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The Frontal Assessment Battery as a Tool for Evaluation of Frontal Lobe Dysfunction in Patients With Parkinson Disease

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Abstract

Background: Frontal-type cognitive deficits are common in patients with Parkinson disease (PD). The Frontal Assessment Battery (FAB) was developed to assess frontal lobe functions. However, many studies found that it also correlated with a variety of other general neuropsychological tests. **Objectives:** To evaluate whether the FAB has an added value over the Mini-Mental State Examination (MMSE) and other bedside neuropsychological tests in reflecting cognitive deficits in patients with PD. **Methods:** Seventy-two consecutive patients with PD underwent cognitive assessment including the FAB, the MMSE, and a variety of other neuropsychological tests. Correlations were examined using the Spearman's r. **Results:** Highly significant correlations were found between the total FAB score and tests of attention, executive functions, and memory. To evaluate the contribution of the FAB beyond that of the MMSE, partial correlation was used. Analyses revealed that the FAB still correlated with most of the tests. Dividing the patients according to the median MMSE score revealed that the high correlation between the FAB and the MMSE was preserved in the low MMSE group, while in the high MMSE group the correlation was relatively low. In the high MMSE group, the FAB correlated with I I tests compared to the MMSE that correlated with one (P < .001), while in the low MMSE group the number of correlations was I3 versus 7, respectively (P = .05). **Conclusions:** In our sample of patients with PD, the FAB correlated with dysfunction in a variety of cognitive domains including attention, memory, and executive functions. The FAB has an added value over the MMSE, particularly among nondemented patients, an advantage that can be used in clinical practice.

Keywords

Parkinson disease, frontal assessment battery, frontal lobe dysfunction

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Introduction

Cognitive impairment may begin early in Parkinson disease (PD). As the disease progresses, patients may develop dementia due to dysfunction of the subcortical dopaminergic, noradrenergic, and cholinergic circuits arising from the accumulation of α-synuclein-related pathology in the brain, as well as from agerelated changes including plaques and tangles and/or vascular changes. Dementia occurs in 15% to 44% of patients with PD, ^{1,2} and 20 years from disease onset it is present in 83% of survivors. ³ Frontal lobe dysfunction is common in patients with PD⁴ and the prototype of dementia is a dysexecutive syndrome with impaired attention, executive functions, visuspatial orientation, and secondarily impaired memory. ^{5,6} These specific deficits, that can affect social adaptation and professional achievements, are difficult to evaluate at bedside or in the clinic and may necessitate

the performance of detailed and time-consuming neuropsychological assessment.

The frontal assessment battery (FAB)⁷ is a recently introduced short bedside test consisting of 6 subtests that explore various functions of the frontal lobes, including (1) similarities

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Table 1. Patient's Baseline Characteristics^a

		MMSE Group			
	All Patients	Low MMSE	High MMSE	P Value	
Gender (males)	46 (63.9)	15 (51.7)	24 (75.0)	0.059	
Age (years)	68.7 ± 1Í.6	74.6 ± 7.7	63.8 ± 1Í.6	<0.001	
Education (years)	$12.0 \frac{-}{\pm} 3.7$	$10.7 \frac{-}{\pm} 3.7$	13.1 ± 3.2	0.008	
Disease duration (years)	6.7 + 4. 7	7.5 + 4.8	6.6 + 5.0	0.515	
Motor UPDRS stage	23.8 + I2.0	27.5 + I3.I		0.034	
Hoehn and Yahr score	$2.3 \frac{-}{\pm} 0.8$	2.4 ± 0.8	$\frac{-}{2.1} \pm 0.7$	0.146	

Abbreviations: MMSE, Mini-Mental State Examination; UPDRS, Unified Parkinson's Disease Rating Scale.

(conceptualization), (2) lexical fluency (mental flexibility), (3) motor series (programming), (4) conflicting instructions (sensitivity to interference), (5) inhibitory control (Go-No-Go), and (6) environmental autonomy. The score for each item is between 0 and 3 and the maximal possible total score is 18 with higher scores indicating better performance.

In the original study presenting the FAB, it was found to be a valid and sensitive test of frontal lobe dysfunction in patients with extrapyramidal disorders. Two additional studies have since claimed that the FAB is useful and reliable for bedside evaluation of frontal lobe function in patients with PD and frontotemporal dementia. 8,9

However, most studies evaluating the validity of the FAB for frontal lobe dysfunction in dementia^{10,11} as well as in PD¹² and other extrapyramidal disorders^{13,14} have consistently found it to be highly and significantly correlated with a variety of other neuropsychological tests. These include measures of general cognitive impairment, such as the Mini-Mental State Examination (MMSE; *r* values ranging from .49 to .73)^{10-12,14} and the Mattis Dementia Rating Score, ¹³ as well as measures of memory¹¹ and executive functions, including the trail making test, ¹² the Wisconsin card sorting test, ¹¹⁻¹³ and verbal fluency tests. ^{10,12,13} While the positive correlations of the FAB with "frontal" tests are expected, its correlation with other tests that do not reflect executive functions may point to a lack of specificity.

The aim of this study was to evaluate whether the FAB has an added value over the MMSE and other bedside neuropsychological tests in reflecting cognitive deficits in general and frontal lobe dysfunction in particular in patients with PD. We therefore tested its correlations with an extensive battery of neuropsychological tests in a large nonhomogenous group of consecutive patients with PD. In order to see whether this potential advantage of the FAB depends on the cognitive level, we also analyzed the FAB as a function of the performance on MMSE.

Methods

Participants

Seventy-two consecutive patients (46 men) with idiopathic PD were recruited from the Movement Disorders Clinic at Sheba Medical Center. The mean age was 68.7 ± 11.6 years (range

42-96 years) and the mean disease duration was 6.7 ± 4.7 years (range: 0.5-27 years). The mean Hoehn and Yahr (H&Y) score was 2.3 ± 0.8 (range 1-4). Sixty-three patients (87%) were treated by levodopa at the time of inclusion in the study. The baseline characteristics of the patients appear in Table 1 (column 1).

Participants were diagnosed by a neurologist specializing in movement disorders, in accordance with the UK Brain Bank Criteria. Patients were excluded if they had 1 or more of the following: another central nervous system disorder (eg, normal pressure hydrocephalus, stroke); a concomitant primary psychiatric disorder; an end stage state (eg, severe parkinsonism), any cranial neurosurgical procedure or head trauma. The study was approved by the Institutional Review Board, and all participants signed an informed consent form.

All patients underwent an interview-based assessment of demographic and clinical data followed by a detailed neurological examination and rating of severity and stage of motor impairment including part III (motor examination) of the Unified Parkinson's Disease Rating Scale (UPDRS)¹⁶ and the H&Y staging.¹⁷

The FAB⁷

The FAB consists of 6 subtests designed to test various functions of the frontal lobe including:

- 1. Conceptualization and abstract reasoning. Participants are asked to determine the category similarity between 2 objects (eg, a banana and an orange).
- 2. Mental flexibility is tested by verbal fluency. This test requires self-organization and cognitive strategies, both of which may be impaired by frontal lobe dysfunction. Participants are asked to list out loud as many words as possible beginning with a specific letter in 1 minute.
- 3. Motor programming. Participants are asked to observe and then perform the Luria maneuver, repeating the pattern (fist-edge-palm) demonstrated by the examiner.
- 4. Sensitivity to interference may be observed in tasks in which the verbal commands conflict with sensory information. The participant is asked to provide an opposite response to the examiner's alternating signal, for example, tapping once when the examiner taps twice.

 $^{^{\}rm a}$ Values are N (%) for categorical variables and mean (\pm SD) otherwise.

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Table 2. Patients' Scores on Various Neuropsychological Tests^a

		MMSE Group			
	All Patients	Low MMSE	High MMSE	P Value	
MMSE	26.8 ± 3.0	24.6 ± 3.1	28.8 <u>+</u> 0.8	<.001	
FAB TS	13.9 ± 3.4	12.3 ± 3.8	15.2 ± 2.2	<.001	
FAB I	2.6 ± 0.6	2.4 ± 0.8	2.7 ± 0.4	.081	
FAB 2	1.7 <u>+</u> 1.1	I.2 <u>+</u> I.0	2.1 <u>+</u> 1.0	.001	
FAB3	2.5 ± 0.8	2.2 ± 1.0	2.8 ± 0.5	.003	
FAB 4	2.5 ± 0.9	2.l <u>+</u> l.l	2.8 ± 0.6	.002	
FAB 5	1.7 <u>+</u> 1.1	1.5 <u>+</u> 1.2	1.8 <u>+</u> 1.0	.279	
FAB 6	2.8 ± 0.6	2.8 ± 0. 7	2.8 ± 0.5	.858	
FAB I-5	11.1 ± 3.2	9.4 ± 3.5	12.4 ± 2.2	<.001	
RCF immediate recall	13.1 <u>+</u> 8.3	10.1 <u>+</u> 7.6	14.8 <u>+</u> 8.4	.053	
RCF delayed recall	13.5 ± 7.9	10.6 ± 8.0	15.3 ± 7.4	.045	
RAVLT trial I	4.4 <u>+</u> 2.4	4.2 <u>+</u> 2.3	4.6 <u>+</u> 2.4	.542	
RAVLT trial 5	9.1 <u>+</u> 3.3	7.9 <u>+</u> 3.4	10.0 <u>+</u> 2.9	.014	
RAVLT delay	7.6 ± 3.7	6.3 ± 3.8	8.6 <u>+</u> 3.4	.021	
Digit forward	7. 8 <u>+</u> 2.4	7.1 <u>+</u> 2.2	8.4 <u>+</u> 2.4	.040	
Digit backward	5.4 <u>+</u> 2.4	4.4 <u>+</u> 1.9	6.3 <u>+</u> 2.6	.003	
TOH time (seconds)	428.7 ± 253.3	575.9 <u>+</u> 297.7	363.2 ± 204.5	.013	
Number cancellation test I (seconds)	147.9 <u>+</u> 70.2	181.8 <u>+</u> 84.6	120.8 <u>+</u> 40.1	.001	
Number cancellation test 2 (seconds)	153.9 <u>+</u> 57.6	174.3 <u>+</u> 64.8	137.5 <u>+</u> 45.8	.018	
Trail making A (seconds)	127.6 ± 127.3	183.8 <u>+</u> 170.4	85.9 ± 55.7	.006	
Trail making B (seconds)	242.4 <u>+</u> 157.5	314.5 <u>+</u> 179.3	194.3 <u>+</u> 122.1	.012	
Phonemic word fluency	7.5 <u>+</u> 3.2	6.5 <u>+</u> 2.9	8.2 <u>+</u> 3.3	.082	
Semantic word fluency	14.2 ± 6.0	11.5 \pm 5.0	16.2 ± 5.9	.004	

Abbreviations: MMSE, Mini-Mental State Examination; FAB TS, frontal assessment battery total score; Rey AVLT Trial I, Rey Auditory Verbal Learning Test: immediate recall; Rey AVLT Trial 5, Rey Auditory Verbal Learning Test: learning; RCFC, Rey-Osterrrieth complex figure test; TOH time, Tower of Hanoi puzzle: time to solution.

- 5. Inhibitory control is tested by using the go-no-go paradigm. The participant is asked to inhibit a response that was previously given to the same stimulus, for example, not tapping when the examiner taps twice.
- 6. Environmental autonomy is evaluated by sensory stimuli anticipated to activate patterns of responses that are normally inhibited. Prehension behavior (loss of environmental autonomy) occurs when the visual or tactile perception of the examiner's hands compels the patient to take them.

For each item a score of a 0-to-3 is given, resulting in a possible range of 0 to 18 points, with lower scores indicating greater impairment.

Neuropsychological Assessment

All patients were assessed by a well-trained Neuropsychologist who performed a battery of questionnaires and semiquantitative tests to evaluate global cognitive functioning, including the MMSE, ¹⁸ the Hebrew version of the FAB (total score and subscores), the Rey-Osterrieth complex figure test (RCFC; including copy, immediate, and delayed tests), ¹⁹ the Hebrew version of the Rey Auditory Verbal Learning Test (RAVLT), ²⁰ the digit span (DS) forward and backward tests, ²¹ the trail making A and B tests (TM), the Tower of Hanoi (TOH) puzzle, the

phonemic and semantic word fluency tests (PWFT and SWFT), and the number cancellation (NC) test.²² In all tests, the raw scores were analyzed.

Statistical Analysis

Correlations between the tests, the MMSE, and the FAB (before and after controlling for MMSE by partial correlation) were examined using Spearman's r. This correlation is based on the ranked observation of the 2 variables and therefore makes no assumption about the distribution of the values and is robust to outliers. When appropriate, P values were corrected to account for multiple comparisons using the false discovery rate (FDR) method.²³ Comparison of the number of correlations between the groups was done using Fisher exact test. P values of less than .05 were considered significant.

Results

The MMSE mean score was 26.8 ± 3.0 (range: 13-30) and the median score 27. The mean FAB score was 13.9 ± 3.4 (range: 3-18). The patient's scores on the various neuropsychological tests are presented in Table 2, column 1.

All the patients that were defined as demented according to their formal testing had the typical features of PD dementia

^a FAB I-5 is the sub score in section I to 5. Number cancellations test I is the I-digit cancellation (8) and number cancellation test 2 is the 2-digit cancellation (5 & 3). P values for comparison between low and high MMSE groups.

Table 3. Correlation Between the FAB and MMSE With Various Baseline Characteristics^a

	FAB TS	MMSE	FAB TS Low MMSE	FAB TS High MMSE
Age	60°	51°	51 ^b .44 ^b 3369 ^c 18	57 ^b
Years of education	.49°	.46°		.27
Hoehn and Yahr stage	44°	29 ^b		50 ^b
Motor UPDRS score	57°	44 ^b		34
Disease duration	19	18		18

Abbreviations: MMSE, Mini-Mental State Examination; FAB TS, frontal assessment battery total score; UPDRS, Unified Parkinson's Disease Rating Scale.

Table 4. Correlations Between the FAB and MMSE and Other Neuropsychological Tests^a

TEST	FAB TS	MMSE	FAB TS pc
MMSE	.54°	1	
FAB	I	.54°	
RCFC immediate recall	.60°	.28	.56°
RCFC delayed recall	.49°	.35 ^b	.44 ^c
RAVLT trial I	.39 ^b	.23	.32 ^b
RAVLT trial 5	.65°	.46°	.55°
RAVLT delay	.56°	.43 ^b	.45°
Digit forward	.28 ^b	.40 ^b	.08
Digit backward	.49°	.50°	.30 ^b
TOH time	−.51°	−.35 ^b	−.48 ^c
Number cancellation test I	−.54 ^c	−. 49 °	−. 4 1 ^b
Number cancellation test 2	55^{c}	−. 4 1 ^b	−.45 ^c
Trail making A	66 ^c	−.51°	−.55 ^c
Trail making B	73^{c}	−. 47 ^b	−.67 ^c
Phonemic word fluency	.66°	.42 ^b	.59°
Semantic word fluency	.66°	.44 ^b	.59°

Abbreviations: MMSE, Mini-Mental State Examination, FAB TS, frontal assessment battery total score; FAB TS pc, frontal assessment battery total score partial correlation after controlling for MMSE; RCFC, Rey complex figure test; Rey AVLT Trial I, Rey Auditory Verbal Learning Test: immediate recall; Rey AVLT Trial 5, Rey Auditory Verbal Learning Test: learning; TOH time, Tower of Hanoi puzzle: time to solution.

(PD-D) and fulfilled the Movement Disorders Society criteria for probable PD-D. $^{24}\,$

When correlations with baseline characteristics were tested it was found that both the FAB and the MMSE inversely correlated with age and disease severity as reflected by UPDRS and H&Y scores. The level of education correlated positively with the FAB and MMSE as highly educated patients achieved higher scores in these tests. No correlation was found between the FAB and MMSE score and the disease duration (Table 3).

When Spearman correlations between the scores of the FAB and the other cognitive tests were calculated, a high and

significant correlation (.54) was found between the FAB and the MMSE. The total FAB score in the entire patient group also significantly correlated with tests of attention (NC, TM, and DS), executive functions (PWFT and SWFT), memory (RCFC and RAVLT), and the skill learning (TOH; Table 4).

As evident in Table 4, the MMSE also highly correlated with other tests. The number of correlations was similar to the number of tests that correlated with the FAB: (12 versus 14 P = .48, Fisher exact test) but r values were generally lower than those of the FAB for the majority of tests.

To evaluate the contribution of the FAB beyond that of the MMSE, partial correlations between the FAB and other tests were performed, with the effects of the MMSE removed. As seen in Table 4, these analyses showed that even_after partial correlation, the FAB still significantly correlated with most (13 out of 14) of the other tests.

As it seemed that the FAB has no advantage over the MMSE in reflecting cognitive decline in the entire group of patients with PD, we wanted to test whether it might be superior to the MMSE in subgroups of patients with different degrees of cognitive impairment. We therefore examined the correlations between the FAB and other tests in 2 subgroups (30 patients in the low MMSE group and 33 patients in the high MMSE group) divided according to the median MMSE score (Table 5). As can be seen, the significant correlation between the FAB and the MMSE was preserved in the low MMSE group (.59), while in the high MMSE group the correlation was relatively low and nonsignificant (.30). This points to the possibility that in the latter group the 2 tests are not sensitive to the same dysfunctions. This trend is further strengthened by the fact that in the high MMSE group the FAB correlated with 11 tests compared to the MMSE that correlated with only 1 test (P < .001, Fisher exact test); while in the low MMSE group, the number of correlations was 12 versus 6, respectively (P = .046, Fisher exact test). Partial correlation analysis revealed a reduction in the number of tests correlated with the FAB in the low MMSE group (from 12 to 8 tests, P = .209) alongside a preservation of the number of correlations in the high MMSE group (the same 11 tests).

Analysis of the subscores for specific FAB items revealed that most patients had similar scores (of 3) on item 6 (environmental autonomy). Moreover, the correlations did not change significantly when this item was omitted (data not shown), reflecting its lack of sensitivity.

Discussion

A number of studies have already examined whether the FAB can be used to detect executive dysfunction in PD,^{7,8} and correlations between the FAB and other executive and non-executive measures, including the MMSE, have also been explored. However these studies were done either in non-PD patients, ^{10,14,25} or in a small number of patients, ¹³ and in most of them the FAB was correlated with a limited number of neuropsychological tests. ^{7,12,14} Our study is therefore unique by performing an extensive battery of tests in a large population of patients with PD.

^a Correlations are expressed as Spearman's r.

^b *P* < .05.

^c P < .001 (both values statistically significant).

^a Correlations are expressed as Spearman's r. Number cancellations test 1 is the 1-digit cancellation (8) and the number cancellation test 2 is the 2-digit cancellation (5 & 3).^b P < .05.

^c *P* < .001 both values statistically significant (after correction for multiple comparisons).

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Table 5. Correlations Between the FAB and MMSE and Other Neuropsychological Tests in Subgroups Divided According to Median MMSE Score^a

	Low MMSE			High MMSE		
	FAB TS	MMSE TS	FAB TS pc	FAB TS	MMSE TS	FAB TS pc
MMSE	.59 ^b	l		.30	ı	
FAB	I	.59 ^b		I	.30	
RCFC immediate recall	.83°	.13	.83°	.50 ^b	.05	.51 ^b
RCFC delayed recall	.64 ^b	.26	.63 ^b	.38 ^b	.14	.36 ^b
RAVLT trial I	.55 ^b	.34	.47 ^b	.23	.30	.14
RAVLT trial 5	.75°	.51 ^b	.66°	.49 ^b	.31	.42 ^b
RAVLT delay	.60 ^b	.38	.51 ^b	. 46 ^b	.33	.39 ^b
Digit forward	.18	.32	09	.26	.42	.16
Digit backward	.54 ^b	.63°	.27	.33	.30	.27
TOH time	14	13	13	60^{b}	11	−.60 ^c
Number cancellation test 1	−.51 ^b	−.63 ^b	26	−.39 ^b	03	−.39 ^b
Number cancellation test 2	−.47 ^b	−.64 ^b	19	61°	05	−.62 ^c
Trail making A	−. 72 °	−.58 ^b	−.62 ^c	−.50 ^b	−. 3 l	−. 46 ^b
Trail making B	−. 48 ^b	−.58 ^b	42	81°	26	−.80 ^c
Phonemic word fluency	.53 ^b	.27	.48 ^b	.69°	.50 ^b	.64 ^c
Semantic word fluency	.58 ^b	.46	.49 ^b	.68°	.14	.67°

Abbreviations: MMSE, Mini-Mental State Examination; FAB TS, frontal assessment battery total score; FAB TS pc, frontal assessment battery total score partial correlation; RAVLT, Rey Auditory Verbal Learning Test; Rey AVLT Trial I, Rey Auditory Verbal Learning Test: immediate recall; Rey AVLT Trial 5, Rey Auditory Verbal Learning Test: learning; TOH time, Tower of Hanoi puzzle: time to solution.

In the current study, a significant correlation was found between the FAB score and various neuropsychological tests including measures of attention, memory, and executive function, in patients with PD. Consistent with previous reports in the literature, ¹⁰⁻¹⁴ the FAB was highly correlated with the MMSE. These high correlations that were preserved even after removing the effect of the MMSE by partial correlation show that the FAB is in accordance with general cognitive impairment in many cognitive domains.

The finding that in the full sample the FAB correlates with more tests than the MMSE could be explained by the assumption that in order to succeed in many tasks, that do not specifically test executive functions, one must use executive skills like divided attention and learning strategies (as tested in the verbal memory test) or spatial organization (as in the DS test or the TM tests). This_assumption is supported by our finding that there seems to be a trend for stronger correlations of the FAB, than those of MMSE, in tests like RAVLT trial 5 (where strategy is needed at the end of the memory test), in the NC2 test (where spatial organization is required), or in TMB test (where one should do shift and control).

When the correlation between the FAB and other tests was examined in 2 groups based on the median MMSE, the high correlation between the FAB and the MMSE was preserved only in the low MMSE group. It seems therefore that when the cognitive function is impaired, patients show dysfunction in both tests; but when the cognitive function is relatively preserved, the FAB and the MMSE detect dysfunction in different

cognitive domains. "In the high MMSE group the proportion of the tests correlated with the FAB was higher than the proportion correlated with the MMSE and this pattern was preserved following partial correlation. This may point to the possibility that the FAB has an added value over the MMSE in capturing cognitive deficits in non-demented PD patients." In other words, it seems that in a patient with PD with a relatively high cognitive function the FAB will be more effective than the MMSE in reflecting various cognitive deficits.

There are a number of possible explanations for the lack of specificity of the FAB total score with respect to frontal dysfunction in our samples. First, our patients had deficits in a variety of cognitive domains, such that the FAB score was correlated with other tests of cognitive dysfunction. This possibility is in accordance with our finding that the correlation between the FAB and MMSE was lower in the subgroup of patients with relatively good cognitive function. It is also supported by previous reports²⁶ that patients with PD exhibit cognitive impairment in many domains including visuospatial functions,²⁷ memory,²⁸ speech and language,²⁹ and attention. 28,30 However, the fact that previous studies found the same pattern of correlation with the MMSE and other tests may point to the possibility that that there is a structural component in the FAB that is not specific to frontal processes, such that the findings cannot be attributed to characteristics of the current sample. Second, frontal dysfunction is known to affect patients' performance in other cognitive domains (eg., attention and memory), and the high correlation between the FAB and

^a Correlations are expressed as Spearman's r. Number cancellation test 1 is the 1-digit cancellation (8) and the number cancellation test 2 is the 2-digit cancellation (5 & 3).

^b P < .05.

^c P < .001 both values statistically significant (after correction for multiple comparisons).

other cognitive tests may be attributed to these causal effects. It is assumed that due to the possible frontal/executive dysfunction, patients with PD have difficulty inhibiting irrelevant resources while performing a task, which may lead to excessive cognitive load. This may, in turn, decrease cognitive processing speed and potentially result in impairment in performing a variety of cognitive tasks. 10 Third, the cognitive processes tested by the FAB may not be specific to frontal lobe function but rather require the integrity of other brain regions. This possibility is supported by the report that the FAB cannot differentiate frontal dementia from Alzheimer disease (AD)¹⁰ and by the finding that patients with PD with a low FAB score have a reduced perfusion in the left inferior parietal lobule and in the left supramarginal gyrus, indicating that decreased FAB scores in these patients may be caused by parietal lobe dysfunction in addition to their preexisting frontal lobe impairment.³¹

The FAB is a feasible bedside test that can be a useful tool in clinical practice, enabling the clinician to screen for initial cognitive dysfunction in patients with PD. This may be especially relevant in nondemented individuals in whom specific deficits are not revealed by the MMSE. Identifying those deficits is important since their presence can predict behavioral problems and impairment of social and professional adaption that can be potentially improved by behavioral or psychological treatment.

In our population, the FAB and the MMSE were correlated with age, disease severity, and the level of education. The inverse correlation with age was previously reported²⁵ and is probably attributed to age-related structural changes in the frontal lobes.³² The effect of education was also previously noted by us³³ and others.^{25,34} The correlation with disease severity, previously noted in patients with amyotrophic_lateral sclerosis, can be attributed to the progression of the degenerative process in PD into cortical regions.³⁵

An additional finding is the lack of sensitivity of the sixth item of the FAB (environmental autonomy or evaluation of prehension behavior) in patients with PD. A similar finding was reported by Lima et al, ¹² as all the patients participating in their study received the maximal score in this item. In contrast, Lipton et al³⁶ reported that this item discriminated between frontotemporal lobar degeneration and AD. If the current finding is reproduced in a larger sample, it may lead to the constriction of the FAB into 5 items.

Conclusion

In the current sample of patients with PD, the FAB correlated with dysfunction in a variety of cognitive domains including attention, memory, and executive functions. Furthermore, it has an added value over the MMSE in reflecting cognitive dysfunction, particularly among nondemented patients, an advantage that can be used in clinical practice.

Authors' Note

The work was done at Sheba Medical Center, Ramat-Gan, Israel, and was presented in the 16th International Congress on Parkinson's

Disease, Berlin, Germany, and published as an abstract in *Parkinsonism and Related Disorders*, 2005;11(suppl 2):154.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

- Mayeux R, Chen J, Mirabello E, et al. An estimate of the incidence of dementia in idiopathic Parkinson's disease. *Neurology*. 1990;40(10):1513-1517.
- Aarsland D, Tandberg E, Larsen JP, et al. Frequency of dementia in Parkinson disease. *Arch Neurol*. 1996;53(6):538-542.
- 3. Hely MA, Reid W, Adena MA, et al. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. *Movement Disorders*. 2008;23(6):837-844.
- Emre M. Dementia in Parkinson's disease: cause and treatment. Curr Opin Neurol. 2004;17(4):399-404.
- Hietanen M, Teravainen H. Cognitive performance in early Parkinson's disease. Acta Neurol Scand. 1986;73(2):151-159.
- Tsai CH, Lu CS, Hua MS, Lo WL, Lo SK. Cognitive dysfunction in early onset parkinsonism. *Acta Neurol Scand*. 1994;89(1):9-14.
- 7. Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: a frontal assessment battery at bedside. *Neurology*. 2000;55(11): 1621-1626.
- 8. Takagi R, Kajimoto Y, Kamiyoshi S, Miwa H, Kondo T. The frontal assessment battery at bed side (FAB) in patients with Parkinson's disease (Japanese). *No To Shinkei*. 2002;54(10):897-902.
- Slachevsky A, Villalpando JM, Sarazin M, Hahn-Barma V, Pillon B, Dubois B. Frontal assessment battery and differential diagnosis of frontotemporal dementia and Alzheimer disease. *Arch Neurol*. 2004;61(7):1104-1107.
- Castiglioni S, Pelati O, Zuffi M, et al. The frontal assessment battery does not differentiate frontotemporal dementia from Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2006;22(2): 125-131.
- 11. Kugo A, Terada S, Ata T, et al. Japanese version of the frontal assessment battery for dementia. *Psychiatry Res.* 2007;153(1): 69-75.
- Lima CF, Meireles LP, Fonseca R, Castro SL, Garrett C. The frontal assessment battery (FAB) in Parkinson's disease and correlations with formal measures of executive functioning. *J Neurol.* 2008;255(11):1756-1761.
- Paviour DC, Winterburn D, Simmonds S, et al. Can the frontal assessment battery (FAB) differentiate bradykinetic rigid syndromes? Relation of the FAB to formal neuropsychological testing. *Neurocase*. 2005;11(4):274-282.
- 14. Rodrigues GR, Souza CP, Cetlin RS, et al. Use of the frontal assessment battery in evaluating executive dysfunction in patients with Huntington's disease. *J Neurol*. 2009;256(11):1809-1815.
- 15. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-

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pathological study of 100 cases. *J Neurol Neurosurg Psychiatry*. 1992;55(3):181-184.

- 16. Fahn S, Elton RL and UPDRS Program Members. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Goldstein M, Calne DB, eds. *Recent Developments in Parkinson's Disease*. Florham Park, NJ: Macmillan Healthcare Information; 1987: 153-163, 293-304.
- Hoehn M, Yahr M. Parkinsonism: onset, progression, mortality. Neurology. 1967;17(5):427-442.
- Folstein MF, Folstein SE, McHugh PR. Mini-mental state.
 A practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*. 1975;12(3):189-198.
- Duley JF, Wilkins J, Hamby S, et al. Explicit scoring criteria for the Rey-Osterrieth and Taylor complex figures. *The Clinical Neuropsychologist*. 1993;7(1):29-38.
- Vakil E, Blachstein H. Rey AVLT: developmental norms for adults and the sensitivity of different memory measures to age. *The Clinical Neuropsychologist*. 1997;11(4):356-369.
- Wechsler D. Wechsler Memory Scale (WMS-III). 3rd ed. San Antonio, TX: Texas Psychological Corporation; 1997.
- Lezak M. Neuropsychological Assessment. 3rd ed. New York, NY: Oxford University Press; 1995.
- 23. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J Royal Statistical Society, Series B (Methodological)*. 1995;57(1):289-300.
- 24. Gotez CG, Emre M, Dubois B. Parkinson's disease dementia: definitions, guidelines and research perspective in diagnosis. *Ann Neurol*. 2008;64 (suppl):S81-S92.
- Appollonio I, Leone M, Isella V, et al. The frontal assessment battery (FAB): normative values in an Italian population sample. *Neurol Sci.* 2005;26(2):108-116.

- Zgaljardic DJ, Borod JC, Foldi NS, Mattis P. A review of the cognitive and behavioral sequelae of Parkinson's disease: relationship to frontostriatal circuitry. *Cogn Behav Neurol*. 2003; 16(4):193-210.
- 27. Raskin SA, Borod JC, Tweedy JR. Set-shifting and spatial orientation in patients with Parkinson's disease. *J Clin Exp Neuropsychol*. 1992;14(5):801-821.
- Raskin SA, Borod JC, Tweedy J. Neuropsychological aspects of Parkinson's disease. *Neuropsychol Rev.* 1990;1(3):185-221.
- 29. Levin BE, Tomer R, Rey GJ. Cognitive impairments in Parkinson's disease. *Neurol Clin.* 1992;10(2):471-485.
- Pahwa R, Paolo A, Troster A, Koller W. Cognitive impairment in Parkinson's disease. *Eur J Neurol*. 1998;5(5):431-344.
- 31. Matsui H, Udaka F, Miyoshi T, et al. Frontal assessment battery and brain perfusion image in Parkinson's disease. *J Geriatr Psychiatry Neurol*. 2006;19(1):41-45.
- 32. Raz N, Lindenberger U, Rodrigue KM, et al. Regional brain changes in aging healthy adults: general trends, individual differences and modifiers. *Cereb Cortex*. 2005;15(11):1676-1689.
- Cohen OS, Vakil E, Tanne D, Nitsan Z, Schwartz R, Hassin-Baer S. Educational level as a modulator of cognitive performance and neuropsychiatric features in Parkinson disease. *Cogn Behav Neurol*. 2007;20(1):68-72.
- 34. Beato RG, Nitrini R, Formigioni AP, Caramelli P. Brazilian version of the FAB. *Dementia Neuropsychol.* 2007;1(1):59-65.
- Braak H, Ghebremedhin E, Rüb U, Bratzke H, Del Tredici K. Stages in the development of Parkinson's disease-related pathology. *Cell Tissue Res.* 2004;318(1):121-134.
- 36. Lipton AM, Ohman KA, Womack KB, et al. Sub scores of the FAB differentiate frontotemporal lobar degeneration from AD. *Neurology*. 2005;65(5):726-731.