UPDRS, Fahn et al., 1987), a quantitative measure of clinical motor disability, including akinesia, rigidity, tremor, and paucity of movement (see Appendix A). Higher scores indicate greater symptom severity. Patients were in the early or middle stage (I to III) of the disease based on the Modified Hoehn and Yahr Staging Scale (Fahn et al., 1987; see Appendix B). Thus, they had either unilateral or bilateral

involvement, with only one patient demonstrating some postural instability while remaining physically independent. At the time of testing, patients were optimally medicated and received antiparkinsonian dopaminergic treatment. None were treated with anticholinergic medications. The clinical features of individual patients are listed in Appendix C.

Normal Controls

Twenty healthy right-handed control subjects (15 men, 5 women), matched for age ($M = 61.7$, $SD = 8.8$) and years of education ($M = 18.1$, $SD = 1.6$), were also involved in the study. With an average Vocabulary score of 63.6 ($SD = 4.1$), the estimated premorbid intelligence level of the control group was high and comparable to that of the patient group (see Table 1). Half of the normal control group consisted of acquaintances and of one relative of the principal investigator. Five subjects were friends of patients who participated in the study and one was a spouse. The remaining four controls were recruited with public advertisements.

General Description of Participants

Participants were high-functioning individuals. This inclusion criterion was defined by the fulfillment of at least one of the following criteria: (a) pursuit of university studies and completion of at least a Bachelor's degree and/or (b) engagement in a professional capacity, past or present, involving either direct or indirect supervision of others (e.g. lawyer, teacher, manager). Someone who met solely the latter criterion was given the equivalency of a Bachelor's level university education since successful performance in a senior level employment position requires a relatively high level of intellectual competency. About half of participants were still employed whereas all others, although retired, remained involved in various committees or groups. Appendix D gives the educational and professional background of each subject.

Individuals who fulfilled DSM-IV (1994) criteria for dementia were excluded. In addition, the Mini-Mental State Examination (MMSE, Folstein, Folstein, & McHugh,

1975) served as a brief quantitative screening tool for dementia. The severity of cognitive dysfunction is revealed by lower scores on the MMSE. Most clinical trials for anti-dementia agents currently utilize a cut-off score of less than or equal to 26 as indicative of dementia sufficient for inclusion in the trials. Accordingly, the current study excluded individuals with MMSE scores of less than or equal to 26. However, all subjects scored within the 28-30 range. Errors occurred in the areas of memory, time orientation, and attention.

Subjects who met criteria for the clinical diagnosis of depression based on the Geriatric Depression Scale (GDS, Brink et al., 1982) were also excluded. This self-report rating scale, designed specifically for and standardized on an older population, has the least amount of overlap with PD symptoms within established depression scales. The GDS mainly assesses cognitive and affective symptoms of depression, with few somatic items that could relate directly to the Parkinsonian patient's physical disability. This scale uses a forced-choice format requiring the subject to respond either "yes" or "no" to each of 30 items. Response bias is controlled by reversal of question wording; therefore, the response that indicates depression is scored with 1 and the other is 0. A total score out of 30 indicates severity of depression, with 10 or less being normal, 11-20 reflecting mild depression, and a score greater than 20 suggesting moderate to severe depression. Patients and controls obtained similar scores on this scale ($M = 4.2$, $SD = 2.7$ and $M = 3.7$, $SD = 3.3$, respectively).

Additional exclusion criteria included a history of major psychiatric illness, alcoholism, head injury, cardiovascular accident or other central nervous system (CNS) disorder, with the exception of PD, and significant vision or hearing-related difficulties which could interfere with subjects' ability to complete the assessment. Participants with a pre-existing medical condition (e.g. hypertension, diabetes) were included in the study only if the condition was adequately controlled.

One patient was excluded as a result of failing the screening for depression. There were no withdrawals from the study. Subjects initially provided written informed consent (see Appendix E) and no compensation was offered to them.

Materials and Neuropsychological Measures

Outcome measures were categorized into four groups: (a) tests of temporal memory; (b) tests of executive functions, including cognitive sequencing skills; (c) a test of episodic memory; and (d) a test of intellectual ability.

Word Sequencing Task

The word sequencing task allows the assessment of temporal order memory. The procedure follows the one used by Shimamura et al. (1990) with frontal lobe and amnesic patients. Fifteen common words printed individually on 4 x 6 in. white index cards were presented in a different random order to each subject at a rate of 3 s per word. The words selected (see Appendix F) contained one or two syllables and had a frequency of occurrence of at least 20 per million ($M = 162$, range = 28-492) in the English language (Kucera & Francis, 1967). Subjects were instructed to read each word aloud and to remember the order in which the words appeared. Appendix G provides verbatim instructions given to participants.

Immediately following presentation of the last item, a duplicate set of word cards were randomly placed in a two-dimensional array on the table in front of the subject. This duplicate set served to ensure that the word cards were indeed randomly arranged and prevented the use of extraneous cues (such as bent cards) to aid performance. Subjects were instructed to rearrange the words in their original order of presentation and were awarded as much time as needed to complete the task. The ability to remember the sequential order of the words was determined by calculating a Spearman rank order correlation between the presentation sequence of the words (the actual order of item presentation) and the order recalled by the subject (perfect score = +1.0). A sample

scoring sheet can be found in Appendix H. The possibility of short-term memory rehearsal of the word presentation sequence was reduced by giving subjects instructions between the study and test phases. Since two other tasks, notably temporal ordering and recency discrimination, assessed item memory, no recognition test was administered.

Temporal Ordering Task

Temporal ordering tasks have been specifically designed as research tools to study memory for the temporal order of sequentially presented items. They require subjects to reconstruct from memory the order in which a series of stimuli are presented. The procedure followed in this study was based on the temporal ordering task developed by Vriezen and Moscovitch (1990). Three sets of nine drawings were constructed; the first served for recall of temporal order, the second for target recognition, and the third as distracters for the recognition task. The three sets of stimuli were randomly distributed among these conditions and counterbalanced within each group as much as possible.

For the temporal ordering task, subjects were presented with nine consecutive line drawings of common objects (Snodgrass & Vanderwart, 1980) mounted on 4 x 6 in. white index cards. Subjects were instructed to remember the order of presentation of the drawings, which were introduced at a rate of one every 3 s. After naming each object to ensure its correct perception, participants engaged in a distracting task for 3 min to prevent rehearsal of the material. They were presented with a similar series of drawings and indicated whether the notion of “man-made” or “part of nature” best applied to the object represented. Subjects were then shown a duplicate set of cards depicting the original drawings. Cards within each series were always introduced in the same order. The restriction that no drawing occupy the same position as it did originally or immediately follow the same stimulus it succeeded when initially presented determined the order of card presentation. Subjects were instructed to rearrange the drawings in their original presentation sequence (see Appendix I). No time limit was imposed.

For the delayed recognition task, subjects were shown nine drawings, different from the ones introduced during the temporal ordering task, at a rate of one every 3 s. Again, subjects named each object and then performed the same distracting task described earlier. Pilot testing conducted by Vriezen and Moscovitch (1990) reveals that with a 3-min distracting activity, performance on the recognition trial falls between chance and ceiling levels. After 3 min, subjects were presented with 18 consecutive cards depicting nine new representational drawings (distracters) randomly interspersed among the nine target items presented immediately prior to the distracting activity. For each drawing, subjects indicated whether or not it had been seen previously. The recognition test allowed for a comparison between memory for item content and temporal order.

The three sets of picture stimuli used for the temporal ordering and recognition components were drawn from the same semantic categories (see Appendix J). The degree of familiarity of the objects depicted ranged from 2.92 to 4.82 out of 5 ($\underline{M} = 4.04$, $\underline{SD} = .59$) whereas image agreement ranged from 2.59 to 4.62 out of 5 ($\underline{M} = 3.83$, $\underline{SD} = .57$) based on the norms established by Snodgrass and Vanderwart (1980). Image agreement refers to how closely each picture corresponds to subjects' mental representation of the object.

For the temporal ordering task, several scores were calculated, the most important being a Spearman rank-order correlation between the positions of the drawings upon presentation and recall. This measure reflects memory for the presentation order of the drawings. The two other measures recorded include (a) an absolute deviation score based on the sum of the distance between each item's presentation and recall position across the nine drawings and (b) a relative deviation score based on the sum of the distance between each item's presentation position and the presentation position of the items placed before or after it upon recall across the nine drawings.

A corrected recognition score was computed by subtracting the number of false positive scores from the number of hits. Hits are described as items that are correctly

recognized as having been presented previously. Conversely, false positive errors are new items that are falsely identified as having been presented earlier. Appendix K provides a sample scoring sheet for the temporal ordering and recognition tests.

Recency Discrimination Task

Recency discrimination tasks have been repeatedly utilized in research settings to compare temporal and content memory. Specifically, these tasks allow the dissociation of cognitive processes involved in recognizing previous events and making judgements of temporal order (Sagar et al., 1988b). The recency discrimination task administered in this study parallels the one employed by Milner et al. (1991).

Subjects first engaged in a practice series to familiarize themselves with the task. They were given a booklet of 16 cards, each bearing two proper names (e.g. John-Mary). In this set of cards, there were 10 white inspection cards (I) and six blue response cards (R). The first five cards within the stimulus booklet were inspection cards, followed by an alternation of response and inspection cards (i.e. I I I I I R I R I R I R I R). When presented with inspection cards, subjects read the words aloud and tried to remember them and their order of appearance. Response cards resembled inspection cards except for a question mark placed between the two words. These response cards served as either content recognition or recency discrimination tests. The former involved the simultaneous presentation of a previously presented word and a foil and required subjects to judge which word was seen before. For the recency discrimination test, subjects had to choose which of the two words was seen most recently. Subjects were blinded to the type of test to be performed when confronted with individual response cards. Instructions were almost identical to those formulated by Milner et al. (1991) (see Appendix L).

For the recency discrimination task, subjects were given a booklet of 184 cards (4 x 6 in.) on which were inscribed two words, one above the other. The words were drawn from the same source as those used by Sagar et al. (1988b) for their version of the recency discrimination task. They contained four to six letters and had a frequency of

occurrence of at least 25 per million in the English language (Kucera & Francis, 1967; see Appendix M).

The booklet was composed of 95 white inspection cards and 89 blue response cards. The first seven cards in the booklet were inspection cards; response and inspection cards alternated thereafter. The task was self-paced. However, to avoid unnecessary frustration and to promote concentration on the task, the experimenter turned over the cards if this proved difficult for the patient.

Of the 89 response cards, 60 assessed recency discrimination whereas only 29 tapped content recognition. The number of words separating the original presentation of a word and its appearance on a recognition trial were as follows: 4, 8, 16, or 32. Each stimulus-test interval was represented equally often during the recognition test, with the exception of one interval. The same intervals separated the original occurrence of a word from its presentation on a recency discrimination trial, with one additional interval: 4, 8, 16, 32, or 128. Therefore, the number of words separating the original presentation of the two stimuli to be compared (i.e. 4, 8, 12, 16, 24, 28, 96, 112, 120, 124) yielded 10 different combinations of recency levels (4 vs. 8; 4 vs. 16; 4 vs. 32; 4 vs. 128; 8 vs. 16; 8 vs. 32; 8 vs. 128; 16 vs. 32; 16 vs. 128; 32 vs. 128). Thus, six instances of each of the 10 combinations of stimulus-test intervals were presented in a fixed random order. No word appeared more than once on a response card to reduce the possibility of proactive interference from the repeated presentation of a single stimulus in different pairings. Furthermore, the correct response was randomly and equally often the top or the bottom word on the card for both the recency and recognition trials.

As illustrated in Appendix N, the number of correct recency discriminations made at each combination of stimulus-test intervals was calculated for each subject. On the other hand, only the total number of correct answers to the recognition trials was computed since this task component constituted solely a control measure.

Wisconsin Card Sorting Test (WCST)

The WCST (Heaton, 1981) is perhaps the most established neuropsychological test of executive function. It taps shifting and maintenance of set, abstract concept formation, and the ability to profit from feedback. This test has been shown to be sensitive (although not specific) to frontal lobe dysfunction, particularly following lesions to the dorsolateral prefrontal cortex (Milner, 1964). The WCST was thus thought to be a useful tool to assess the hypothesis of frontal system disruption in high-functioning Parkinsonians. Impairments on this test by nondemented and nondepressed patients with PD have been reported by several studies (e.g. Bondi et al., 1993; Cooper et al., 1991).

Using the Milner (1964) 128-card version of the test, subjects were given two decks of 64 response cards and were instructed to match each of the cards to one of four stimulus cards laid out on a table in front of them. These stimulus cards were placed from left to right (from the subject's point of view) in the following order: one red triangle, two green stars, three yellow crosses, and four blue circles. Similarly, one to four identical designs, colored either red, green, yellow, or blue, were depicted on each deck card. The cards could thus be matched along three dimensions: color, geometric form, and number of designs.

However, at any given time, response cards could be matched correctly along one sorting criterion only. No cues as to the matching principle were offered but subjects were told whether they were right or wrong upon each card placement. They were required to use this information to guide their next move. However, the correct matching principle shifted without warning after 10 consecutive correct responses. The WCST (Heaton, 1981) was administered until all six sorting categories (color, form, number, color, form, number) had been completed or until all deck cards had been placed under the stimulus cards. Where motor symptoms interfered with a patient's ability to pick up

deck cards, these were handed to him(her) by the experimenter to avoid unnecessary frustration and to keep the patient's attention focused on the task.

Performance was scored by computer according to the method of Heaton (1981). The following scores were of interest for this study: (a) the number of categories completed, (b) the number of perseverative errors, and (c) the number of trials to achieve the first category.

Picture Arrangement Subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R)

Picture Arrangement assesses an executive skill, cognitive sequencing, by tapping the ability to order multiple events chronologically in order to form a logical story-line. This WAIS-R subtest (Wechsler, 1981) consists of 10 sets of cartoon pictures which can be sequenced to depict a story. For each item (or set), a series of three to six pictures were placed on the table in front of subjects in a predetermined, mixed-up order. Subjects were then instructed to rearrange the cards from left to right in an order that tells a coherent story. Card sets were presented in a fixed order of increasing difficulty and all 10 items were administered to all subjects. No time limit was imposed in order to provide an adequate appraisal of cognitive sequencing ability unaffected by the motor deficits of Parkinsonian patients. A total score out of 20 points was derived according to standardized procedures.

Backward Digit Span Subtest of the WAIS-R

Sequencing ability is also necessary for successful performance on Backward Digit Span, which is a subtest of both the WAIS-R (Wechsler, 1981) and the Wechsler Memory Scale-Revised (WMS-R, Wechsler, 1987). Backward Digit Span specifically involves the cognitive manipulation and ordering of digits, placing additional demands on mental tracking and working memory.

Backward Digit Span requires subjects to memorize a sequence of digits (e.g. 5-3-9-4-1-8) and to repeat them in the reverse order (in this example, 8-1-4-9-3-5). Since

sequences range from two to eight digits in the WAIS-R version (Wechsler, 1981), compared to the two to seven digit sequences of the WMS-R (Wechsler, 1987), only the former was administered. Digits were read at the rate of one digit per second. Two examples were provided before subjects undertook the task, which was discontinued after failure on both trials of any item. A maximum score of 14 points could be obtained on Backward Digit Span based on standardized scoring procedures.

Digit Ordering Test

Digit Ordering (see Appendix O) has been described as a measure of executive ability, particularly of cognitive sequencing, and of working memory (Cooper et al., 1993). This study follows the procedure employed by Cooper et al. (1991) with nondemented Parkinsonian patients. On each of 15 trials, subjects were read a random selection of seven digits (e.g. 1-6-4-1-3-9-3) at the rate of one digit per second and were asked to rearrange the items in memory in order to repeat them in ascending fashion (in this example, 1-1-3-3-4-6-9). Digits were chosen to appear with similar frequency.

For each trial, one point was awarded for each digit correctly positioned within the ascending sequence, until a digit was given which broke this sequence. A digit that did not come from test presentation, but nonetheless maintained the ascending order, was accepted but not scored. Whenever more than seven digits were reported within a trial, only the first seven responses were scored. A score out of 7 was obtained for each of the 15 trials for a maximum score of 105 points for the entire task.

Wechsler Memory Scale-Revised (WMS-R)

The WMS-R (Wechsler, 1987) provided a general measure of memory capacity. Selected subtests from this standardized assessment battery allowed the evaluation of immediate memory for meaningful and abstract material presented in the verbal or visual modality. Two separate composite or index scores, Verbal Memory and Visual Memory, were calculated. Their sum yielded the General Memory Index (or Memory Quotient

[MQ]) which has a mean of 100 and a standard deviation of 15. Age is taken into account in the determination of index scores.

The following subtests were administered: (a) Figural Memory, which taps immediate visuospatial pattern recognition memory; (b) Logical Memory I, which evaluates immediate recall of stories; (c) Visual Paired Associates I, which assesses immediate recall and learning of visual paired associates; (d) Verbal Paired Associates I, which assesses immediate recall and learning of verbal paired associates; and (e) Visual Reproduction I, which measures immediate recall of geometric designs.

Vocabulary Subtest of the WAIS-R

Vocabulary is the WAIS-R subtest (Wechsler, 1981) which is thought to give the relatively best indication of premorbid intellectual functioning. Evidence suggests that performance on this task remains unchanged in the Parkinsonian population (Mohr et al., 1990; Taylor et al., 1986). Given its low sensitivity to bilateral or diffuse brain injury (Lezak, 1995, p. 540) and its high correlation with the full scale WAIS-R IQ, Vocabulary served to demonstrate the intellectual equivalence of patients and normal controls and to further substantiate the recruiting criterion. A list of 35 words were read, as well as shown, to subjects who attempted to define each word. A neutral inquiry was made when in doubt as to whether or not subjects knew the meaning of a word or when a response was unclear or too vague to be scored. Test administration began with the fourth word but if any of items 4 to 8 were failed, items 1 to 3 were given. Performance was scored according to the guidelines provided in the WAIS-R manual for a maximum of 70 points.

Procedure

The research protocol was approved by both the Research Ethics Committee of the Ottawa Civic Hospital and Carleton University. Potentially eligible patients were contacted by phone by the clinic nurse or by the principal investigator or else a Parkinson's Clinic neurologist briefly described the study upon a patient's regular clinic

visit. When the initial contact was made by a nurse or by a physician, the principal investigator then called those who were interested in participating to schedule appointments and to provide further information.

Patients with PD and control subjects were individually assessed by the same experimenter. After participants provided written informed consent and had the opportunity to ask questions, screening was undertaken by the principal investigator. The MMSE (Folstein et al., 1975) and the GDS (Brink et al., 1982) were completed to rule out the presence of dementia and depression, respectively. Demographic information was then collected from all subjects. The medication regimen of patients was additionally recorded and their current motor status was rated by the clinic nurse using the motor examination section of the UPDRS (Fahn et al., 1987). The nurse also assessed the stage of motor disease based on the Modified Hoehn and Yahr Staging Scale (Fahn et al., 1987). The interval between the neurological rating and neuropsychological testing varied from the same day to three months.

If screening was successful, the principal investigator administered the nine neuropsychological tasks assessing general executive functions, sequencing ability, temporal memory, episodic memory, or intellectual function. Tests were presented in the following order: (a) recency discrimination task, (b) WCST (Heaton, 1981), (c) word sequencing task, (d) Digit Ordering Test, (e) WMS-R (Wechsler, 1987), (f) Backward Digit Span subtest of the WAIS-R (Wechsler, 1981), (g) Picture Arrangement subtest of the WAIS-R, (h) temporal ordering task, and (i) Vocabulary subtest of the WAIS-R. By following this test sequence, memory and executive function tasks were alternately administered, providing a change in task demands in an effort to maintain an optimal level of subject interest. Furthermore, the last task administered did not place demands on memory processes since performance on memory tests may be compromised by fatigue in subjects completing all tasks within a single testing session. Although all subjects were bilingual, tests were administered in French when available.

The testing session, including screening, lasted approximately two hours. Most participants completed the tests in a single session but a few subjects in each group required two sessions due either to fatigue or to time constraints. Some PD patients treated with L-dopa manifest marked fluctuations in motor functions, ranging from normal or near-normal (on) to severe disability (off). Since severe motor disability could confound the results, patients were tested at times of the day when they functioned optimally (in the “on” state) according to their self-reports. The tests were usually administered at subjects’ home although sessions were held at the clinic for six of the patients and for two controls.

Statistical Data Analysis

The Statistical Package for the Social Sciences (SPSS, version 6.1) was utilized to run the analyzes. Table 1 provides the means and standard deviations obtained by each group on screening measures, notably on age, years of education, MMSE (Folstein et al., 1975), and GDS (Brink et al., 1982). Twenty scores obtained on tasks assessing temporal memory, episodic memory, executive skills, and premorbid intellectual function constituted the outcome measures. Group membership (control subjects and PD patients) was the independent variable for univariate inferential statistics performed on the group means of each outcome measure.

Prior to analysis, the 20 dependent variables were examined for accuracy of data entry, missing values, and fit between their distributions and the univariate assumptions. Since statistical analyses are performed on grouped data, data screening was carried out for each group separately. The normality assumption was verified using the Shapiro-Wilks test (Norusis, 1994) whereas homogeneity of variance was assessed with the Levene test (Levene, 1960). Outliers, defined as data points lying at least 2.5 standard deviations from the average value for a dependent variable, were sought within each group.

Univariate two-tailed t-tests for two independent samples were used to identify reliable differences among the group means on all outcome measures with the exception of the recency discrimination task. Although the univariate assumptions were violated for certain dependent variables, the t statistic has been reported to be robust to deviations from normality (Stevens, 1995, p. 240). It has also been shown to be relatively robust to violations of the assumption of homogeneity of variance, especially when t-tests are two-tailed and performed on equal sample sizes (Stevens, p. 238). Thus, no transformations were applied to the data. The Mann-Whitney test served to corroborate the results obtained through standard parametric analyses for the dependent variables whose distribution violated the univariate assumptions (see Appendix P).

T-tests were run both with and without the outliers, to ascertain that the significance or non-significance of results was not overly determined by the outlier(s) but represented most of the data. This approach to dealing with outliers was preferred over data transformation since the latter can render the interpretation of results quite difficult.

The alpha level was set at .05 for each of 14 analyses but the remaining six t-tests were each carried out with an alpha of .10. These levels of significance were chosen partly because of the low power associated with a sample size of 20 subjects per group. The sample size was small due to the nature of the patient population and the inclusion criteria. However, it was equivalent or superior to the sample sizes drawn in many studies on PD (e.g. Bondi et al., 1993; Ogden et al., 1990; Sagar et al., 1988). With a sample size of 20, a more stringent alpha level (e.g. .01) would lead to a reduction of power, in which case even substantial differences in the population might not be detected. It was therefore concluded that an alpha level of .05 or .10 provides a good balance between the probability of type I and II errors.

Whenever group means were not expected to differ on a dependent variable based on previous findings, an alpha level of .10 vs. .05 was used to evaluate the significance of the differences. When no group differences were expected, type II error was a greater

concern than type I error. The probability of making a type II error, that is not detecting a difference in the sample when there is one in the population, is lower if an alpha level of .10 is used since type I and II errors are inversely related. In other words, the adjusted alpha level increases power and thus guards against the possibility of not detecting a difference between the groups because of low power rather than because of a lack of such a difference in the population. Given that this is an exploratory study, power is of great importance. Thus, power and effect size analyses were carried out for all dependent variables but particular attention was paid to their outcome when similar group performance was anticipated.

Temporal memory and executive functions, including cognitive sequencing, have often been found to be impaired in nondemented Parkinsonian patients (Bondi et al., 1993; Cooper et al., 1993; Fisher et al., 1990; Vriezen & Moscovitch, 1990). Therefore, group means were compared with an alpha level of .05 on the following tests: word sequencing, temporal ordering (rank-order correlation, absolute deviation, and relative deviation score measures), Picture Arrangement (Wechsler, 1981), Backward Digit Span (Wechsler, 1981), Digit Ordering, and WCST (number of categories completed, number of perseverative errors, and trials to achieve the first category; Heaton, 1981).

Within groups of nondemented Parkinsonian patients, the dissociation often found between performance on (1) free recall measures requiring self-generated search and retrieval strategies and on (2) cued recall and recognition measures (e.g. Mohr et al., 1990; Taylor et al., 1986, 1990) suggested that groups may differ only on the Logical Memory and Visual Reproduction subtests of the WMS-R (Wechsler, 1987). Group means on each of these subtests were thus compared with alpha level set at .05, as were the groups' average MQs. On the other hand, mean scores on the Figural Memory, Visual Paired Associates, and Verbal Paired Associates subtests were submitted to inferential analyses with alpha adjusted to .10 since no group differences were expected on these

subtests. This alpha level was also used to test for mean group differences on the recognition component of both the temporal ordering and recency discrimination tasks.

The t-test comparing patients and controls' mean scores on Vocabulary (Wechsler, 1981) was also analyzed with alpha adjusted to .10. Groups were not expected to differ on this task since it is relatively insensitive to the effects of brain injury (Lezak, 1995, p. 540).

Performance on the recency discrimination task was originally analyzed using a repeated measures analysis of covariance (ANCOVA), with performance on the recognition trials as a covariate. This was based on findings of a significant effect of item recognition on recency judgments (Milner et al., 1991). ANCOVA was thus used to test whether, after adjusting for the effects of recognition, there were any significant group differences in recency judgments. In this ANCOVA, there was one between groups (BG) factor (group) with two levels (patients and controls) and one within subjects (WS) factor (combination of recency levels) with 10 levels (4 vs. 8, 4 vs. 16, 4 vs. 32, 4 vs. 128, 8 vs. 16, 8 vs. 32, 8 vs. 128, 16 vs. 32, 16 vs. 128, 32 vs. 128). A single recognition score was computed for each subject by summing the scores obtained on the four stimulus-test intervals (4, 8, 16, and 32).

Although the primary objective of this study concerned the assessment of temporal memory and executive skills in high-functioning Parkinsonian patients to provide a clearer picture of frontal lobe function in the illness in the absence of dementia, a secondary goal was to investigate the relationship between temporal memory deficits and other cognitive impairments in Parkinsonian patients. It was hypothesized that the patients' performance on the tests of temporal memory would be correlated with their performance on cognitive sequencing tests since both processes depend on the integrity of the frontal lobes (Stuss & Benson, 1984, 1986) and require the temporal organization of information (Vriezen & Moscovitch, 1990). Furthermore, deficits in these cognitive

abilities have previously been found to be correlated in nondemented Parkinsonian patients (Cooper et al., 1993).

To test this hypothesis, Pearson Product-Moment correlations were carried out between Parkinsonian patients' performance on temporal memory tasks and on cognitive sequencing tests. Since there are three temporal memory tasks, one of which yields three scores, and three cognitive sequencing tests, 15 correlations were performed. This particular correlation matrix was examined for significance with alpha level set at .05 for the set of correlations. Each correlation was therefore considered to be significant only if $p < .003$. Use of this Bonferroni test statistic approach controlled for type I error.

While it is generally accepted that executive functions are subserved by the frontal lobes, this relationship is less certain in the case of temporal memory function. In patients with frontal lobe injury or with Parkinson's disease, impairment on temporal memory tasks has been found to be related to poor executive function performance on the WCST (Heaton, 1981), a well-established measure of frontal lobe functioning (Cooper et al., 1993). Assessment of the relationship between performance on the WCST and on temporal memory tasks may thus lend some support to the notion of frontal lobe involvement in temporal memory function.

To test this hypothesis, Parkinsonian patients' performance on temporal memory tasks was correlated with their scores on the WCST (Heaton, 1981) measures. Since there are five dependent variables for the temporal memory tasks and three dependent variables for the WCST, this analysis yielded 15 correlations. The Bonferroni test statistic was again utilized to adjust the overall alpha level to .05 for the number of correlations being performed.

This study is of an exploratory nature in its attempt to determine the relationship between temporal memory deficits in Parkinsonian patients and executive dysfunction, particularly with respect to cognitive sequencing. Correlations whose probability values were greater than .003 and thus did not meet the stringent Bonferroni criterion were

nevertheless examined to see if they were associated with a probability value inferior or equal to .05.

Correlational analyses were run between Parkinsonian patients' scores on neuropsychological tasks and their motor disability scores, disease stage, and disease duration (see Table 3). Previous studies have generally failed to detect a significant relationship between disease stage and duration and performance on neuropsychological tests (e.g. Bondi, Kaszniak, Bayles, & Vance, 1993; Mohr et al., 1990; Taylor, Saint-Cyr, & Lang, 1986), including both temporal memory and sequencing tasks (Beatty & Monson, 1990; Cooper et al., 1993; Fisher et al., 1990). The lack of an association between the motor and cognitive symptoms of PD supports the neuroanatomical model developed by Alexander et al. (1986), which postulates the existence of structurally and functionally (e.g. motor/cognitive) parallel frontal-subcortical circuits. Since the variables relating to the motor aspects of the disease were not expected to influence performance on neuropsychological tests, the significance level was set at .10.

Results

Data Screening

Data screening procedures revealed that seven out of the 20 neuropsychological test variables were non-normally distributed in either or both the patient and control groups ($p < .01$). Non-normality was found for the rank-order correlation, absolute deviation, and recognition scores of the temporal ordering task, for the three WCST (Heaton, 1981) measures, and for the Vocabulary subtest of the WAIS-R (Wechsler, 1981). The homogeneity of variance assumption was violated for three dependent variables, notably for perseverative errors and categories completed on the WCST as well as for Visual Reproduction (Wechsler, 1987) ($p < .001$).

Data screening also revealed the presence of nine outliers among the 800 individual data points. Outliers were detected on the following tests: Backward Digit Span (Wechsler, 1981), Digit Ordering, Figural Memory (Wechsler, 1987), temporal ordering (absolute and relative deviation measures), WCST (categories completed and perseverative errors; Heaton, 1981), and Vocabulary (Wechsler, 1981). Two outliers were found within the patient group and seven belonged to the normal control group. T-tests were re-run with the outlier data points removed from the analysis. Since no differences were noted in the pattern of results, outliers remained in the analyses. The only exception to this was the rank-order correlation measure of the temporal ordering task, on which a trend became significant once an outlier was removed from the analysis. Two sets of results are thus reported for this measure of temporal memory, including and excluding the outlier.

Inferential Statistics

Table 2 summarizes the results obtained by the patient and control groups on each of the neuropsychological tests and provides the significance level of observed differences. Non-parametric analyses produced the same pattern of results (see Appendix

P). Power analysis yielded low to high power, even within each conceptual category. With the alpha level set at .05, power ranged from .04 to .77 whereas it increased slightly when alpha was .10 (.18 to .81). Effect sizes were also quite variable, ranging from 0 to .15.

Temporal Memory

Contrary to prediction, no group differences were found on the word sequencing task ($t(1,38) = 1.83, p = .074$). However, two of the three measures derived from the temporal ordering task yielded significant results. The mean absolute deviation score obtained by the patient group was significantly higher than that observed in the control group ($t(1, 38) = -2.17, p = .036$). Similarly, group performance differed on the relative deviation measure ($t(1, 38) = -2.15, p = .038$). There was a trend for the patient group to obtain lower rank-order correlations on the temporal ordering task compared to the normal control group ($p = .054$). When the analysis was re-run without the outlier from the normal control group, group differences on this measure of temporal memory became highly significant ($t(1, 37) = 2.78, p = .009$).

The repeated measures ANCOVA performed on the recency discrimination task (using the recognition measure as the covariate) failed to show any effect of item recognition on recency judgments. Indeed, item recognition accounted for only 2% of the variance in recency judgments. A repeated measures analysis of variance (ANOVA) was therefore performed on mean recency discrimination scores of patient and control groups and yielded similar results as the ANCOVA ($p = .337$). Neither the main effect of group nor the group-by-interval interaction reached significance, with an F-ratio inferior to 1.0 in both instances. The main effect of interval was, however, significant. In both groups, performance on the recency discrimination task declined with increasing stimulus-test intervals ($F(9, 342) = 2.96, p = .002$). Therefore, the accuracy of recency judgments increased as a greater number of words separated the original presentation of the two stimuli to be compared.

Executive Functions

As shown in Table 2, no significant group differences emerged on the cognitive sequencing tests. Patients did not differ from normal controls on the Backward Digit Span (Wechsler, 1981), Digit Ordering, and Picture Arrangement (Wechsler, 1981) tests ($p = .570$, $.116$, and $.891$, respectively). On the WCST (Heaton, 1981), the two groups committed a similar number of perseverative errors ($p = .094$). They also did not differ significantly in the number of trials required to achieve the first category ($p = .286$). On the other hand, significant differences were found between the groups on the categories measure of the WCST, with the Parkinsonian patients completing fewer categories than normal controls ($t(1, 38) = 2.28$, $p = .028$).

Episodic Memory

As predicted, the global index of episodic memory derived from the WMS-R (MQ; Wechsler, 1987) revealed significant differences between the patient and normal control groups ($t(1, 38) = 2.29$, $p = .028$). However, no impairment was found on free recall measures for the patient group. Patients and controls did not differ on the verbal test of free recall (Logical Memory) ($p = .259$) although group differences on the visual test of free recall (Visual Reproduction) approached significance ($p = .052$). Cued recall revealed significant group differences in the auditory modality only. Thus, the patient group obtained lower scores than the control group on the Verbal Paired Associates subtest of the WMS-R ($t(1, 38) = 2.56$, $p = .015$) but was not significantly impaired on the Visual Paired Associates subtest ($p = .390$). The Figural Memory subtest, assessing recognition, did not yield significant results ($p = .679$). Although the alpha level was $.10$ for this subtest, power remained very poor ($.18$). Similarly, differences between the groups on the recognition test that followed the temporal ordering task did not reach significance ($p = .150$). On the other hand, Parkinsonian patients recognized fewer words than the normal controls during the recency discrimination task ($t(1, 38) = 2.10$, $p = .043$).

Vocabulary

As predicted, the performance of patients on the Vocabulary subtest of the WAIS-R (Wechsler, 1981) did not differ from that of the normal controls ($p = .191$).

Correlational Analyses

Contrary to prediction, the Parkinsonian patients' group performance on each of the five measures of temporal memory did not correlate with their performance on any of the three cognitive sequencing tests nor with their scores on any of the three WCST (Heaton, 1981) measures with an alpha level of .05.

Table 3 presents the correlations between neuropsychological test performance and clinical variables of Parkinsonian patients. Although the significance of each correlation was assessed with an alpha level of .10, it must be noted that correlations with a probability value between .05 and .10 are regarded as possibly spurious in light of the large number of correlations performed.

Hoehn and Yahr ratings of disease stage (Fahn et al., 1987) were slightly correlated with the Parkinsonian patients' rank-order correlation and absolute deviation scores on the temporal ordering task ($r = .41$, $p = .075$ and $r = .41$, $p = .074$, respectively) as well as with their ability to order series of digits in ascending order (Digit Ordering; $r = -.386$, $p = .093$). Verbal cued recall was also slightly associated with disease stage ($r = -.393$, $p = .086$).

Parkinsonian patients with longer disease duration achieved significantly lower scores on Picture Arrangement ($r = -.580$, $p = .007$), Verbal Paired Associates ($r = -.569$, $p = .009$), Visual Paired Associates ($r = -.615$, $p = .004$), and on the recognition component of the recency discrimination task ($r = -.579$, $p = .007$). The patients' MQ and their scores on the recency discrimination and Visual Reproduction tests were also slightly related to disease duration ($p = .020$, $.035$, and $.039$, respectively). Additionally, there were trends for the duration of PD to correlate with performance on the word

sequencing and Digit Ordering tests as well as with the rank-order correlation and absolute deviation measures of the temporal ordering task ($p = .062, .076, .085$, and $.062$, respectively).

Finally, severity of motor dysfunction of patients showed a slight positive correlation with performance on the Digit Ordering, Verbal Paired Associates, and Vocabulary tests ($p = .033, .015$, and $.035$, respectively).

Discussion

The main purpose of this study was to clarify the issue of frontal lobe function in the absence of dementia in PD by assessing cognitive skills typically associated with this brain region in nondemented, nondepressed, and high-functioning individuals with the disease. Executive ability and temporal memory, shown to depend on the integrity of the PFC, were examined. A secondary goal of this investigation was to explore the possibility of an association between deficits in temporal memory and cognitive sequencing ability.

High-functioning individuals were chosen because, among the PD population, they were deemed relatively least likely to evidence neuropsychological deficits. Most executive skills appeared to be intact in this group of high-functioning patients, notably sequencing, set-shifting, and set-formation. Nevertheless, impairments were noted on a test of planning and organization (WCST; Heaton, 1981). Subtle and selective deficits were also evident on tests of episodic memory (Verbal Paired Associates; Wechsler, 1987), temporal memory (temporal ordering), and recognition. Given the relatively conservative approach adopted for this study, findings of selective compromise of certain executive skills and memory even in this subgroup of patients suggests that cognitive decline may indeed be a consistent feature of the illness in the absence of dementia. However, no clear evidence for the functional sequelae of involvement of the frontal lobes in the pathophysiology of PD could be obtained in this subset of the PD population.

Temporal Memory

Although no study had yet assessed performance on the word sequencing test in individuals with PD, the lack of a significant difference in group performance was unexpected since patients evidence deficits on several other tests of temporal memory (e.g. Bondi et al., 1993; Fischer et al., 1990; Sagar et al., 1988b). The difficulty of the word sequencing task may account for the lack of impairment. The number of words

whose order of presentation had to be remembered greatly exceeded the average STM capacity of 7 ± 2 chunks of information. Indeed, recalling the presentation sequence of 15 words proved to be difficult for both groups. The average correlation between presentation and recall order for the control group fell just slightly above chance level at .61.

On the temporal ordering task, a greater difference was noted between the presentation order of nine line drawings and the order in which these items were recalled by the patient group compared to the control group. Parkinsonian patients were also impaired in their estimation of each item's position within the set of stimuli independently of other items' positions. Their difficulty in judging whether each drawing was presented towards the beginning, middle, or end of card presentation was reflected in the patients' higher absolute deviation scores. Similarly, the patient group's high relative deviation scores indicate a difficulty in remembering item relationships along a time continuum. These results are consistent with those reported by Vriezen and Moscovitch (1990) in nondemented patients with PD. These authors had interpreted their findings as reflecting a decrease in the efficiency of strategic retrieval processes. Such processes, thought to depend on the integrity of the frontal lobes, are largely self-generated and involve the organization, estimation, and formation of relational judgments between items in memory (Moscovitch, 1992). They are likely involved in the reconstruction of stimuli presentation order, a necessary ability to perform the temporal ordering task (Vriezen & Moscovitch, 1990).

This test also taps working memory, attention, and sequencing skills, which seem to be intact in this subgroup of PD patients given their adequate performance on the Backward Digit Span, Digit Ordering, and Picture Arrangement tests. Deficiencies in these skills thus cannot account for the patients' difficulties on the temporal ordering task.

The deficient performance of patients on the temporal ordering task does not appear to stem from difficulties with item retrieval either since performance on tests of free recall was comparable to that of controls. Impairment of the ability to reconstruct the order of item presentation can be excluded given adequate performance on the word sequencing test. Both impaired visual perception and recognition can also be ruled out as contributing factors to the impairment of temporal ordering. All subjects correctly named each object drawing both during presentation of test stimuli and during the distracting activity. Furthermore, the patient and control groups performed similarly on the recognition test administered after the temporal ordering task.

Although both the word sequencing and temporal ordering tasks require subjects to engage in similar cognitive processes, several differences inherent to the tasks may explain the differential impairment of patients on these tests. Fewer items were presented in the temporal ordering task and their presentation order appeared to be easier to retain for controls (77% accuracy) as opposed to the word sequencing task. Adequate performance by the control group would tend to increase a test's sensitivity to even subtle deficits in the patient group. Indeed, compromise of patients' performance on the temporal ordering and word sequencing tasks reveals a higher correlation between the presentation order of items and the order in which the items were recalled for the temporal ordering task. Another likely explanation for the differential impairment noted on the two tasks concerns the 3-min distracting activity separating item presentation and temporal order recall in the temporal ordering task. The fact that PD patients had more difficulty than controls in reconstructing the presentation order of nine vs. 15 items may be explained by their heightened sensitivity to interference on the temporal ordering task. The deleterious effects of competition between stimuli may thus be magnified in patients with PD. However, no effects of interference were observed on the recognition test that followed another 3-min distracting activity within the temporal ordering task. This may signify that patients experience a heightened sensitivity to interference only when the

recall or organization of items is required. Such a hypothesis is consistent with findings that such heightened sensitivity to interference is prominent when recall is required following a distracting activity on the Brown-Peterson Distracter Task (Cooper et al., 1991). Taylor et al. (1990) also observed this effect when PD patients had to recall a list of words after the presentation of a different list of words.

No group differences were found on the recency discrimination task. This finding is in direct contrast to earlier reports stipulating that recency judgments are impaired in PD patients (e.g. Fischer et al., 1990; Sagar et al., 1988b). The most likely explanation for the lack of significant results lies in the presence of floor effects on this particular version of the recency discrimination test. The average number of correct recency estimations for each group was much lower than chance level performance. On average, the control group correctly identified the more recent of two previously seen items for 33% of the word pairs. Similarly, only 28% of the recency judgments performed by patients were correct. Furthermore, the fact that responses such as “Neither word was seen before” and “I don’t remember” were allowed may have obscured possible group differences by giving subjects the option of skipping items about which they were unsure.

This particular version of the recency discrimination task had been administered by Milner et al. (1991) to patients with frontal lobe lesions. The discrepancy between the current results and those reported by other investigators in nondemented patients with PD may also be related to differences between tests used and/or sample characteristics. Contrary to this study, in which all PD patients were nondemented and scored between 28 and 30 on the MMSE, there was greater variability on dementia rating scales in studies by Sagar et al. (1988b) and Cooper et al. (1991). In the former, 3 out of 15 patients were classified as demented. The poor performance on the verbal and nonverbal recency discrimination tasks administered in that study may have been associated with the presence of dementia. Findings of a negative correlation between recency

performance and scores on the Blessed Dementia Scale (Cooper et al., 1991) support this hypothesis.

The other study which reported deficits in nondemented PD patients' ability to perform recency judgments utilized 22 line drawings rather than words as stimuli (Fischer et al., 1990). This suggests that nondemented PD patients may experience selective deficits when dealing with pictorial vs. verbal stimuli, at least in temporal memory tasks. This hypothesis is supported by current findings of selective impairment on the temporal memory test utilizing line drawings rather than words.

The combination of recency discrimination and recognition trials within the same task resulted in a bias towards providing recognition responses. Several subjects also seemed to forget the instructions and provided almost solely recognition responses until reminded that the task also occasionally required recency judgments. The combination of the two tasks may also have contributed to the difficulty of the test since, prior to judging which of two words was seen last, subjects had to decide whether one or both words had been presented before. This contrasts with the explicit instruction given to subjects on each test card ("Which of these words did you see most recently" or "Which of these words have you seen on this test" in studies by Cooper et al. (1991) and by Sagar et al. (1988b).

The patient and control groups performed similarly at all stimulus-test intervals, a result inconsistent with findings of a disproportionate impairment by a group of nondemented Parkinsonian patients at the shortest intervals (Cooper et al., 1991; Sagar et al., 1988b). However, consistently with the study by Sagar et al. (1988b), both groups had more difficulty performing recency judgments when fewer words separated the original presentation of the items to be compared.

Variations in the demands of each task could account for the fact that significant group differences were found only on the temporal ordering vs. recency discrimination tasks. Whereas the former requires one to recall the order in which a series of items were

presented, the latter task calls for a relational judgment to be made between only two stimuli. Performance on the recency discrimination task may rely less on working memory than the temporal ordering task because it does not require subjects to manipulate several stimuli at once. Similarly, Cooper et al. (1991) have proposed that the absence of deficits on the recency discrimination task could be due to recency judgments being performed under 2-choice conditions and to the fact that the order of item presentation must not be reconstructed while taking into account all items presented. Nevertheless, this explanation does not explain the adequate performance of the patient group on the word sequencing test.

In summary, the temporal memory task performed with the highest accuracy rate (77%) by the control group revealed temporal ordering-difficulties in PD patients. Conversely, the two other tests assessing temporal memory were performed near chance level by controls and thus may not have been able to detect the potential presence of subtle deficits in the patient group. Another plausible explanation for the differential performance of patients on temporal memory tasks may be related to the nature of the stimuli (pictorial or verbal). If this is the case, it could indicate greater involvement of the right (vs. left) frontal lobe in PD. However, this explanation is weakened by the fact that a test of cued recall revealed group differences for verbal stimuli only. The most likely explanation remains that the tasks tap different abilities besides temporal memory and that deficiencies in some of these skills account for the sole impairment noted on the temporal ordering task. This subset of the PD population may thus not have problems organizing information in its proper temporal context and retrieving it but rather they may have difficulty with other cognitive processes (e.g. enhanced sensitivity to interference).

Order vs. Item Memory

Deficient performance on temporal memory tasks has been suggested to result from a lack of spontaneous organizational strategies necessary to retrieve information in memory (Milner et al., 1991). The similar recall of stories (Logical Memory; Wechsler, 1987) by patient and control groups raises doubts as to whether such retrieval deficits account for decreased temporal order memory. The adequate performance of patients on this free recall measure was unexpected since selective deficits on similar tests relative to intact performance on recognition measures has previously been reported in high-functioning patients with PD (Mohr et al., 1990). The discrepancy between the results obtained in this study and those reported by Mohr et al. (1990) may be due to sampling differences. Only one of the 20 patients involved in the current study was in stage III of the disease whereas seven out of ten patients in Mohr et al. (1990)'s study were in stages III or IV. However, there was a trend for the current patient group to do poorly relative to normal controls upon recall of simple geometric figures (Visual Reproduction; Wechsler, 1987).

Of the WMS-R (Wechsler, 1987) subtests, only a STM measure of verbal cued recall (Verbal Paired Associates) yielded significant group differences. It is unclear whether such an impairment is indicative of frontal and/or temporal lobe damage since both the DLPFC (Rugg, Fletcher, Frith, Frackowiak, & Dolan, 1996) and hippocampal region (Schacter, 1996) may become activated when healthy subjects engage in cued recall tests.

Patients did perform significantly more poorly than controls on Verbal Paired Associates (Wechsler, 1987). The selective deficit noted for cued vs. free recall is surprising since the latter is generally viewed as more difficult, requiring self-initiated spontaneous organization of material in memory and its retrieval in the absence of external cues. One possible explanation for the selective deficit on Verbal Paired Associates is that this test requires one to manipulate several independent pairs of stimuli

and remember which two words are associated together while a list of eight pairs of words are read. The subject must keep the word pairs apart whereas in Logical Memory, the information is provided in a logical sequence and all details relate to a unique topic.

The ability of nondemented PD patients to recognize previously encountered stimuli was generally within the normal range, at least when the number of stimuli did not exceed their STM span. Adequate performance on recognition tests has been associated with the integrity of the temporal lobe memory system (Milner et al., 1991). A neuroimaging study has shown a correlation between the amount of activation in the hippocampal region and the accuracy of responses on a recognition test (Nyberg et al., 1996).

On the Figural Memory subtest of the WMS-R (Wechsler, 1987), patients scored within the normal range. These results are in agreement with the majority of studies on nondemented Parkinsonian patients, which found recognition ability to be intact (e.g. Beatty et al., 1989; Mohr et al., 1990; Taylor et al., 1990) regardless of the medication status of patients and of their disease stage (Owen et al., 1993). According to Owen et al. (1993), sparing of pattern recognition memory would suggest the relative intactness of the temporal lobes. The patient and control groups could also differentiate familiar from novel line drawings on the recognition task that followed temporal ordering. However, Parkinsonian patients were impaired on the recognition trials of the recency discrimination task. These results are at odds with reports of intact performance of patients in similar tasks (Cooper et al., 1991; Sagar et al., 1988b). It must be noted, however, that deficits in STM recognition of abstract designs have been found by some investigators (Sahakian et al., 1988; Sullivan & Sagar, 1989, 1991).

Considering that two out of the three tests assessing recognition memory failed to indicate an impairment by Parkinsonian patients and that the performance of both groups was near chance level on the third test, it is thought that the lower scores obtained on the recognition component of the recency discrimination task are probably not due to

encoding deficits. Rather, the selective deficit for this particular type of recognition task may stem from two major differences between the test requirements associated with the recognition trials of the recency discrimination task and those associated with the temporal ordering and Figural Memory tests.

Only the latter tests assess solely recognition whereas in the former, subjects may have seen both stimuli previously. Therefore, they don't have a 50-50 chance of providing the correct answer but rather one chance in three. Furthermore, the recency discrimination task is quite long and a much greater number of stimuli are presented to be encoded. Since 29 words appear on the recognition trials and another 120 on cards assessing recency ability, this requires a total of 149 words to be recognized. On the other hand, subjects must point out only nine out of 18 drawings on the temporal ordering task and three out of nine designs on Figural Memory (Wechsler, 1987). If the different level of difficulty inherent to the recognition tasks indeed accounts for the unique impairment observed on the recency discrimination test, patients may be able to register and store information accurately in memory. The results of this study do not warrant an explanation such as that proposed by Mohr et al. (1990), in which effortful episodic memory processes are selectively impaired. Performance on tests of recall and recognition were not found to be differentially impaired in this group of high-functioning Parkinsonian patients.

Consistent with the findings of Cooper et al. (1991) and of Mohr et al. (1990), the overall MQ obtained by patients on the WMS-R (Wechsler, 1987) was lower than that of controls by almost one standard deviation. This global index of STM reveals an impairment of episodic memory even in high-functioning patients with PD. The impairment contrasts with their preserved intellectual functions.

Executive Functions

This study sought to explore the relationship between temporal memory and cognitive sequencing on the basis of Cooper et al.'s (1993) suggestion that deficient sequencing ability could account for temporal memory decrements. Although patients were impaired on one of the temporal memory tasks, they performed within the normal range on the three cognitive sequencing tests, notably on Backward Digit Span (Wechsler, 1981), Digit Ordering, and Picture Arrangement (Wechsler, 1981).

The present findings do not support the hypothesis that temporal memory deficits stem from a broader impairment of sequencing ability. Furthermore, the association found between performance on temporal memory and cognitive sequencing tests by Cooper et al. (1993) was not present in this study. Deficits in several other cognitive processes can also be ruled out as underlying temporal memory deficits. One such process is working memory. Efficiency in this type of memory, which holds information "on-line" during manipulation of other information, may be especially crucial to performance on Backward Digit Span (Wechsler, 1981) and Digit Ordering, tests adequately performed by the patient group.

A decrease in attentional resources also cannot account for impairment of temporal memory function given that patients were generally able to repeat series of digits backward or in ascending order and to recognize previously seen stimuli. It has been argued that patients with PD are impaired when tasks require self-directed, task-specific planning (Taylor et al., 1986, 1990). However, no evidence for this was found, with relatively good performance by patients on a test of free recall.

As mentioned previously, the expected deficits on cognitive sequencing tests were not observed. Whereas studies by Cooper et al. (1991) and by Sullivan et al. (1989) revealed impaired performance on Backward Digit Span (Wechsler, 1981), high-functioning PD patients' scores fell in the normal range. The lack of group differences on this test may be associated with the fact that 17 out of 20 patients had received higher

education. Performance on the Backward Digit Span test has been shown to correlate with years of education (Wechsler, 1981). Group performance also did not differ on Digit Ordering. This test was slightly more effort-demanding since it does not involve solely an inversion of digit order but requires the mental manipulation of individual digits to organize them in ascending order.

Picture Arrangement (Wechsler, 1981) was viewed as a purer measure of cognitive sequencing ability since mnemonic requirements are minimal compared to Backward Digit Span (Wechsler, 1981) and Digit Ordering. The impairment found on this test in an otherwise unselected sample of nondemented patients (Bondi et al., 1993; Cooper et al., 1991; Ogden et al., 1990) could not be replicated. The higher education obtained by the patients in this study is unlikely to have contributed to the absence of deficits since education level accounts for only 13% of the variance on Picture Arrangement in 55-74 year-old individuals (Wechsler, 1981).

The fact that the current results are inconsistent with several findings of cognitive sequencing impairments in nondemented PD patients may suggest one of two things. High-functioning PD patients may form a subset of the Parkinsonian population without sequencing deficits or else this subgroup of patients have subtle deficits which cannot be detected with the tests administered. However, it must be noted that findings of cognitive sequencing impairments are not universal (e.g. Beatty & Monson, 1990; Canavan et al., 1989b).

Although deficits of executive function, as assessed by the WCST (Heaton, 1981), are frequently observed in nondemented PD patients (Cooper et al., 1991; Paolo et al., 1996; Pillon et al., 1997; Venneri et al., 1997), these skills were shown to be preserved in high-functioning individuals with PD (Mohr et al., 1990). Performance on the WCST was comparable to that of controls, leading investigators to suggest that their selection criteria may have contributed to the absence of executive deficits. A strong impact of IQ (Taylor et al., 1986) and education (Beatty et al., 1989; Sullivan et al., 1989) on WCST

performance has been reported. However, the present study shows that some high-functioning individuals with PD do evidence executive deficits. Indeed, the patient group completed fewer categories than the control group on the WCST, suggesting impaired maintenance of set. Conversely, set-formation and set-shifting abilities appear to be preserved in these patients, as revealed by the similar number of trials required by patients and controls to achieve the first category and the lack of a tendency to perseverate in their errors. Two points worth noting are 1) the selectivity of deficits within the executive realm in these high-functioning PD patients and 2) the fact that these deficits are not observed in all patients, as indicated by the large within group variability in the patients's scores on the WCST (see Table 2).

The Frontal Lobe Hypothesis in PD in the Absence of Dementia

The sensitivity of temporal memory to frontal lobe disruption is well-established (Milner & Petrides, 1984; Milner et al., 1985, 1991). Patients with frontal lobe lesions are frequently reported to experience deficits on tasks of temporal memory. They evidence impairment on the word sequencing task utilized in this study (Shimamura et al., 1990), as well as on a very similar version of the recency discrimination task (Milner et al., 1991). PD patients' differential impairment on various tests of temporal memory suggests that, while the three tests may rely on the same basic processes, additional task-specific cognitive mechanisms likely mediate performance on such tests. These task-specific processes could potentially be impaired to various degrees or follow a different course of decline if they are mediated by different brain areas, including different subdivisions of the PFC (e.g. DLPFC vs. orbitofrontal cortex).

The sole deficit noted on the temporal ordering task may be attributed to an enhanced sensitivity to interference, a feature usually associated with orbitofrontal cortex involvement. Patients with frontal lobe lesions show an increased sensitivity to competition between stimuli (e.g. Vilkkii, Virtanen, Surma, & Servo, 1996). Lesions to

the DLPFC, on the other hand, have been linked to impaired processing of temporal information (Milner & Petrides, 1984; Milner et al., 1985, 1991). If patients are assumed to adequately process temporal information but to have difficulty processing it in the presence of interference, it may suggest that cognitive processes associated with the orbitofrontal cortex decline more rapidly than do those mediated by the DLPFC. On the other hand, it could signify that temporal information processing remains relatively intact in high-functioning PD patients.

The functional status of the DLPFC is difficult to infer from the results of this study because of an inconsistency of performance on tests thought to tap cognitive processes associated with this prefrontal area. None of the temporal memory measures in this study were correlated with Parkinsonian patients' scores on the WCST (Heaton, 1981), described as a classic test of dorsolateral function (Milner, 1963, 1964, 1971). A similar lack of correlation between these tests has been reported in patients with damage to the frontal lobes (Shimamura et al., 1990). Two explanations are proposed to account for this. First, temporal memory may not, in fact, be mediated by the DLPFC. The other possibility is that the WCST is not as good a measure of DLPFC function as it was suggested to be by Milner (1963).

Regarding the first hypothesis, research has been fairly consistent in linking impairments on temporal memory tasks to frontal lobe dysfunction (Milner & Petrides, 1984; Milner et al., 1985, 1991; Shimamura et al., 1990). However, such tasks are experimental and their construct validity generally remains to be determined. In the event that the DLPFC does not mediate the processing of temporal information, the relative integrity of this structure in high-functioning patients with PD is nevertheless suggested by adequate performance on cognitive sequencing tests.

Additionally, the perseverative errors and trials to the first category measures of the WCST (Heaton, 1981) did not indicate impairment. These executive functions have been linked to the PFC, particularly the dorsolateral region (Milner, 1963, 1964, 1971).

However, recent studies have concluded that the WCST cannot be used as a single predictor of focal frontal lobe damage (e.g. Mountain & Snow, 1993), although they acknowledge the sensitivity of this measure to frontal lobe injury (Arnett et al., 1994; Rezaei et al., 1993). On the other hand, one study reported comparable performances by those with frontal lobe injury and normal controls on the WCST (Cantor-Graae, Warkentin, Franzen, & Risberg, 1993). This test has also been conceived as a complex measure of executive abilities requiring not only the activation of the frontal lobes but also the integration of several brain regions (Axelrod et al., 1996).

These studies caution against interpreting the fewer number of categories completed on the WCST (Heaton, 1981) as reflecting a dysfunction within the DLPFC. Furthermore, in Milner's (1963) study, those with excisions of the DLPFC (vs. the orbitofrontal and posterior brain regions) had an increased number of perseverative errors rather than a difficulty in completing categories. Therefore, completion of fewer categories on the WCST by the patient group may not necessarily suggest compromise of the DLPFC, but that of another brain region. Specifically, it may indicate a difficulty with the maintenance of set, an executive function associated with the orbitofrontal cortex (Stuss & Benson, 1984, 1986). This region of the PFC may thus be affected in PD although, as noted earlier, the WCST is not specific to frontal lobe damage despite being sensitive to it (Heaton, 1981).

Alternatively, the pattern of deficits evidenced by this group of nondemented high-functioning Parkinsonian patients may not be related to compromise of the frontal lobes but rather to dysfunction of other brain regions. A study by Piccirilli, D'Alessandro, Finali, and Piccinin (1997) reported four patterns of cognitive impairments in patients with PD, reflecting either generalized impairment, selective dysfunction of the frontal lobes, dysfunction of non-frontal areas only, or an absence of cognitive decrements.

Whatever the neuroanatomical focus of disruption that underlies the cognitive and executive deficits exhibited by the patient group, the relative integrity of the DLPFC

would explain why the cognitive sequencing tests, perseverative errors and trials to the first category measures of the WCST (Heaton, 1981), and most of the temporal memory tasks, assessing DLPFC function, did not yield impairment. The ability to generate and use self-directed, task-specific strategies to organize information in memory may also be mediated by the DLPFC in addition to the diencephalon and medial temporal lobes (Poldrack & Gabrieli, 1997). This ability is thought to be problematic in nondemented PD patients (Bondi et al., 1993; Taylor et al., 1986, 1990), as judged by poor performance on tests of free recall. However, nondemented high-functioning patients did not differ from normal controls on the Logical Memory and Visual Reproduction subtests of the WMS-R (Wechsler, 1987), again suggesting relatively intact DLPFC function in this subpopulation of PD patients.

The absence of generalized executive deficits in high-functioning individuals with PD, noted in both this study and that of Mohr et al. (1990), may be attributed to a “protective” effect of higher education against the decline of executive functions usually associated with the illness. Indeed, Taylor et al. (1995) reported that IQ may have a protective effect on neuropsychological integrity. Furthermore, the high-functioning criterion for participation in the study implied that individuals had high organizational skills and an ability to adapt to novel situations. It is therefore plausible that this higher absolute level of executive function in patients contributed to the lack of group differences on executive tests.

Nondemented PD patients are often thought to experience dysfunction of the frontal lobes (e.g. Bondi et al., 1993; Pillon et al., 1997; Vriezen & Moscovitch, 1990), with cognitive deficits that appear to overlap with those that occurring after damage to the frontal lobes (Brown & Marsden, 1990). However, the extent of the neurochemical dysfunction is hypothesized to be limited to the basal ganglia (Bondi et al., 1993). Previous studies have hypothesized, based on a neuroanatomical model developed by Alexander et al. (1986), that depletion of DA within the caudate nucleus, and subsequent

dysfunction of the subcortical-frontal circuits, leads to abnormal function of the DLPFC and accounts for executive deficits in nondemented PD patients. The idea that the presence or absence of deficits may depend on different degrees of DA depletion in the caudate nucleus was raised by Canavan et al. (1989a). The selective and subtle cognitive impairments noted in high-functioning patients with the disease suggests a more restricted extent of frontal lobe dysfunction in this subpopulation, possibly due to a lesser depletion of DA within their caudate nucleus compared to other nondemented Parkinsonian patients. A relatively lesser degree of disruption of subcortical-frontal circuits would follow, meaning that the DLPFC would still have sufficient DA input to function adequately. A longitudinal study examining performance on a battery of executive tests in groups of high-functioning and non-high-functioning nondemented patients with PD could test this hypothesis. Nevertheless, the high variability within the patient group on WCST (Heaton, 1981) measures may reflect different degrees of compromise to neurological systems within the high-functioning nondemented Parkinsonian population.

The possibility of additive effects of “subthreshold” DA depletion within the caudate nucleus and the PFC on level of cognitive functioning has been raised by Brown and Marsden (1990) to account for the increased cognitive dysfunction associated with longer disease duration. In an attempt to explain the differential performance on neuropsychological tests by high-functioning and non-high-functioning patients, such “subthreshold” depletions could be evoked. It may be that the high-functioning patients in this study only experienced a “subthreshold” DA depletion within the caudate nucleus and thus, did not evidence any frontally-associated cognitive deficits. With longer disease duration, depletion may also occur within the PFC, thereby explaining the correlations found between performance on most neuropsychological measures and disease duration.

Alternatively to the hypotheses presented earlier, it may be the case that nondemented high-functioning Parkinsonian patients do have impairments of executive

functions but that the deficits are so subtle that the tests administered lacked the sensitivity to detect them. Only robust differences would have been uncovered, such as those on the categories measure of the WCST (Heaton, 1981).

Clinical Correlates of Neuropsychological Test Performance

Caution is necessary when interpreting the correlations between neuropsychological test performance and clinical variables since up to six of the 57 correlations were expected to reach significance by chance alone with an alpha level of .10. Nevertheless, the pattern of results is quite striking. Disease duration was significantly correlated with patient performance on the three tests of temporal memory, on two cognitive sequencing tasks, and on three WMS-R (Wechsler, 1987) subtests assessing free or cued recall. On the other hand, none of the WCST (Heaton, 1981) and recognition measures were associated with length of illness.

These correlations suggest that only selective areas within the PFC (e.g. the orbitofrontal cortex) may be affected in the early stages of the disease (I and II), with other subdivisions becoming disrupted later on (e.g. the DLPFC). Such a suggestion has been made by Owen et al. (1992), who found the performance of nondemented Parkinsonian patients in stages I and II to be deficient on only two of three tests shown to be sensitive to frontal lobe disruption. With a single exception, the patient sample was in stages I and II of the disease.

These findings support the dopaminergic hypothesis in which depletion of this neurotransmitter in the caudate nucleus disrupts cognitive functions associated with the integrity of the PFC as the disease progresses. With the exception of the WCST (Heaton, 1981), whose specificity to frontal lobe function has recently been questioned, all tests shown to be sensitive to frontal lobe dysfunction were linked to disease duration whereas

recognition test performance, associated with the temporal lobes, appears to be largely independent of length of illness.

Several other neuropsychological measures were also correlated with disease stage or with the severity of motor symptoms but no coherent pattern emerged. Few significant correlations may have been found between neuropsychological variables and Hoehn and Yahr disease stage (Fahn et al., 1987) because of the low variability in the latter. Indeed, 80% of patients were in stage II of the disease. Nevertheless, these results are consistent with several others showing no relation between neuropsychological performance and disease stage in nondemented Parkinsonian patients (e.g. Beatty & Monson, 1990; Bondi et al., 1993; Mohr et al., 1990).

Severity of motor symptoms, measured with the UPDRS (Fahn et al., 1987), was also associated with very few neuropsychological variables. The UPDRS encompasses several symptoms, including rigidity, bradykinesia, and tremor. These cardinal motor symptoms of PD have often been found to be differentially linked to cognitive deterioration. The first two symptoms are often associated with impaired performance on neuropsychological tests whereas tremor usually is not (see Levin, Tomer, & Rey, 1992, chap. 8 for a review). Correlating the severity of individual motor symptoms of PD with neuropsychological performance may have provided clues as to whether motor and cognitive deficits share a common pathophysiological mechanism (Levin et al., 1992).

Overall, the pattern of correlations suggests an increased dysfunction of the caudate nucleus, and thus a greater disruption of frontal lobe functioning and of the cognitive skills mediated by it, with longer disease duration. Consistent with this idea, Levin et al. (1992) stated that the chronic progressive nature of PD “implies that disease duration must, by definition, exert some influence on the mental status changes observed during the course of the illness” (chap. 8, p. 100). The lack of an association between both disease stage and motor symptom severity and neuropsychological test scores supports the hypothesis that the deterioration of cognitive and motor skills, associated

with disturbance of the caudate nucleus and putamen respectively, are relatively independent in PD (Taylor & Saint-Cyr, 1995).

The twenty patients who participated in the study were medicated with dopaminergic agents. While this reduced the possibility of motor confounds, the effects of such treatment on cognitive performance remain uncertain (see Levin et al., 1992 for a review) and may be related to such variables as length of treatment, type of medication, and dosage. Furthermore, no consensus has been reached regarding the neuropsychological performance of patients during “on” and “off” states. Therefore, the influence of medications in the present study cannot be determined although doses were optimized for the motor symptoms.

Conclusions

It was anticipated that nondemented patients with PD would perform more poorly than controls on temporal memory and executive function tests due to disruption of subcortical-frontal circuits arising from lesions in the basal ganglia. Executive function deficits do not appear to be a prominent feature of the cognitive decline experienced by high-functioning patients with PD. In a previous study with high-functioning patients, performance on the WCST (Heaton, 1981), used as a primary measure of executive ability, was not impaired (Mohr et al., 1990). Similarly, the current study found performance to be spared on two measures derived from the WCST assessing set-formation and set-shifting. Assessment of an additional executive ability, cognitive sequencing, revealed that it is also preserved in high-functioning patients. Sequential deficits thus could not have accounted for impaired performance noted on one of the three tests of temporal memory, as had been hypothesized. The only observed executive impairment lies in poor maintenance of set, as measured by the WCST.

Results do not provide clear-cut evidence of frontal lobe involvement in all PD patients in the absence of dementia. The functional status of the DLPFC is difficult to

infer from the results of this study because of an inconsistency of performance on tests thought to tap cognitive processes associated with this prefrontal area. However, relative preservation of its integrity seems to best account for the pattern of preserved performance on all but one executive function test. This latter measure has recently been shown not to be specific to frontal lobe damage.

Executive functions comprise a heterogeneous class of cognitive processes (Van Spaendonck et al., 1996) which may be differentially affected in the disease and which are assessed by different tasks. Thus, no firm conclusion can be drawn regarding the status of frontal lobe functioning since several other executive skills remain to be assessed in high-functioning patients with the illness.

The hypothesis of frontal lobe dysfunction in PD stems largely from observations of a parallel between performance by Parkinsonians and patients with frontal lobe lesions on neuropsychological tests. However, few studies have compared their performance directly. By doing this, confounding variables linked to the research setting (e.g. experimenter, assessment tools, statistical analyses) would be eliminated. Nevertheless, the use of neuropsychological tests only permits the specific foci of regional dysfunction to be inferred.

Parkinsonian patients showed a preservation of executive and temporal memory functions on most tests. However, the current study suggests that impairment of specific executive abilities, notably deficient set-maintenance, and heightened sensitivity to interference, may account for the deficits observed on selective tests of temporal memory, cued recall, and on one WCST (Heaton, 1981) measure. The hypothesis of a heightened sensitivity to interference could be further explored by administering the Stroop, CVLT, and Brown-Peterson Distracter Task to a group of such patients. With respect to temporal memory, results suggest that this current subset of the PD population may thus not have problems organizing information in its proper temporal context and retrieving it.

Several factors may contribute to the absence of generalized executive deficits in the sample of patients. First, the PD patients may form a subset of the Parkinsonian population without such generalized impairments. It is also possible that high-functioning patients do evidence impairments of executive functions but that the deficits are so subtle that the tests employed in the present study lacked the sensitivity to detect them. It is noteworthy, however, that there are PD patients without executive deficits.

Disease duration was found to be associated with performance on the majority of the tests sensitive to frontal lobe dysfunction. These results are interpreted as suggesting a limited involvement of the DLPFC in the cognitive deficits of nondemented patients with a short disease duration, with greater DA depletion and frontal lobe dysfunction as length of illness increases. Cognitive deficits were not correlated with the severity of motor symptoms nor with disease stage, suggesting that the cognitive and motor decline associated with PD are relatively independent. This suggestion is consistent with the hypothesized network of segregated circuits linking the caudate nucleus and putamen with different frontal lobe areas and with cognitive and motor function, respectively (Alexander et al., 1986).

Nevertheless, caution must be exercised when interpreting the results of this study because a large number of tests and correlations were performed on the data, increasing the likelihood of spurious results. It must be noted, however, that this study adopted a relatively conservative approach in its search for executive and temporal memory deficits in PD. In addition to the sample characteristics previously described, none of the patients were in the advanced stages of the disease (Hoehn & Yahr stages IV and V) and all patients were medicated and tested while in the "on" state. Several factors which could potentially have accounted for, or exacerbated cognitive deficits were thus reduced or eliminated.

Finally, findings of cognitive decline even in a group of high-functioning nondemented PD patients, deemed relatively unlikely to manifest neuropsychological

dysfunction, confirm that such decrements are indeed part of the clinical presentation of the illness. Care must be taken in extending the specific pattern of results of this study to the Parkinsonian population. Importantly therefore, the sample of patients was not representative of all individuals with PD due to the highly selective criteria employed.

However, these findings highlight the need for the development of treatment strategies for the cognitive symptoms associated with PD. Development of such treatment interventions is essential, especially given the high prevalence of this illness in people over the age of 60 (Golbe, Langston, & Shaulson, 1990).

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Table 1

Demographic Characteristics and Screening Results for Subject Groups

Group	Gender	Age in	Education	WAIS-R	MMSE	GDS
	ratio M/F	years	in years	Vocabulary	score	score
Parkinsonians						
	18 : 2					
<u>M</u>		62.0	18.2	61.4	29.7	4.2
<u>SD</u>		7.7	2.3	6.2	.49	2.7
range		51-78	16-25	41-69	29-30	1-9
Controls						
	15 : 5					
<u>M</u>		61.7	18.1	63.6	29.5	3.7
<u>SD</u>		8.8	1.6	4.1	.69	3.3
range		50-75	16-21	54-68	28-30	0-10

Note. WAIS-R = Wechsler Adult Intelligence Scale-Revised; MMSE = Mini-Mental State Examination; GDS = Geriatric Depression Scale.

Table 2

Mean Performance of Patient and Control Groups on Neuropsychological Tests

Test	Parkinsonian patients		Normal controls		p
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>	
WCST					
No. categories	4.90	1.68	5.80	.52	<.05
No. perseverative errors	18.55	16.44	11.85	5.87	
Trials to first category	18.70	23.66	12.85	5.09	
Digit Ordering	86.20	9.28	90.15	5.88	
Picture Arrangement	13.60	5.03	13.80	4.10	
Backward Digit Span	8.00	1.75	8.30	1.56	
Word sequencing	.44	.32	.61	.28	
Temporal ordering task					
Rank-order correlation	.62	.27	.77	.22	<.01,
Absolute deviation	13.40	5.73	9.60	5.34	<.05
Relative deviation	42.05	12.65	34.75	8.40	<.05
Recognition test	7.55	1.39	8.15	1.18	
Recency discrimination task					
Recency test	16.95	9.00	19.60	8.58	
Recognition test	12.40	5.14	15.60	4.49	<.05
WMS-R					
MQ	99.25	12.32	108.40	12.98	<.05
Figural Memory	6.65	2.03	6.90	1.74	
Logical Memory	21.55	5.72	23.60	5.60	
Visual Paired Associates	12.00	4.18	13.05	3.43	
Verbal Paired Associates	14.55	4.47	17.80	3.50	<.05
Visual Reproduction	32.35	5.74	35.20	2.75	

Note. MQ = memory quotient; WCST = Wisconsin Card Sorting Test;

WMS-R = Wechsler Memory Scale-Revised.

. = significant level with the outlier removed from the analysis.

Table 3

Correlations Between Neuropsychological Test Performance and Clinical Variables in Parkinsonians

Neuropsychological test	Disease duration	Hoehn & Yahr stage	UPDRS
Word sequencing	-.43*	-.13	-.19
Recency discrimination	.47**	.26	.11
Temporal ordering rank-order correlation	-.39*	-.41*	-.26
Temporal ordering absolute deviation score	.43*	.41*	.37
Temporal ordering relative deviation score	.19	.17	-.01
Backward Digit Span	-.16	.11	-.32
Digit Ordering	-.41*	-.39*	-.48**
Picture Arrangement	-.58***	.01	.02
WCST categories completed	-.34	.00	.02
WCST perseverative errors	.32	-.10	-.02
WCST trials to first category	.02	-.10	-.22
WMS-R MQ	-.52**	-.31	-.15
Logical Memory	-.24	-.28	-.17
Visual Reproduction	-.46**	-.09	-.17
Verbal Paired Associates	-.57***	-.39*	-.54**
Visual Paired Associates	-.61***	.02	-.10
Figural Memory	-.06	.07	.07
Recognition test (Temporal ordering task)	-.11	.11	.12
Recognition test (Recency discrimination task)	-.26	.26	.11

Note. UPDRS = Unified Parkinson's Disease Rating Scale; WCST = Wisconsin Card Sorting Test; WMS-R = Wechsler Memory Scale-Revised; MQ = memory quotient.

* $p < .10$. ** $p < .05$. *** $p < .01$.

APPENDIX A

**Motor Examination Section of the Unified Parkinson's Disease Rating Scale
(UPDRS) - Version 3.0**

18. Speech:

- 0=Normal.
- 1=Slight loss of expression, diction and/or volume.
- 2=Monotone, slurred but understandable; moderately impaired.
- 3=Marked impairment, difficult to understand.
- 4=Unintelligible.

19. Facial expression:

- 0=Normal.
- 1=Minimal hypomimia, could be normal "Poker Face".
- 2=Slight but definitely abnormal diminution of facial expression.
- 3=Moderate hypomimia; lips parted some of the time.
- 4=Masked or fixed facies with severe or complete loss of facial expression; lips parted 1/4 inch or more.

20. Tremor at rest:

- 0=Absent.
- 1=Slight and infrequently present.
- 2=Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present.
- 3=Moderate in amplitude and present most of the time.
- 4=Marked in amplitude and present most of the time.

21. Action or postural tremor of hands:

- 0=Absent.
- 1=Slight; present with action.
- 2=Moderate in amplitude, present with action.
- 3=Moderate in amplitude with posture holding as well as action.
- 4=Marked in amplitude; interferes with feeding.

22. Rigidity: (Judged on passive movement of major joints with patient relaxed in sitting position. Cogwheeling to be ignored.)

- 0=Absent.
- 1=Slight or detectable only when activated by mirror or other movements.
- 2=Mild to moderate.
- 3=Marked, but full range of motion easily achieved.
- 4=Severe, range of motion achieved with difficulty.

23. Finger taps: (Patient taps thumb with index finger in rapid succession with widest amplitude possible, each hand separately.)

- 0=Normal.
- 1=Mild slowing and/or reduction in amplitude.
- 2=Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
- 3=Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
- 4=Can barely perform the task.

24. *Hand movements: (Patient opens and closes hands in rapid succession with widest amplitude possible, each hand separately.)*
 0=Normal.
 1=Mild slowing and/or reduction in amplitude.
 2=Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
 3=Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
 4=Can barely perform the task.
25. *Rapid alternating movements of hands: (Pronation-supination movements of hands, vertically or horizontally, with as large an amplitude as possible, both hands simultaneously.)*
 0=Normal.
 1=Mild slowing and/or reduction in amplitude.
 2=Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
 3=Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
 4=Can barely perform the task.
26. *Leg agility: (Patient taps heel on ground in rapid succession, picking up entire leg. Amplitude should be about 3 inches.)*
 0=Normal.
 1=Mild slowing and/or reduction in amplitude.
 2=Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement.
 3=Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement.
 4=Can barely perform the task.
27. *Arising from chair: (Patient attempts to arise from a straight-back wood or metal chair with arms folded across chest.)*
 0=Normal.
 1=Slow; or may need more than one attempt.
 2=Pushes self up from arms of seat.
 3=Tends to fall back and may have to try more than one time, but can get up without help.
 4=Unable to arise without help.
28. *Posture:*
 0=Normal erect.
 1=Not quite erect, slightly stooped posture; could be normal for older person.
 2=Moderately stooped posture, definitely abnormal; can be slightly leaning to one side.

3=Severely stooped posture with kyphosis; can be moderately leaning to one side.

4=Marked flexion with extreme abnormality of posture.

29. *Gait:*

0=Normal.

1=Walks slowly, may shuffle with short steps, but no festination or propulsion.

2=Walks with difficulty, but requires little or no assistance; may have some festination, short steps, or propulsion.

3=Severe disturbance of gait, requiring assistance.

4=Cannot walk at all, even with assistance.

30. *Postural stability:* (Response to sudden posterior displacement produced by pull on shoulders while patient erect with eyes open and feet slightly apart. Patient is prepared.)

0=Normal.

1=Retropulsion, but recovers unaided.

2=Absence of postural response; would fall if not caught by examiner.

3=Very unstable, tends to lose balance spontaneously.

4=Unable to stand without assistance.

31. *Body bradykinesia and hypokinesia:* (Combining slowness, hesitancy, decreased arm swing, small amplitude, and poverty of movement in general.)

0=None.

1=Minimal slowness, giving movement a deliberate character; could be normal for some persons. Possibly reduced amplitude.

2=Mild degree of slowness and poverty of movement which is definitely abnormal. Alternatively, some reduced amplitude.

3=Moderate slowness, poverty or small amplitude of movement.

4=Marked slowness, poverty or small amplitude of movement.

IV. COMPLICATIONS OF THERAPY(In the past week)

A. *Dyskinesias*

32. *Duration:* What proportion of the waking day are dyskinesias present? (Historical information)

0=None

1=1-25% of day.

2=26-50% of day.

3=51-75% of day.

4=76-100% of day.

33. *Disability:* How disabling are the dyskinesias? (Historical information; may be modified by office examination.)

0=Not disabling.

1=Mildly disabling.

2=Moderately disabling.

3=Severely disabling.

4=Completely disabled.

APPENDIX B**Modified Hoehn and Yahr Staging Scale**

- Stage 0 = No signs of disease.
- Stage 1 = Unilateral disease.
- Stage 1.5 = Unilateral plus axial involvement.
- Stage 2 = Bilateral disease, without impairment of balance.
- Stage 2.5 = Mild bilateral disease, with recovery on pull test.
- Stage 3 = Mild to moderate bilateral disease; some postural instability; physically independent.
- Stage 4 = Severe disability; still able to walk or stand unassisted.
- Stage 5 = Wheelchair bound or bedridden unless aided.

APPENDIX C

Clinical Features of Parkinson's Disease Within the Patient Group

Patient no.	Disease duration in years	Hoehn & Yahr stage	Motor disability rating (UPDRS)	Antiparkinsonian medications
1	5	2.0	9	Pramipexole
2	7	2.5	48.5	Sinemet
3	9	2.5	48.5	Sinemet Sinemet CR Bromocriptine
4	7	1.5	13	Sinemet CR
5	6	2.0	19.5	Amantadine
6	8	2.0	19.5	Sinemet Sinemet CR
7	17	2.0	20	Sinemet
8	12	2.0	21	Sinemet Sinemet CR Permax
9	8	2.5	23	Sinemet Sinemet CR Tolcapone
10	8	2.0	12	Sinemet Permax
11	7	1.0	8.5	Prolopa
12	11	2.0	17.5	Sinemet Sinemet CR Deprenyl

Patient no.	Disease duration in years	Hoehn & Yahr stage	Motor disability rating (UPDRS)	Antiparkinsonian medications
13	5	2.0	26	Eldepryl
14	15	2.0	53.5	Sinemet Bromocriptine
15	4	1.5	11.5	Eldepryl Sinemet Tolcapone
16	28	3.0	42	Sinemet Bromocriptine Symmetrel
17	4	2.0	13	Sinemet CR
18	6	2.0	21	Sinemet Sinemet CR Mirapex Tolcapone
19	6	2.0	31	Sinemet CR
20	6	2.0	8	Sinemet Eldepryl Tolcapone Artane

Note. UPDRS = Unified Parkinson's Disease Rating Scale.

APPENDIX D

Educational and Professional Background of Study Participants

Participant no.	Education in years	Occupation
1	17	scholarship program officer
2	19	physicist / manager
3	16 (15)	school teacher
4	18	teacher / computer programmer
5	19	trade commissioner
6	21	university professor
7	17	college teacher
8	17	lawyer
9	17	public servant / military
10	16 (13)	manager / teacher
11	17	researcher / manager
12	20	public servant
13	21	guidance counselor
14	19	military / college teacher
15	18	school principal
16	17	engineer
17	17	diplomat
18	25	diplomat / senior manager
19	16 (15)	civil servant
20	16 (14)	general manager
21	16	school teacher
22	20	rehabilitation counselor

Participant no.	Education in years	Occupation
23	18	social worker
24	18	researcher / statistician
25	21	school teacher
26	17	director / auditor
27	19	chief librarian
28	18	translator / editor
29	16	school teacher
30	16	school teacher
31	16	computer programming analyst
32	19	editor
33	19	architect
34	21	engineer
35	19	university professor
36	17	accountant
37	17	school principal
38	18	regional superintendant of education
39	19	regional superintendant of education
40	17	advisor

Note. () = actual number of years of education completed.

APPENDIX E

Information Sheets and Consent Forms**INFORMATION SHEET AND CONSENT FORM (PATIENTS)**

TITLE: Temporal Memory and Executive Functions in High-Functioning Parkinsonian Patients

TELEPHONE
830-7788

PRINCIPAL INVESTIGATOR: Brigitte Patry, BA

ASSOCIATE INVESTIGATORS: E. Mohr, PhD
C. L. Barclay, MD
T. Mendis, MD
J. D. Grimes, MD
Peggy Gray, RN

PURPOSE OF THE STUDY: Several studies have reported changes in mental functioning in people with Parkinson's disease. However, not all studies are in agreement and it remains unclear whether certain areas of the brain are involved in the physical and mental changes occurring in this illness. Better insight as to their involvement may be gained by the study of high-functioning individuals, thought to be least likely to have experienced changes in mental functions.

The purpose of this study is thus to examine the ability to remember not actual items but the order in which they are presented (temporal memory). The study will also focus on general problem solving skills as well as on the ability to organize items in a logical or predetermined sequence (sequencing ability) in high-functioning individuals with Parkinson's disease. It has previously been suggested that to remember the order of presentation of items, a person must be able to organize information in a specific sequence. The same brain areas appear to be involved in these particular mental functions. Therefore, this study will look at the relationship between temporal memory and sequencing ability.

STUDY PLAN AND PROCEDURES: Twenty people with Parkinson's disease attending the Parkinson's Disease Clinic of the Ottawa Civic Hospital and twenty people without a chronic illness will be asked to participate in this study. If you decide to enter the study, a nurse will assess your motor symptoms. This will take about 10 minutes.

The principal investigator will then ask you some questions to assess mental status. Afterwards, you will be given a questionnaire to answer. The questions are designed to detect the presence of depressive symptoms. Another 10 minutes will be required to complete these questions. Following this initial visit, you may decide to continue with the

testing sessions right away (if you are judged to be eligible to participate in the study). If you choose to wait, you will be contacted at a later date about your eligibility to participate in the study.

If you are eligible and still interested in participating, an appointment will then be made for you to return to the Ottawa Civic Hospital. There, the principal investigator will give you a total of eight paper and pencil tasks to perform in order to assess your memory, sequencing, and problem solving abilities. You will have the option of completing all the tasks in one session or to spread them out in many sessions based on your schedule. Together, the tasks will take about 2 hours to complete. Your total time in the study will range from one day to approximately 4 weeks. If you would prefer that the testing sessions take place at your home, this can be arranged with Brigitte Patry, the principal investigator.

STANDARD CARE AND TREATMENT: Your treatment for your Parkinson's disease will not change as a result of participating in this study. The assessments are for research purposes, and are more than the usual standard of care for Parkinson's patients.

RISKS AND BENEFITS: There are no known risks associated with this study. The benefit of the study is that it will help further knowledge about mental function in people with Parkinson's disease. This study may also provide clues as to the involvement of specific brain areas in Parkinson's disease, an important issue for drug studies on the prevention of mental decline in this illness.

PARTICIPATION AND WITHDRAWAL: Your participation in this study is completely voluntary. You may choose not to participate, and you may withdraw at any time. Such a decision will not affect your present and future care at this hospital.

CONFIDENTIALITY: The investigators and representatives from the Research Ethics Committee of the Ottawa Civic Hospital may review your medical records in relation to this study. No records bearing your name will leave the Ottawa Civic Hospital. You will be identified only by code on study information. If the results of this study are reported or published, your name or other identifier will not be used.

COMPENSATION: You will not be paid for participation in this study, and no alternate compensation will be offered to you.

PROBLEMS AND QUESTIONS: You are urged to discuss any questions you have about this study with the principal investigator. Please call the principal investigator at any time if you have any further questions about the study or the rights of research participants.

LEGAL RIGHTS: You do not waive any legal rights by signing the consent form to participate in this study.

CONSENT SIGNATURE PAGE

TITLE OF STUDY: Temporal Memory and Executive Functions in High-Functioning Parkinsonian Patients

I have read and received a copy of the information and consent package.

I have had the opportunity to discuss it and ask questions.

I understand the possible risks and benefits of the study.

I, _____, consent to take part in this study.
Patient's Name (please print)

Signature of Patient

Date

Signature of Witness

Date

Name of Witness (please print) _____

I, _____ (investigator), have explained this study and certify that, to the best of my knowledge, the subject signing this consent understands the nature, demands, and benefits involved in participating in this study.

Signature of Investigator

Date

INFORMATION SHEET AND CONSENT FORM (CONTROLS)

TITLE: Temporal Memory and Executive Functions in High-Functioning Parkinsonian Patients

TELEPHONE
830-7788

PRINCIPAL INVESTIGATOR: Brigitte Patry, BA

ASSOCIATE INVESTIGATORS: E. Mohr, PhD
C. L. Barclay, MD
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PURPOSE OF THE STUDY: Several studies have reported changes in mental functioning in people with Parkinson's disease. However, not all studies are in agreement and it remains unclear whether certain areas of the brain are involved in the physical and mental changes occurring in this illness. Better insight as to their involvement may be gained by the study of high-functioning individuals, thought to be least likely to have experienced changes in mental functions.

The purpose of this study is thus to examine the ability to remember not actual items but the order in which they are presented (temporal memory). The study will also focus on general problem solving skills as well as on the ability to organize items in a logical or predetermined sequence (sequencing ability) in high-functioning individuals with Parkinson's disease. It has previously been suggested that to remember the order of presentation of items, a person must be able to organize information in a specific sequence. The same brain areas appear to be involved in these particular mental functions. Therefore, this study will look at the relationship between temporal memory and sequencing ability.

In order to judge the performance of people with Parkinson's disease adequately, their results must be compared with that of people who do not have a chronic illness such as Parkinson's disease. Therefore, both patients with Parkinson's disease and people without a chronic illness are needed to participate.

STUDY PLAN AND PROCEDURES: Twenty people with Parkinson's disease attending the Ottawa Civic Hospital Parkinson's Clinic and twenty people without a chronic illness will be asked to participate in this study.

The principal investigator will ask you some questions to assess mental status. Afterwards, you will be given a questionnaire to answer. The questions are designed to detect the presence of depressive symptoms. Approximately 10 minutes will be required to complete these questions.

Following this initial visit, you may decide to continue with the testing sessions right away (if you are judged to be eligible to participate in the study). If you choose to wait, you will be contacted at a later date about your eligibility to participate in the study. If you are eligible and still interested in participating, an appointment will then be made for you to return to the Ottawa Civic Hospital. There, the principal investigator will give you a total of eight paper and pencil tasks to perform in order to assess your memory, sequencing, and problem solving abilities. You will have the option of completing all the tasks in one session or to spread them out in many sessions based on your schedule. Together, the tasks will take about 2 hours to complete. Your total time in the study will range from one day to approximately 4 weeks. If you would prefer that the testing sessions take place at your home, this can be arranged with Brigitte Patry, the principal investigator.

RISKS AND BENEFITS: There are no known risks associated with this study. The benefit of the study is that it will help further knowledge about mental function in people with Parkinson's disease. This study may also provide clues as to the involvement of specific brain areas in Parkinson's disease, an important issue for drug studies on the prevention of mental decline in this illness.

PARTICIPATION AND WITHDRAWAL: Your participation in this study is completely voluntary. You may choose not to participate, and you may withdraw at any time. Such a decision will not affect your present and future care at this hospital.

CONFIDENTIALITY: The investigators and representatives from the Research Ethics Committee of the Ottawa Civic Hospital may review your medical records in relation to this study. No records bearing your name will leave the Ottawa Civic Hospital. You will be identified only by code on study information. If the results of this study are reported or published, your name or other identifier will not be used.

COMPENSATION: You will not be paid for participation in this study, and no alternate compensation will be offered to you.

PROBLEMS AND QUESTIONS: You are urged to discuss any questions you have about this study with the principal investigator. Please call the principal investigator at any time if you have any further questions about the study or the rights of research participants.

LEGAL RIGHTS: You do not waive any legal rights by signing the consent form to participate in this study.

CONSENT SIGNATURE PAGE

TITLE OF STUDY: Temporal Memory and Executive Functions in High-Functioning Parkinsonian Patients

I have read and received a copy of the information and consent package.
I have had the opportunity to discuss it and ask questions.
I understand the possible risks and benefits of the study.

I, _____, consent to take part in this study.
Subject's Name (please print)

Signature of Subject

Date

Signature of Witness

Date

Name of Witness (please print) _____

I, _____ (investigator), have explained this study and
certify that, to the best of my knowledge, the subject signing this consent understands the
nature, demands, and benefits involved in participating in this study.

Signature of Investigator

Date

APPENDIX F

**Word Sequencing Task: Words Selected and their Frequency of Occurrence
(per Million) in the English Language (Kucera & Francis, 1967)**

<u>Words</u>	<u>Frequency of Occurrence</u>	<u>Syllables</u>
cloud	28	1
fruit	35	1
pocket	46	2
foot	70	1
kitchen	90	2
glass	99	1
season	105	2
story	153	2
island	167	2
road	197	1
tax	197	1
mother	216	2
music	216	2
door	312	1
school	492	1

APPENDIX G

Word Sequencing Task Instructions

I will show you 15 cards, one at a time. On each card, there will be a word. I want you to read that word aloud. Try to remember the order in which the words are presented. You will have 3 s to look at each word.

After showing you all 15 cards, I will place 15 different cards with the same words you read on the table. They will not be in the same order as you saw them before. (Demonstrate with 4 cards with different words).

I want you to rearrange the 15 cards so that the words appear in the same order as when you read them. Make 3 rows of 5 cards each. Place the card with the first word you read to the top left, the second word to its right, and so on, always moving from left to right, until you reach the last word you read. You will place that card at the bottom right. Take your time when you rearrange the cards.

APPENDIX H

Word Sequencing Task Scoring Sheet

Order and Words Presented	Sequence of Words upon Recall	Order
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.		
12.		
13.		
14.		
15.		

APPENDIX I

Temporal Ordering Task Instructions

Picture Presentation and Distracting Activity

I will show you nine cards. On each card, there will be a black-and-white picture of an object. You will have 3 s to look at each picture and tell me the name of the object. As you look at the pictures, try to remember the order in which you see them.

After I will have shown you all nine cards, I will show you other cards with different pictures. For each one, I want you to tell me if the object is part of nature or if it's man-made.

Temporal Ordering Task

The pictures on these nine cards are the same ones that you named but they are not in the same order as before. I want you to rearrange the cards so that the pictures appear in their original order. Place the card with the first picture you saw to the top left, the second one to its right, and so on, always moving from left to right, until you reach the last picture you saw. You will place that card at the bottom right. There is no time limit for this test.

Recognition Targets and Distracting Activity

I will now show you nine pictures that you haven't seen before. Tell me the name of each object and try to remember them. I will then show you other pictures. Again, I want you to tell me if the object is part of nature or man-made.

Delayed Recognition Test

I will now show you the pictures that you named earlier as well as new pictures that you haven't seen before. For each picture, I want you to say "yes" if you saw it before and "no" if you did not.

APPENDIX J

**Temporal Ordering Task: Semantic Categories of the Three Sets of Drawings
Utilized as Temporal Ordering Stimuli, Recognition Targets and Distracters**

	<u>Set 1</u>	<u>Set 2</u>	<u>Set 3</u>
<u>Fruits:</u>	apple	pear	lemon
<u>Vegetables:</u>	carrot	celery	corn
<u>Furniture:</u>	dresser	table	desk
<u>Glassware:</u>	cup	wineglass	glass
<u>Tools:</u>	scissors	saw	pliers
<u>Means of Transportation:</u>	truck	bus	car
<u>Parts of the Human Body:</u>	hand	foot	arm
<u>Articles of Clothing:</u>	shirt	coat	vest
<u>Domestic Animals:</u>	dog	cat	rabbit

APPENDIX K

Temporal Ordering Task Scoring Sheet Example

Correct Order	Order Recalled
1. rabbit	
2. glass	
3. pliers	
4. corn	
5. arm	
6. car	
7. lemon	
8. desk	
9. vest	

Absolute deviation score:

Relative deviation score:

Items Presented	Items "Recognized"	Hits	False Positives
celery			
<u>car</u>			
<u>vest</u>			
table			
<u>rabbit</u>			
pear			
foot			
<u>arm</u>			
wineglass			
cat			
<u>glass</u>			
<u>pliers</u>			
bus			
<u>corn</u>			
saw			
coat			
<u>lemon</u>			
<u>desk</u>			

APPENDIX L

Recency Discrimination Task InstructionsSample

As you can see, there are two names written on each of these cards. What I want you to do is to read each name aloud and then to turn the card over and read the next one, and so on. The first few cards are white.

As you go down the stack you will, from time to time, come to a blue card with a question mark between the two names. When this happens, I want you to tell me which of the two names you have read more recently. Do you understand? (These instructions are repeated if the subject has difficulty understanding).

Sometimes on the blue card one name will be new, one that has not come before in this series, and the other name you will have read before. In this case just tell me which of the two names you have read before.

Test

Now, instead of people's names, you will read this bigger stack of ordinary words. I want you to do the same thing as you did before. Read the words aloud and when you come to a blue card with a question mark on it, tell me which word you read more recently. For example, say "I saw 'apple' more recently". If you have read only one of the two words on the blue card before, tell me which one. For example, say "I only saw 'rabbit' before".

APPENDIX M

Recency Discrimination Task: Words Selected and Frequency of Occurrence (per Million) in the English Language (Kucera & Francis, 1967)

year	660	theory	129	legal	72
house	591	spring	127	wine	72
home	547	farm	125	danger	70
water	442	plant	125	animal	68
hand	431	game	123	career	67
city	393	radio	120	dress	67
room	383	chief	119	jury	67
power	342	window	119	birth	66
light	333	horse	117	chair	66
family	331	corner	115	forest	66
week	275	pool	111	desk	65
money	265	ball	110	belief	65
office	255	price	108	wind	63
street	244	stress	107	beach	61
south	240	health	105	duty	61
land	217	doctor	100	metal	61
child	213	energy	100	speech	61
class	207	film	96	travel	61
north	206	park	94	garden	60
sound	204	dinner	91	moon	60
peace	198	weight	91	nose	60
table	198	king	88	scale	60
book	193	poetry	88	budget	59
fire	187	battle	87	tree	59
space	184	bank	83	stone	58
heart	173	ship	83	artist	57
wall	160	winter	83	bear	57
floor	158	train	82	uncle	57
paper	157	trip	81	wood	55
market	155	watch	81	lake	54
hall	152	coffee	78	breath	53
earth	150	judge	77	grass	53
food	147	bottle	76	gold	52
letter	145	rock	75	hero	52
hour	144	frame	74	player	51
summer	134	valley	73	stream	51
trial	134	writer	73	driver	49
friend	133	boat	72	mantle	48
month	130	hill	72	poem	48

suit	48	guide	36	mirror	27
cook	47	shadow	36	ranch	27
humor	47	bench	35	shirt	27
luck	47	fish	35	bath	26
mail	47	bright	35	beard	26
opera	47	knee	35	card	26
ring	47	yard	35	cellar	26
artery	46	corn	34	fist	26
decade	46	crime	34	storm	26
dollar	46	golf	34	widow	26
brain	45	ocean	34	noon	25
mold	45	pencil	34	parade	25
sheet	45	sugar	34	penny	25
brush	44	branch	33	pond	25
path	44	bride	33	saddle	25
snake	44	gift	33	star	25
coat	43	jacket	33		
drama	43	lunch	33		
lawyer	43	prince	33		
reader	43	rice	33		
route	43	debate	32		
salary	43	bird	31		
golden	42	maid	31		
skill	42	panel	31		
wire	42	studio	31		
bread	41	trail	31		
match	41	tube	31		
queen	41	fence	30		
tissue	41	meal	30		
talent	40	root	30		
tool	40	barn	29		
guest	39	belt	29		
palace	38	lesson	29		
piano	38	movie	29		
sister	38	silver	29		
gate	37	stem	29		
noise	37	dawn	28		
paint	37	powder	28		
supper	37	prize	28		
baker	36	sand	28		
camera	36	butter	27		
cash	36	chin	27		
error	36	fiber	27		

APPENDIX N

Recency Discrimination Task Scoring Sheets

Words Presented	Saw More Recently	Saw Before
Joe - <u>Jack</u>		*
Ann - <u>Lynn</u>	*	
Mary - <u>Carol</u>	*	
<u>Peter</u> - George		*
<u>Sarah</u> - Jim		*
<u>Paul</u> - Julie	*	

Scoring Sheet for Test

Words Presented	Saw More Recently	Saw Before	Correct	Recency Interval
<u>home</u> - house				
<u>ship</u> - fire				4 vs 16
<u>bear</u> - winter				4 vs 8
<u>food</u> - wood				
spring - <u>summer</u>				
bath - <u>path</u>				
<u>letter</u> - powder				8 vs 16
<u>hour</u> - month				
floor - <u>cook</u>				
<u>hero</u> - yard				
window - <u>branch</u>				4 vs 32
trip - <u>gift</u>				4 vs 16
<u>supper</u> - dress				16 vs 32
bank - <u>office</u>				8 vs 32
dinner - <u>lunch</u>				

Words Presented	Saw More Recently	Saw Before	Correct	Recency Interval
<u>space</u> - penny				
north - <u>ranch</u>				8 vs 16
storm - <u>root</u>				4 vs 32
<u>mail</u> - snake				8 vs 32
<u>sheet</u> - heart				4 vs 16
bread - <u>brush</u>				
uncle - <u>route</u>				8 vs 32
battle - <u>bottle</u>				
train - <u>match</u>				8 vs 32
<u>queen</u> - king				8 vs 16
<u>palace</u> - paint				16 vs 32
<u>mirror</u> - wire				
bird - <u>barn</u>				16 vs 32
<u>tree</u> - skill				16 vs 32
<u>grass</u> - valley				16 vs 128
<u>pond</u> - metal				32 vs 128
career - <u>mold</u>				4 vs 32
jacket - <u>market</u>				
<u>poem</u> - artist				
<u>land</u> - travel				4 vs 32
<u>widow</u> - friend				32 vs 128
gate - <u>book</u>				8 vs 32
<u>health</u> - breath				
water - <u>power</u>				32 vs 128
card - <u>horse</u>				4 vs 16
lawyer - <u>ocean</u>				16 vs 128
sister - <u>belt</u>				16 vs 32
noise - <u>artery</u>				

Words Presented	Saw More Recently	Saw Before	Correct	Recency Interval
<u>rice</u> - studio				32 vs 128
<u>year</u> - decade				
<u>knee</u> - guest				8 vs 16
shirt - <u>family</u>				16 vs 128
<u>talent</u> - bench				
<u>reader</u> - street				4 vs 8
<u>golden</u> - suit				8 vs 128
<u>camera</u> - film				
coat - <u>boat</u>				
salary - <u>coffee</u>				
chair - <u>error</u>				4 vs 8
<u>wind</u> - stress				8 vs 16
<u>rock</u> - stone				
south - <u>panel</u>				4 vs 128
birth - <u>fish</u>				4 vs 32
<u>trial</u> - class				8 vs 128
<u>fiber</u> - frame				4 vs 8
meal - <u>golf</u>				
baker - <u>tissue</u>				32 vs 128
guide - <u>peace</u>				4 vs 32
<u>fence</u> - crime				4 vs 8
<u>city</u> - money				4 vs 128
<u>nose</u> - chin				
lesson - <u>dollar</u>				4 vs 16
<u>scale</u> - bride				16 vs 32
<u>hill</u> - shadow				16 vs 128
theory - <u>chief</u>				8 vs 128
hall - <u>wall</u>				
sound - <u>farm</u>				4 vs 128

Words Presented	Saw More Recently	Saw Before	Correct	Recency Interval
<u>danger</u> - animal				8 vs 128
maid - <u>poetry</u>				32 vs 128
lake - <u>desk</u>				
<u>noon</u> - plant				4 vs 16
garden - <u>saddle</u>				4 vs 128
<u>butter</u> - movie				4 vs 128
<u>parade</u> - doctor				16 vs 128
<u>cellar</u> - table				
tube - <u>duty</u>				8 vs 128
<u>corn</u> - sugar				
<u>gold</u> - pool				16 vs 128
watch - <u>game</u>				8 vs 16
week - <u>wine</u>				
moon - <u>stem</u>				8 vs 32
writer - <u>judge</u>				8 vs 128
paper - <u>radio</u>				4 vs 128
<u>forest</u> - ball				4 vs 8

Number of correct recency discriminations at each combination of recency levels:

4 vs 8:

4 vs 16:

4 vs 32:

4 vs 128:

8 vs 16:

8 vs 32:

8 vs 128:

16 vs 32:

16 vs 128:

32 vs 128:

Number of words correctly recognized:

APPENDIX O

Digit Ordering Test Instructions and Scoring Sheet

I am going to say some numbers. Listen carefully, and when I stop I want you to say them in ascending order, from the smallest number to the biggest one. Sometimes a number will be repeated more than once within a sequence. When it does, I want you to say that number as many times as you have heard it, but remember that you are to repeat the numbers in ascending order. For example, if I say 1 6 4 1 3 9 3, what would you say?

If subject fails the example

No, you would say 1 1 3 3 4 6 9. I said 1 6 4 1 3 9 3, so to say it in ascending order you would say 1 1 3 3 4 6 9. Now try these numbers. Remember, you are to say them in ascending order: 5 4 8 1 7 2 3. (Answer is 1 2 3 4 5 7 8).

Item	Digits	Response	Score
1.	6 4 8 6 1 9 8		
2.	1 3 7 2 5 9 4		
3.	5 3 6 2 7 2 1		
4.	2 5 7 1 5 6 3		
5.	9 1 4 7 3 4 8		
6.	7 6 3 2 5 9 3		
7.	3 5 1 6 8 9 4		
8.	1 7 4 6 8 2 7		
9.	5 9 3 9 4 2 8		
10.	4 1 8 5 3 2 9		
11.	8 2 6 9 5 8 7		
12.	9 7 2 6 7 1 6		
13.	2 7 4 5 9 3 1		
14.	5 7 8 4 6 1 3		
15.	3 4 6 2 8 1 5		

APPENDIX P

Mann-Whitney U - Wilcoxon Rank Sum W Tests

WCSTCAT

by GROUP group

Mean Rank Cases

23.35 20 GROUP = 1 NC

17.65 20 GROUP = 2 PD

--

40 Total

		Exact	Corrected for ties	
U	W	2-Tailed P	Z	2-Tailed P
143.0	467.0	.1274	-1.9619	.0498

WCSTPERS

by GROUP group

Mean Rank Cases

19.80 20 GROUP = 1 NC

21.20 20 GROUP = 2 PD

--

40 Total

		Exact	Corrected for ties	
U	W	2-Tailed P	Z	2-Tailed P
186.0	396.0	.7180	-.3797	.7042

WCSTTRY

by GROUP group

Mean Rank	Cases	
20.20	20	GROUP = 1 NC
20.80	20	GROUP = 2 PD
	--	
	40	Total

U	W	Exact 2-Tailed P	Corrected for ties Z	2-Tailed P
194.0	404.0	.8831	-.1837	.8542

TORANK

by GROUP group

Mean Rank	Cases	
23.73	20	GROUP = 1 NC
17.27	20	GROUP = 2 PD
	--	
	40	Total

U	W	Exact 2-Tailed P	Corrected for ties Z	2-Tailed P
135.5	474.5	.0810	-1.7475	.0805

TOABSDEV

by GROUP group

Mean Rank	Cases	
16.45	20	GROUP = 1 NC
24.55	20	GROUP = 2 PD
	--	
	40	Total

U	W	Exact 2-Tailed P	Corrected for ties Z	2-Tailed P
119.0	329.0	.0283	-2.2066	.0273

TORECOGN

by GROUP group

Mean Rank Cases

23.17 20 GROUP = 1 NC

17.83 20 GROUP = 2 PD

--

40 Total

U	W	Exact 2-Tailed P	Corrected for ties Z	2-Tailed P
146.5	463.5	.1493	-1.5258	.1271

VR

by GROUP group

Mean Rank Cases

22.70 20 GROUP = 1 NC

18.30 20 GROUP = 2 PD

--

40 Total

U	W	Exact 2-Tailed P	Corrected for ties Z	2-Tailed P
156.0	454.0	.2423	-1.1953	.2320

VOCAB

by GROUP group

Mean Rank Cases

22.88 20 GROUP = 1 NC

18.13 20 GROUP = 2 PD

--

40 Total

U	W	Exact 2-Tailed P	Corrected for ties Z	2-Tailed P
152.5	457.5	.2012	-1.2891	.1974

IMAGE EVALUATION TEST TARGET (QA-3)

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