Cognitive profile of patients with newly diagnosed Parkinson's disease

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Abstract

Cognitive deficits can occur even in the early stages of Parkinson disease (PD). In many instances these deficits may not be clinically apparent, but they are detectable with specific neuropsychological tests. However, the exact pattern of these impairments and their frequencies are still subjects of considerable controversy. To investigate the cognitive profile of patients with newly diagnosed Parkinson disease (PD) and to determine the demographic and medical variables those contribute to the cognitive outcome. Forty three consecutive patients with newly diagnosed PD and 30 healthy controls were given a neuropsychological test battery investigating psychomotor speed, attention, language, memory, executive and visuospatial functions. Patients also received quantitative ratings of motor symptom severity. Neuropsychological performance of PD patients was compared with that of healthy controls and with available normative data. Independent demographic and clinical predictors of cognitive impairment were identified with multiple logistic regression analysis. Relative to controls, PD patients performed significantly worse on most cognitive measures. However, further analysis revealed that group differences in cognitive performance could mainly be explained by measures of immediate memory and executive function. Comparison with normative data showed that impairments were most frequent on measures of executive function, memory and psychomotor speed. In all, 25.6% of PD patients (6.7%of controls) displayed defective performance on at least three neuropsychological tests and were classified as cognitively impaired. Late onset of disease was an independent predictor of cognitive dysfunction in PD.The observed cognitive impairments in patients with newly diagnosed Parkinson disease are more than expected for normal aging, with deficits being most prominent in the domains of memory and executive functions. Older age at disease onset is likely to be an important determinant of cognitive dysfunction in Parkinson disease.

Introduction

Parkinson's disease (PD) is an age-related, progressive neurodegenerative disorder initially characterized by resting tremor, rigidity, or bradykinesia *(Gelb et al, 1999)*. Cognitive changes can complicate the long-term management of PD and are estimated to occur in 20% to 40% of all diagnosed patients who have PD, leading to a diagnosis of Parkinson's disease with dementia (PDD). Alternatively, cognitive deficits can occur even in the early stages of Parkinson disease (PD) *(Elmer, 2004)*. In many instances these deficits may not be clinically apparent, but they are detectable with specific neuropsychological tests. Some deficits resemble those seen in patients with frontal lobe damage, which is consistent with the anatomic model of basal ganglia thalamocortical circuits *(Louis, 1997)*. However, the exact pattern of these impairments and their frequencies are still subjects of considerable controversy. In support of the hypothesis of "frontal-type dysfunction," isolated deficits have been found in newly diagnosed, nonmedicated PD patients on tests known to be sensitive

to frontal lobe damage *(Mayeux et al, 1981; Dooneief et al, 1992; Cummings et al, 1988 and Fenelon et al, 2006)*. Other studies, however, have found a more generalized pattern of cognitive dysfunction *(Tandberg et al, 1996 and Aarsland et al 1999)*. Furthermore, some investigators found no evidence of "frontal deficit" in their sample, suggesting that such impairment is not a universal cognitive feature of early PD (*Tandberg et al, 1996)*. More over Regardless of the specific classification of cognitive impairment accompanying the extrapyramidal features of PD, dementia has a great impact on the course and management of PD symptomatology *(Elmer, 2004)*. In an attempt to resolve these discrepancies, we examined the frequency and pattern of cognitive impairments in a group of patients with newly diagnosed PD using a comprehensive battery of neuropsychological tests. In addition to comparing the patients' performance to that of healthy controls, standard scores were derived for each measure from published normative data to assess the cognitive profile in a more clinically meaningful manner and with greater external validity. Furthermore, we sought to identify demographic and clinical correlates of cognitive dysfunction in early PD.

Subjects and Methods

Subjects

The patient sample consisted of forty three patients with Parkinson disease (PD) who fulfilled the clinical criteria for the diagnosis of PD *(Calne et al, 1992 and Elmer, 2004)*. They were recruited from the neurology outpatient clinics of Saudi German hospital, Madinah Elmonawarah, King Saudi Arabia. Exclusion criteria were age of 85 years or older, global cognitive decline (Mini-Mental State Examination [MMSE] < 24), and the presence of somatic illness with a life expectancy of less than 1 year. Neurologic examination was conducted for all patients. At the time of the examination, 14 patients were not receiving any medication. Of the remaining 29 patients, 15 were treated with levodopa plus a peripheral levodopa-decarboxylase inhibitor, 6 with a dopamine agonist (pramipexol), two with levodopa in combination with a dopamine agonist (pramipexol in both cases), four with amantadine, one with levodopa in combination with a dopamine agonist and amantadine, and one with amantadine plus an anticholinergic drug. To calculate levodopa dose, we pooled different drugs in a levodopa equivalent dose (LED) *(Emre, 2003)*. None of the patients received antidepressants, benzodiazepines, or antipsychotics. None of the patients had undergone neurosurgical operation for relief of motor symptoms.

Thirty normal control subjects (NCs), who were neurologically intact and age matched to the PD patients, were also recruited. None of the controls had impairment in hearing and visual acuity, history of a major psychiatric disorder, head injury with loss of consciousness in excess of 1 hour, cerebrovascular disease or other CNS illness, drug or alcohol abuse, and were currently taking psychoactive medication. Control subjects underwent only neuropsychological assessment. Written informed consent was obtained from all subjects after the nature of the study was fully explained.

Procedure

Neuropsychological assessment was conducted within 1 to 4 weeks after the neurologic examination.

Neurological examination

A detailed neurologic examination was performed in all patients to check the diagnosis of PD. Information about the onset and course of the disease, initial symptoms, side of onset of disease, medical history, medication, and response to levodopa therapy was obtained with a semistructured interview. The severity of extrapyramidal symptoms was rated using the motor section of the Unified Parkinson Disease Rating Scale (UPDRS) *(Aarsland et al, 2005)*. The stage of disease was determined with the Hoehn and Yahr rating scale. The duration of disease was defined as the time between the appearance of the first symptom of PD as reported by the patient and the moment of assessment.

Neuropsychological assessment

Neuropsychological tests were administered in a fixed order during a period of 2 to 3 hours with suitable rest periods. In addition to assessment of global cognitive functioning (MMSE) *(Louis et al 1997 and Aarsland et al, 2000)* neuropsychological testing examined functions in six cognitive domains: psychomotor speed, attention, language, memory, executive functions, and visuospatial/constructive skills *(Rippon and Marder, 2005)*. Psychomotor speed was evaluated using the Wechsler Adult Intelligence Scale–Revised (WAIS–R), Digit Symbol test (This subtest of the WAIS-III presents the patient with a row of numbers one through nine, each paired with nonsense symbols (e.g., inverted T). Below this key are empty boxes with numbers above each box. The patient is required to transcribe the symbol corresponding to the number above the box as quickly as possible. This measure requires focused attention and switching behavior between the key and the target boxes. One advantage of this test is the extensive WAIS-III norms available on performance expectations) *(Levy et al, 2000)* and Trail Making Test Part A (This test requires the patient to connect randomly positioned numbered circles in numeric order as quickly as possible) *(Berg et al, 1982 and McKeith et al, 2005)*. Attention was assessed with an adapted version of WAIS–R forward and backward digit span (three trials were administered per length of digit strings; the score was the total number of correct responses for each condition, maximum 21) *(Berg et al, 1992)*, and Trail Making Test Part B (The patient is required to connect the circles in numeric and alphabetic order as quickly as possible, alternating between numbers and letters. Both Trail Making forms A and B require focused attention for successful performance) (*McKeith et al, 2005)*. Language function was examined with the Boston Naming Test (Patients are required to name 60 objects depicted in line drawings. The objects range from simple and common objects such as a tree to complex and uncommon objects such as an abacus. If a patient is unable to name an object, he or she is given a phonemic cue and a semantic cue) (BNT; short form, the score was extrapolated to the full-length score) *(Rubin e al, 1998)*. Memory was assessed with the Rey Auditory Verbal Learning Test (This test of verbal memory presents the patient with multiple trials of learning a list of 10 words. Following each presentation of the study list, the patient is asked to recall as many words as possible. Following the fifth repetition of this study list, a new study list is introduced followed by a recall trial. Following this recall, the patient is asked to recall as many of the words from the first list as possible. Finally, a recognition test is given if delayed recall is defective) (RAVLT; trials 1 to 5, 20-

minute delayed free recall and recognition of a list of 15 unrelated words) *(Biggins et al, 1992)*, Logical Memory Test (immediate and 20-minute delayed recall of two stories) *(Aarsland et al, 2001)*, the Wechsler Memory Scale III (WMS–III; faces recognition test immediate and 30-minute delayed recognition) *(Morris, 1993)*, and Visual Association Test (VAT; subjects are shown six pictures of two common objects; recall is tested without a delay by showing one object and asking what other object is missing; one point was awarded for each correctly recalled object; two trials are given resulting in a score range of 0 to 12) *(Morris et al, 2001)*. Executive functions were examined with the Modified Wisconsin Card Sorting Test (MWCST: Patients are presented with four "target" cards with simple colored designs that can be sorted by three concepts. The patients match probe cards with identical colored design to the target cards according to whatever concept they generate. The only feedback to the patient after each trial is whether his or her response is correct. The order of sorting concept is fixed, but unbeknownst to the patient, changes after a set number of correct responses. Thus, patients must be able to switch the concept they were using for the previous trials) *(Petersen et al, 1985)*, and WAIS–III Similarities (This subtest of the WAIS-III requires the patient to identify the common elements between seemingly uncommon stimuli. The test begins with simple problems (e.g., "How are an orange and banana alike?"), and progress to more difficult problems. Scoring awards full credit for complete abstractions, partial credit for concrete responses, and no credit for incorrect responses) *(McKhann et al, 1984)*. Visuospatial and constructive abilities were assessed with the Groningen Intelligence Test (GIT) spatial test (it is a test in which subjects were instructed to select the figures which they thought were needed to fill up a geometric design; one point was awarded for each correct response, range 0 to 20) *(Rockwood et al, 2000)*, and Clock Drawing Test (This test of visual construction in which the patient is required to draw a clock with all the numbers and "set" the clock at 20 minutes to four o'clock) *(National Institute on Aging, Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer's Disease, 1997)*.

Statistics

Differences in demographic and clinical characteristics between the PD and control groups were analyzed with independent two-tailed t-tests. Mann-Whitney test was used to analyze ordinal data, whereas the χ^2 test was used to analyze nominal variables. Cognitive dysfunction was considered to be present if performance on three or more neuropsychological tests was impaired. This criterion was chosen to minimize the possibility that compromised performance reflects a chance finding due to the large number of measures employed. Based on this criterion, PD patients were assigned into cognitively impaired or cognitively intact group.

Results

Demographic and clinical characteristics

PD patients were older and had lower educational level than controls (table 1). There were no differences between the groups with respect to sex distribution, MMSE score, or handedness. The average degree of motor disorder for the PD group fell within the mild-to-moderate range as

evaluated by the Hoehn and Yahr rating scale and the UPDRS motor section.

Neuropsychological performance of PD patients and control subjects

Patients with PD performed worse than controls on most of the neuropsychological measures employed in the present study (table 2). Within the domain of psychomotor speed, differences were significant for each of the two measures after univariate analyses. On tests of attention, univariate differences on Digit span backward and Trail Making Test B accounted for multivariate results. The PD group showed poorer performance on a measure of language function. Within the memory domain, PD patients performed consistently worse than controls on all tests except on measures of delayed word recognition and visual associative learning. Univariate differences with respect to MWCST number of categories, and WAIS Similarities test accounted for the multivariate differences in executive functioning. Multivariate difference between the PD and control groups in the visuospatial domain was due to GIT spatial task.

To determine which tests had greatest ability to differentiate PD patients from controls, we conducted a logistic regression analysis (forward stepwise method). All cognitive measures were entered into the regression analysis as independent variables, whereas the diagnosis (PD vs control group) was the dependent variable. This analysis identified four tests as best discriminating cognitive measures between the PD and control groups: WAIS Digit Symbol Test, RAVLT Trials 1 to 5, WMS–III Faces Immediate Recognition Test and Trail Making Test A. The Digit Symbol Test and Trail Making Test A involve a strong motor component and time constraints. Therefore, differences between PD patients and controls on these tests might be due to the motor disorder. To address this possibility, the logistic regression analysis was repeated excluding the Digit Symbol Test and Trail Making Test A. The results indicated that RAVLT Trials 1 to 5 and WMS-III Faces Immediate Recognition Test were measures that most effectively differentiated patients from controls. This set of variables correctly classified 77% of the cases (86% of PD patients and 63% of controls).

Clinical significance of cognitive impairments in PD patients

To determine to what degree cognitive impairments in PD patients were clinically significant, their performance on each measure was compared with published normative data. The highest frequency of impairment was observed on the Trail Making Test B (16%), followed by WAIS Similarities (14%), Digit Symbol Test (12%) and Clock Drawing Test (11%). The frequency of impairment was less than 10% on the remaining tests (table 3).

Frequency of cognitive dysfunction

Eleven (25.6%) PD patients exhibited cognitive dysfunction, defined as impaired performance on at least three neuropsychological tests (table 4). In comparison, two (6.7%) controls had evidence of cognitive impairment based on this criterion ($\chi^2 = 10.8$; $p = 0.001$).

The cognitively impaired PD group displayed deficits on measures of psychomotor speed, language, attention and executive functions, memory, and visuospatial abilities (figure 1). The lowest frequency of impairment was observed in the domain of language (22%), whereas deficits were found to be most frequent in

the domain of attention/executive functions (100%).

Demographic and clinical variables associated with cognitive dysfunction in PD

The cognitively impaired PD patients were older, disproportionally more male, had a later onset of disease, greater overall severity of disease and more severe axial symptoms and speech impediments than the cognitively intact PD group. There were no differences between the groups with respect to education, duration of PD, severity of tremor, bradykinesia, rigidity and facial mobility or functional status. No difference was observed between cognitively intact and cognitively impaired PD groups with regard to the MMSE score, suggesting mild degree of cognitive dysfunction (table 5).

Those variables shown to be associated with cognitive dysfunction after univariate analyses were submitted to a multiple logistic regression model (backward stepwise method). Because all normative data sets used in this study include adjustment for effects of age, and thus age was accounted for already by the assignment of patients into cognitively intact and impaired groups, this variable was not included in the regression analysis. Furthermore, the UPDRS motor section score and the Hoehn and Yahr scale were not included in the analysis. Although these two variables differed significantly between cognitively intact and cognitively impaired patients in the univariate analyses, differences on these measures were probably due to axial impairment and speech disorder, because other motor symptoms were comparable across the two PD groups. Thus, four variables were submitted to the regression analysis: sex, age at disease onset, axial symptoms and speech disorder. The results showed that only age at disease onset was an independent predictor of cognitive dysfunction in PD (OR = 1.06; 95% CI = 1.01 to 1.12; $p = 0.02$).

Table (1) Demographic and clinical characteristics of Parkinson disease patients and healthy controls

Variable	Patients with PD	Healthy controls	p Value
n	43	30	
Sex, M/F	23/20	16/14	0.98
Duration of PD, mo	15.8 (9.7)		
Age	65.2 (10.1)	62.7 (7.3)	0.05
Education, y	11.7 (2.4)	12.4 (2.2)	0.04
Handedness, R/L	38/5	27/3	0.81
Mini-Mental State Examination	27.8 (1.6)	28.2 (1.4)	0.09
UPDRS (motor section)	16.7 (7.8)		
Hoehn and Yahr scale	1.8 (0.7)		

Data are means (SD) unless noted.
PD=Parkinson disease; UPDRS=Unified Parkinson's Disease Rating Scale.

Table (2): Neuropsychological test findings (raw scores) of PD patients and controls

Measures	PD (n = 43)		HCS (n = 30)		F	p-value	Cohen's d
	M	SD	M	SD			
Psychomotor speed – MANCOVA: F = 15.76; p < 0.001							
Digit Symbol test	36.9	12.0	49.8	10.9	61.41	< 0.001	-0.93†
Trail Making Test A	49.4	19.4	39.8	13.9	8.26	0.005	-0.55
Attention – MANCOVA: F = 4.58; p = 0.002							
Digit span forward	11.9	2.8	11.9	3.1	0.42	0.517	0
Digit span backward	7.9	2.6	9.5	2.7	11.99	0.001	-0.61
Trail Making Test B	136.5	84.4	86.9	31.2	8.79	0.003	-0.51†
Language							
Boston Naming Test	53.5	4.1	55.5	3.1	9.00	0.003	0.003
Memory – MANCOVA: F = 11.17; p < 0.001							
RAVLT trial 1-5	39.0	9.7	48.5	8.9	41.09	< 0.001	-1.01
RAVLT delayed recall	7.9	2.8	10.3	3.0	23.77	< 0.001	-0.83
WMS-III Faces immediate	31.4	4.3	34.7	3.8	23.49	< 0.001	-0.70
Visual Association Test	11.6	0.8	11.8	0.5	2.23	0.137	-0.29
Executive functions – MANCOVA: F = 5.19; p < 0.001							
MWCST, no categories	3.9	1.8	3.9	1.8	17.22	< 0.001	< 0.001
MWCST, no errors	10.2	5.7	7.7	5.7	4.25	0.041	-0.44
MWCST, no perseverations	6.2	6.1	3.4	4.3	7.02	0.009	-0.51
WAIS-III Similarities	20.6	6.0	24.5	5.0	19.93	19.93	19.93
Visuospatial/constructive skills – MANCOVA: F = 4.93; p = 0.003							
GIT spatial task	9.2	3.3	11.3	3.4	11.96	0.001	0.001
Clock Drawing Test	12.6	1.3	12.6	1.3	2.77	0.098	-0.33

MANCOVA=multivariate analysis of variance with age, premorbid IQ as covariates. †Cohen's *d* corrected for processing speed. RAVLT=Rey Auditory Verbal Learning Test; WMS=Wechsler Memory Scale; MWCST= Modified Wisconsin Card Sorting Test; WAIS=Wechsler Adult Intelligence Scale; GIT= Groningen Intelligence Test.

Table 3): Neuropsychological tests and percentages of impaired PD patients and healthy controls (HC) on each test. Impairment was defined as a score below –2SD of age and (if possible education) norms.

Measure	N*	% PD patients impaired	N	% HC impaired
Psychomotor speed				
Digit symbol test	106	12	70	1
Trail Making Test A	115	7	70	1
Attention				
Trail Making Test B	115	16	70	0
Language				
Boston Naming Test	114	9	70	6
Memory				
RAVLT trial 1 -5	115	1	70	0
RAVLT delayed recall	115	1	70	0
WMS -III Faces immediate	115	1	70	0
WMS -III Faces delayed	115	0	70	0
Visual Association Test	113	0	70	0
Executive functions				
MWCST, no categories	115	5	70	0
MWCST, no errors	112	0	70	0
MWCST, no perseverations	112	0	70	0
WAIS -III Similarities	115	14	70	4
Visuospatial/constructive skills				
GIT spatial task	115	9	70	4
Clock Drawing Test	115	11	70	4

RAVLT=Rey Auditory Verbal Learning Test; WMS=Wechsler Memory Scale; MWCST= Modified Wisconsin Card Sorting Test; WAIS=Wechsler Adult Intelligence Scale; GIT= Groningen Intelligence Test. *Varies due to missing values or unavailable norms for older subjects.

Table 4. Number of impaired tests and percentages of Parkinson disease patients and healthy controls demonstrating impairments

No. of tests impaired	Patients with Parkinson disease,%	Healthy controls,%
0	37.4	68.6
1	24.3	20.0
2	14.8	7.1
3	8.7	2.9
4	3.5	1.4
<5	11.3	

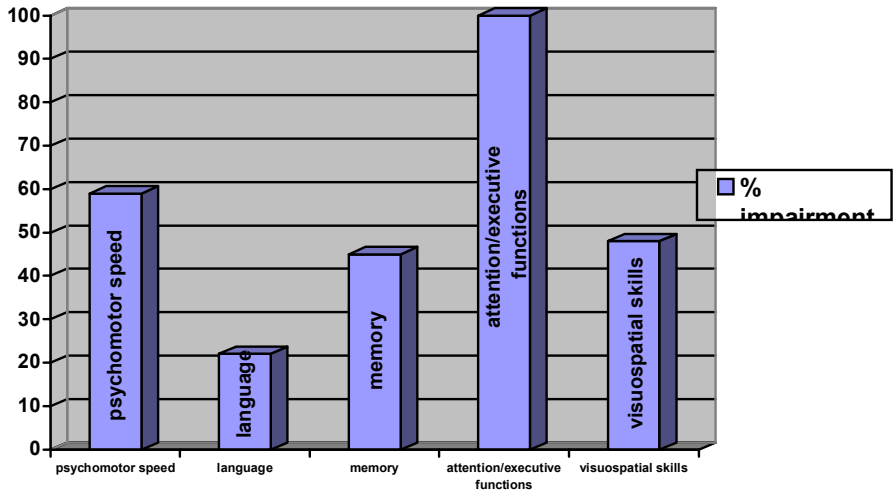

Figure (1): The frequency of impairment across different cognitive domains within the group of cognitively impaired Parkinson disease patients (n = 11).

Table (5): Demographic and clinical characteristics of cognitively intact and cognitively impaired PD patients.

Variable	Intact PD group (n = 32)		Impaired PD group (n = 11)		p-value
	M	SD	M	SD	
Age	62.9	10.4	68.3	8.1	0.02
Gender (M/F)	15/17		8/4		0.04
Education (years)	11.6	2.3	11.7	2.7	0.83
MMSE	28.0	1.5	27.4	1.6	0.06
Age at onset of PD	61.4	10.4	66.6	8.1	0.02
Duration of PD (months)	16.5	10.9	19.9	10.4	0.54
UPDRS (Motor section)	16.0	7.8	19.5	7.5	0.02
Tremor	2.4	1.9	2.2	1.9	0.56
Bradykinesia	5.9	3.1	7.1	3.3	0.08
Rigidity	2.9	2.2	3.7	2.3	0.08
Axial symptoms	1.5	2.0	2.4	1.9	0.01
Speech	0.4	0.5	0.7	0.7	0.03
Face	1.0	0.7	1.3	0.7	0.10
Hoehn & Yahr scale	1.7	0.7	2.1	0.7	0.01
LED (mg/day)[10]	132.9	144.8	186.7	128.8	0.09

UPDRS=Unified Parkinson Disease Rating Scale; MMSE=Mini Mental State Examination; LED=Levodopa equivalent dose.

Discussion

Most of the Available knowledge of cognitive dysfunction in Parkinson's disease (PD) has largely been obtained from studies of chronically treated patients in whom effects of disease chronicity, treatment, depression and dementia are confounding factors (*Cooper et al, 1991)*.

The present study examined the frequency and nature of cognitive impairments in a group of patients with newly diagnosed PD by comparing their performance on a comprehensive battery of neuropsychological tests with that of healthy control subjects. The results indicate that 25.6% of patients in our PD sample showed evidence of cognitive dysfunction. In comparison, 6.7% of control subjects were cognitively impaired. PD patients exhibited impaired performance on a wide range of standardized neuropsychological tests. However, further analysis of individual test performances revealed that deficits in the domains of memory, and attention and executive function constitute the core impairment. The proportion of PD patients with cognitive dysfunction in this study is somewhat lower than in one previous report, in which evidence of cognitive impairment was found in 36% of 159 newly diagnosed patients from a community sample *(Foltynie et al, 2004)*. However, we used more stringent criteria to define cognitive dysfunction; this is probably the reason for a lower frequency of impairment.

When the magnitude of cognitive deficits as expressed in effect sizes was taken into consideration, only deficits in certain aspects of memory function (i.e., immediate and delayed recall) and more complex tests of attention (i.e., Digit Symbol test) appeared to be substantial, whereas decrements on simple measures of attention and processing speed, as well as on tests of language and visuospatial functions were found to be minimal or moderate. Similar findings were observed when the logistic regression analysis was performed on the neuropsychological test battery. This analysis indicated that the Digit Symbol Test differentiated patients with PD from control subjects more effectively than other neuropsychological tests. After excluding tests that depend on processing speed, measures of immediate memory and executive functioning could account for many of the observed group differences in cognitive performance. In contrast, none of the tests purported to measure language and visuospatial functions were entered in the final regression model, suggesting that decreased performance of PD patients on these tests may not reflect truly independent deficits.

The highest frequency of clinically significant cognitive impairments in the PD group was observed on tests of attention and executive functions, and memory (see table 3). Thus, comparison to normative data confirms that deficits in attention and executive function and memory are most prominent features of cognitive dysfunction in patients with PD relative to other cognitive domains.

Although fairly frequent impairment was also observed on the Clock Drawing Test (11%), this finding should be viewed with some caution. The possible explanation for a relatively high rate of impairment on the Clock Drawing Test is that, in addition to measuring constructive ability, this test also involves aspects of executive functions.

Similarly, other measures used to assess visuospatial functions (i.e., GIT spatial task) also require one or more executive components such as spatial reasoning and strategy formation, which are likely to influence performance on these tasks. Thus, it is possible that the observed changes on visuospatial tasks may be due to executive deficits. Our findings from the logistic regression analysis also argue against an independent deficit in visuospatial abilities.

Our results indicate that later onset of disease is an independent predictor of cognitive impairment in patients with PD. This finding is in accordance with a number of cross-sectional *(Katzen et al, 1998)* and longitudinal studies *(Locascio et al, 2003)* in which older age at disease onset was reported to be associated with greater cognitive decline in patients with PD, although such a relationship was not consistently observed *(Huber et al, 1991)*.

In this study, levodopa equivalent dose (LED) was comparable across the cognitively impaired and cognitively intact PD groups. Moreover, only one patient in our sample was taking anticholinergic medication. Thus, cognitive disturbances in our PD patients cannot be attributed to drug treatment, but are likely to be directly related to the pathology of the disease.

Examination of the relationship between impairment of motor functions and the degree of cognitive disturbance in PD has been regarded as a standard clinical approach to determine whether the pathology underlying both types of disorders involves the same neural systems. In this study, the degree of cognitive dysfunction was not associated with the severity of any of the cardinal motor symptom triad of bradykinesia, tremor, or rigidity, which are thought to result from nigrostriatal dopaminergic deficiency. This finding suggests that cognitive dysfunction in early PD patients may reflect neuropathological changes that are distinct from those responsible for the motor disorder.

Similarly the findings of Cooper *et al, 1991* indicate that there is a dissociation of cognition and motor control in early PD and accordingly they suggest that cognitive dysfunction is largely independent of frontostriatal dopamine deficiency underlying motor disability. They concluded that the pathogenesis of the cognitive deficits shown here appears to involve extranstriatal dopamine systems or non-dopaminergic pathology.

Furthermore in the present study as additional support for this assumption is the lack of association between cognitive impairment and dopaminergic medication. In addition, the observation that cognitively impaired PD patients exhibited greater severity of speech deficits and axial impairments (disorders of gait and posture), which are believed to be predominantly mediated by nondopaminergic systems, also provides support for the contention that neural changes distinct from those underlying the motor disorder are likely to play a substantial role in the pathogenesis of cognitive dysfunction in PD.

This study also has some limitations. An important consideration in studies of patients with early PD concerns the accuracy of the clinical diagnosis. Clinicopathological studies indicate that, for a certain percentage of patients with clinical diagnosis of PD, the diagnosis may not be confirmed by neuropathological examination *(Hughes et al, 1992)*. Although

we cannot exclude that some patients in our sample might have been misdiagnosed, we minimized this possibility by including only patients whose diagnoses were confirmed by the neurologic examination performed as a part of the study. Furthermore, because the degree of motor disorders and cognitive impairments in our PD sample was relatively mild, it is possible that meaningful associations between cognitive functioning and motor symptoms may have been left undetected. Finally Logitudinal study in necessary to determine whether increasing disease duration exacerbates the early cognitive deficits and affects new cognitive domains, in addition to producing increasing motor disability.

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طبيعة القدرات الذهنية في مرضى الشلل الرعاشي التشخيص

أن تدهور القدرات الذهنية في مرضى الشلل الرعاشي يمكن أن يحدث في المراحل الأولى من المرض وفى أحيانا كثيرة يكون هذا التدهور غير واضح إكلينيكيا ولكن يمكن اكتشافة بواسطة اختبارات القدرات الذهنية المتخصصة ومع ذلك فأن طبيعة هذا التدهور ومعدل حدوثة لا يزال مجال جدال وخلاف واضحين. ولذلك يهدف هذا البحث لدراسة طبيعة وخصائص القدرات الذهنية في مرضى الشلل الرعاشي الحديث التشخيص وتحديد العوامل الديموجرافية و الإكلينيكية المؤثرة في تحديد طبيعة هذة القدرات. شملت هذة الدراسة ثلاثة وأربعون مريض بالشلل الرعاشي الحديث التشخيص وثلاثون شخصا أصحاء. وقد تم اختبار جميع المشتركين بواسطة مجموعة مختارة من الاختبارات المتخصصة لبحث ١. سرعة التوافق الحركي الذهني النفسي ٢. درجة الانتباة وقدرة التركيز ٣.مهارة استخدام اللغة ٤. الذاكرة ٥. الوظائف الحركية-المرئية-الفضائية. وقد تم مقارنة نتائج الاختبارات لمرضى الشلل الرعاشي بنتائج نفس الاختبارات لأفراد الأصحاء و بالبيانات المعيارية المتاحة لهذة الاختبارات كما تم أجراء تحليل منطقي لمعرفة العوامل المؤثرة في حدوث التدهور الذهني في مرضى الشلل الرعاشي الحديث التشخيص وقد أوضحت النتائج أن معدل حدوث الاضطراب الذهني في مرضى الشلل الرعاشي الحديث التشخيص كان أعلى بصورة ذو دلالة إحصائية (٢٥,٦%) عنة في الأفراد الأصحاء (٦,٧%) ولكن الذاكرة الفورية والوظائف الحركية التنفيذية و سرعة التوافق الذهني الحركي كانوا أكثر القدرات الذهنية اضطرابا و تدهورا في مرضى الشلل الرعاشي الحديث التشخيص عنة في الأفراد الأصحاء كما أوضحت الدراسة أن بداية حدوث المرض في سن متأخر كان من أهم العوامل المؤثرة والمصاحبة لحدوث التدهور الذهني في مرضى الشلل الرعاشي الحديث التشخيص. وقد استنتجت الدراسة أن معدل حدوث التدهور الذهني في مرضى الشلل الرعاشي الحديث التشخيص كان أكثر مما هو متوقع سابقا وان أكثر القدرات الذهنية العرضة للتدهور في هؤلاء المرضى هي الذاكرة والوظائف الحركية-التنفيذية كما استنتج البحث أن سن المريض عند حدوث الشلل الرعاشي هو من أهم العوامل المؤثرة لحدوث التدهور الذهني المبكر بحيث أنة كلما زاد سن المريض عند ظهور مرض الشلل الرعاشي كلما زاد معدل حدوث التدهور الذهني ال