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Executive functions and disease characteristics in Parkinson's disease

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(Received 27 May 1995; accepted 5 October 1995)

Abstract—In the present study, we investigated the association of two executive functions with disease characteristics in Parkinson's disease (PD), especially with severity of motor symptoms. We operationalized two executive functions, viz. fluency and cognitive shifting, each in a number of tests with heterogeneous materials, but with an identical format. We calculated the correlations between test performance and disease characteristics, including the factor scores of the Unified Parkinson's Disease Rating Scale (UPDRS). The results of this study show that only cognitive shifting was consistently associated with the severity of motor symptoms in PD, in particular with rigidity. None of the fluency tests had a significant association with severity of motor symptoms. The present study indicates that PD, as reflected by the severity of motor symptoms, is not associated with a general decrease in executive function. In spite of the fact that both are executive functions and both require generation of items, fluency and cognitive shifting are differentially related to PD. Copyright © 1996 Elsevier Science Ltd.

Key Words: Parkinson's disease; executive functions; motor symptoms.

Introduction

Most studies dealing with the relationship of cognitive dysfunction and other disease characteristics in non-demented patients with Parkinson's disease (PD) found a rather scattered pattern of associations between single test performance and motor symptoms [39, 42, 46]. This pattern may result from the fact that these studies aimed at a large variety of tests in order to cover a great diversity of cognitive functions and also from the heterogeneity of the patients under study. Some other studies [13, 45] made a selection of tests on the basis of established differences between PD patients and control subjects (CS). With regard to this, the frequently observed impairment of so-called frontal or executive functions in PD should be mentioned. Executive functions are defined as functions which are involved in the self-regulation of problem solving strategies [36], a rather theoretical and non-specific definition. It is not surprising, therefore, that there is no unanimity about whether a particular function is executive or not. For example, Lezak [36] and Taylor et al. [53], unlike Litvan et al. [38] and Cooper et al. [14], include verbal fluency in the executive functions. Memory tasks are sometimes included [38, 41, 51], sometimes not [13, 50]. Accordingly, the tests in which the concept of executive functions is operationalized, are very heterogeneous. Recently, David [16] and Stuss [49] pointed out that the concept of frontal and executive function lacks specificity and an empirical basis. Thus, even in studies in which tests assessing executive functions are selected, the heterogeneity of the tests predominates. The lack of corresponding findings in these studies may be due to this heterogeneity.

In the present study we investigated the relationship of cognitive functioning and disease characteristics of PD, especially the severity of motor symptoms. Instead of speculating whether associations between single test performance and motor symptoms reflect a hypothetical common feature, we no longer focused on the diversity, but on the communality of tests to be performed. From the cluster of executive functions, we selected fluency and cognitive shifting as the core variables in this study for two reasons. In a previous study [10], we found that PD patients were impaired on fluency and cognitive shifting, the latter assessed with sorting tests. For the present study, we adopted a distinction of Kolb and Whishaw

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developed an empirically based model of human intelligence [25], fluency and cognitive shifting share a common trait, in that both are tests of divergent production. In tasks of convergent production, the subject has to generate an item which encompasses all items presented: he has to find one superordinate item, i.e., a class or category. Actually, all tests of abstraction and categorization are tests of convergent production. In tasks of divergent production, the subject has to generate different items within a given set: he has to find a series of juxtaposed items. In fluency tests, the subject has to generate items within a given category; in card sorting tests, the subject has to generate categories which cover varying subsets of elements. Although each separate class in card sorting tests is generated along the lines of convergent production, the shift from one class to another requires divergent production in addition. Fluency and cognitive shifting were each operationalized in a group of tests. Within each group, the materials were heterogeneous, i.e., representing distinct cognitive modalities (e.g., verbal, spatial), but the format was identical. As a matter of fact, the format of the fluency tests differed from that of the card sorting tests. Thus, the fluency tests had identical instructions, which required the subject to generate as many elements as possible within a number of different classes. Likewise, the card sorting tests had identical instructions, being the feedback in terms of ‘correct’ and ‘not correct’, which enabled the subject to derive categories from varying sets of elements. This allowed us to investigate not only whether cognitive function is related to the severity of motor symptoms of PD, but also at which level of communality: the level of single, modality-related test performance, the level of a cognitive function, which goes beyond modalities and finally the level of a more comprehensive function, which goes beyond modalities and formats (e.g., divergent production). In the latter case the scores of fluency, cognitive shifting and motor symptoms have to be interrelated despite the heterogeneity of materials and instructions so that a common feature of all these tests, e.g., divergent production, prevails over the heterogeneity of materials and instructions.

A correlational study like this requires that the group of patients under study show a varying degree of severity of symptoms. Therefore, both patients distinguished by a slight severity of symptoms (de novo patients) and patients distinguished by mild to moderate severity (patients on pharmacotherapy) were included in the present study.

### Materials and methods

#### Subjects

Originally, we started with a group of 60 PD patients. We had to exclude 15 PD patients from the partial correlational analysis, merely because their neuropsychological data were incomplete. Accordingly, 45 patients were included in the present study: 23 males and 22 females. All gave informed consent. The diagnosis of idiopathic PD was based on the presence of at least two of the following symptoms: tremor, rigidity, bradykinesia and postural disturbances. The symptoms were evaluated by a neurologist (M.H.) a week before psychological testing. Patients with non-PD symptoms, EEG and CT scan abnormalities, cerebrovascular disease and dementia according to DSM III-R criteria were excluded. In a previous study [55], we obtained evidence that anticholinergic therapy diminishes the performance of PD patients on card sorting tests and so we excluded patients on anticholinergic therapy. The group was composed of 34 de novo patients and 11 PD patients on pharmacotherapy. Five patients were on levodopa plus carbidopa, three on bromocriptine and six on amantadine. Depression was measured by the Zung Depression Scale [58]. Table 1 presents some demographic and clinical data of the group.

The sum score of the following subscales of the Unified Parkinson’s Disease Rating Scale (UPDRS) was used as a measure of severity of PD: 1. bradykinesia; 2. rigidity; 3. posture; 4. arm swing; 5. gait; 6. tremor; 7. face; 8. speech; and 9 activities of daily life. Given the number of patients, the number of subscales to be included in the factor analysis should be restricted to four. In order to establish whether it would be permissible to include the maximum of six subscales of the UPDRS in the factor analysis, we also analyzed the original group of 60 PD patients which showed the same profile of disease characteristics and cognitive performance as the group of 45 PD patients. Therefore, we added the UPDRS scores of the 15 patients who had to be excluded from the present study because of incomplete neuropsychological data to those of the 45 patients. We selected bradykinesia, rigidity, gait, tremor, face and speech. The factor analysis of the group of 45 patients and that of the group of 60 patients provided the same factors and similar loadings as the factor analysis of the group of 45 PD patients, which legitimates the inclusion of six subscales in the present study.

### Tests

#### Reference tests.

To assess intelligence, we selected four subtests from the Wechsler Adult Intelligence Scale-Revised (WAIS-R); vocabulary and similarities, measuring verbal intelligence, and picture completion and block design, measuring visuoperceptual intelligence [15]. Memory was assessed by means of the Rey Auditory Verbal Learning Test [36]. A list of 15 semantically unrelated words was presented five times orally. The subject was asked to enumerate the memorized words after each presentation. The number of correct words after five presentations was the score of memory performance. Attention was assessed with the Stroop Color Word Test [32]. Only part B

| Table 1. Demographic and clinical characteristics of the PD patients (n = 45) |
|-----------------------------|---------------------------|
|                            | Means | S.D.    |
| Age (years)                | 57.4  | 10.5    |
| Onset disease (years)      | 52.6  | 10.7    |
| Duration (years)           | 5.8   | 3.7     |
| Sum UPDRS*                 | 9.7   | 3.5     |
| Zung score†                | 47.3  | 9.4     |

*Sum UPDRS = sum score of the principal subscales of the Unified Parkinson’s Disease Rating Scale. †Zung score = score of the Zung Depression Rating Scale.
We presented four fluency tests. The Semantic Fluency Tests (SFT) required the subjects to enumerate as many animals as possible during 1 min (SFT 1), and next, as many boys' names as possible (SFT 2). The Controlled Word Association Tests (CWAT) [1, 5] required the subjects to generate as many words as possible in 1 min, beginning with the letter p (CWAT 1), and next, ending with the letter k (CWAT 2). Score was the number of different words. Next, these scores were transformed into z-scores. The sum of these z-scores was the total fluency score.

We presented three card sorting tests: the Wisconsin Card Sorting Test (WCST) [24] and a verbal and spatial variation, in order to enlarge the heterogeneity of the sorting criteria. In each test the subject began to sort on the basis of trial and error according to a criterion which was only known to the experimenter. A false response was corrected by the experimenter. This was the acquisition phase. To minimize the impact of memory, the correct (or corrected) matchings were laid down just below the appropriate stimulus cards. After a fixed number of correct responses the experimenter changed the criterion twice without informing the subject. These were the two shifting phases. In order to exclude biasing differences in speed of information processing there were no time constraints. The verbal variation of the WCST was the Animals Sorting Test (AST). This test consisted of three series of 24 cards and two stimulus cards. Initially, subjects had to match 'bird' versus 'mammal'. After seven consecutive correct responses the experimenter changed the sorting criterion to 'herbivore' versus 'carcivore' and finally to 'native' versus 'exotic'. The Spatial Sorting Test (SST) consisted of two stimulus cards and three series of 20 response cards, each depicting two figures in a varying spatial relationship (see Fig. 1). The instructions given to the subjects were analogous to those for animal sorting. For detailed information, we refer to other studies [55, 56].

With respect to the WCST, we used the original form [24] in which over half the cards are ambiguous, i.e., sharing more than one criterion with a stimulus card (e.g., the same in colour and the same in shape), and the instruction is restricted to feedback. Previous research [50, 51] has shown that PD patients are impaired in the ability to generate efficient strategies spontaneously. In the modified form [43], all ambiguous cards are eliminated and the instruction tells the subject exactly what to do, which reduces the appeal to the spontaneous generation of efficient strategies. For this reason we preferred the original form to the modified one. Consequently, studies involving the modified form are omitted from consideration in the discussion.

Since inclusion of ambiguous cards prevents a clear distinction of perseverative and non-perseverative responses [43, 55] and perseverative responses in the acquisition essentially differ from those in the shifting phases [28], we did not analyze the card sorting tests according to perseverative/non-perseverative error pattern. In addition, to rule out chance, generation of a correct class can only be assessed conclusively after a number of correct trials in succession. The same holds true for perseveration. However, unlike, for example, the California Verbal Learning Test [23], the WCST manual [28] does not provide scoring formulae to correct perseverative and non-perseverative responses for chance, which is about one-third.

In most studies, the WCST is stopped when all cards (n = 64) are presented twice. In the present study, the cards of the three card sorting tests were presented once. The tests were stopped when the subject had sorted all cards, or had achieved the three categories of each test. In the present study, we presented three card sorting tests once, so that the maximum number of categories to be found was nine. In our series of card sorting tests, the WCST was the only one with a restricted number of classes embedded in the cards (colour, form and number), which implies that there is only one class left in the second shifting phase. As indicated elsewhere [10, 11], this enables the subject to solve the problem by heading for the only class that is left, instead of generating one, which is incompatible with the homogeneity of tests which we aimed at. Therefore, we continued the WCST by presenting the first class once again and omitted the second shifting phase from our analysis. Cognitive shifting was reflected in two scores: the number of categories achieved and the standardized sum of trials of all card sorting tests taken together. The first measure is a conventional one [4, 6, 35, 53]; the more the subject is able to shift to a new grouping, the more categories a subject discovers. Among the scores provided by the Heaton manual, the number of categories is the only one which reflects directly the number of shifts which the subject has achieved, and consequently, may be considered as the most appropriate measure to reflect cognitive shifting. In a previous study these measures proved to be almost identical [55], but the sum of trials has a much wider range of measurement. Standardization was performed by transforming the number of trials that a subject needed, into the percentage of the maximum number of trials.

**Statistics**

Factor analysis was performed in accordance with the procedures of principal components and varimax rotation (statistical package: SAS). Correlations and partial correlations were established with the Pearson Product-Moment Correlation Coefficient r. In addition, differences between performance of the patients above and below the mean of each UPDRS factor were tested using Student's t-test. Result with P values less than 0.05 (two-sided) were considered significant.

**Results**

Means and standard deviations of neuropsychological test performance are present in Table 2. Since the reader might be interested in normal performance of our experimental tests (AST and SST), we added the scores of 33 control subjects (age: mean = 57.4 years; S.D. = 8.7) of the same intelligence, who participated in a different study of ours [56]. The performance of both groups was fairly similar and, consequently, did not differ significantly.

Age and onset of disease, being the age at which the first symptoms of PD became apparent, showed an identical pattern of correlations with the cognitive variables. Their extremely high intercorrelation [r = 0.96, P < 0.0001] confirms a strong collinearity and, as a result, it is statis-
Table 2. Means and standard deviations of neuropsychological test performance of PD patients (n = 45) and CS (n = 33)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal IQ</td>
<td>115.2</td>
<td>13.4</td>
<td>114.9</td>
<td>14.9</td>
</tr>
<tr>
<td>Visuoperceptual IQ</td>
<td>119.0</td>
<td>18.1</td>
<td>117.8</td>
<td>16.8</td>
</tr>
<tr>
<td>Memory (15 words test)</td>
<td>40.5</td>
<td>8.8</td>
<td>42.8</td>
<td>10.9</td>
</tr>
<tr>
<td>Stroop C-B</td>
<td>44.5</td>
<td>26.6</td>
<td>47.9</td>
<td>27.9</td>
</tr>
<tr>
<td>Semantic Fluency Test 1</td>
<td>18.4</td>
<td>4.0</td>
<td>18.6</td>
<td>5.0</td>
</tr>
<tr>
<td>Semantic Fluency Test 2</td>
<td>20.8</td>
<td>4.7</td>
<td>19.5</td>
<td>4.7</td>
</tr>
<tr>
<td>Controlled Word Association Test 1</td>
<td>13.9</td>
<td>4.1</td>
<td>13.2</td>
<td>5.4</td>
</tr>
<tr>
<td>Controlled Word Association Test 2</td>
<td>11.3</td>
<td>6.1</td>
<td>12.8</td>
<td>5.9</td>
</tr>
<tr>
<td>Sum trials Animals Sorting Test</td>
<td>17.3</td>
<td>14.0</td>
<td>17.2</td>
<td>14.3</td>
</tr>
<tr>
<td>Sum trials Spatial Sorting Test</td>
<td>24.6</td>
<td>18.0</td>
<td>20.6</td>
<td>18.5</td>
</tr>
<tr>
<td>Sum trials WCST</td>
<td>16.9</td>
<td>14.8</td>
<td>23.9</td>
<td>17.4</td>
</tr>
<tr>
<td>Sum categories Card Sorting Tests</td>
<td>7.6</td>
<td>1.5</td>
<td>7.6</td>
<td>1.2</td>
</tr>
</tbody>
</table>

As far as the reference tests were concerned, the scores of visuoperceptual intelligence and the Stroop Color Word Test correlated significantly with age. Memory performance correlated significantly with age and severity of symptoms.

The internal consistency of the four fluency tests was satisfactory: the two SFT scores correlated significantly \( r = 0.50, P < 0.001 \), as did the two CWAT scores \( r = 0.53, P < 0.0005 \); the sum of the SFT \( z \)-scores also correlated significantly with the sum of CWAT \( z \)-scores \( r = 0.43, P < 0.005 \), which allows us to transform the

Table 3. Correlations of age/onset disease and severity of motor symptoms with test performance in PD patients (n = 45)

<table>
<thead>
<tr>
<th></th>
<th>Age/onset disease</th>
<th>Sum UPDRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal IQ</td>
<td>-0.07</td>
<td>-0.19</td>
</tr>
<tr>
<td>Visuoperceptual IQ</td>
<td>-0.44†</td>
<td>-0.27</td>
</tr>
<tr>
<td>Memory performance (15 words test)</td>
<td>-0.32*</td>
<td>-0.40‡</td>
</tr>
<tr>
<td>Stroop C-B</td>
<td>0.44‡</td>
<td>0.14</td>
</tr>
<tr>
<td>Standardized sum Fluency Tests</td>
<td>-0.18</td>
<td>0.02</td>
</tr>
<tr>
<td>Sum of categories Card Sorting Tests</td>
<td>-0.10</td>
<td>-0.38*†</td>
</tr>
<tr>
<td>Standardized sum trials Card Sorting Tests</td>
<td>0.07</td>
<td>0.42‡</td>
</tr>
</tbody>
</table>

(The number of categories increases, and the total number of trials decreases, as test performance improves.)

\*P < 0.05; †P < 0.01; ‡P < 0.005.

Table 4. Correlations of severity of motor symptoms with test performance in PD patients (n = 45), after partialling out age/onset of disease

<table>
<thead>
<tr>
<th></th>
<th>Sum UPDRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal IQ</td>
<td>-0.18</td>
</tr>
<tr>
<td>Visuoperceptual IQ</td>
<td>-0.24</td>
</tr>
<tr>
<td>Memory performance (15 words test)</td>
<td>-0.38*</td>
</tr>
<tr>
<td>Stroop C-B</td>
<td>0.44†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Sum UPDRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardized sum Fluency Tests</td>
<td>0.04</td>
</tr>
<tr>
<td>Sum of categories Card Sorting Tests</td>
<td>-0.37*</td>
</tr>
<tr>
<td>Standardized sum trials Card Sorting Tests</td>
<td>0.41†</td>
</tr>
</tbody>
</table>

(The number of categories increases, and the total number of trials decreases, as test performance improves.)

\*P < 0.01; †P < 0.005.
The standardized sum scores of the fluency tests neither were significant [AST versus SST: \( r = 0.57, P < 0.0001 \),
AST versus WCST: \( r = 0.14, P = 0.35 \); SST versus WCST: \( r = 0.30, P = < 0.05 \)], which is probably due to the pursued heterogeneity of the materials (see Introduction),
each of the three card sorting tests was similarly associated with the UPDRS sum score [AST versus UPDRS: \( r = 0.32; P < 0.05 \); SST versus UPDRS: \( r = 0.30; P < 0.05 \); WCST versus UPDRS: \( r = 0.35; P < 0.05 \)].
The standardized sum scores of the fluency tests neither correlated with age nor with severity of motor symptoms.
The sum of categories and the standardized sum of trials of the card sorting tests showed a very high intercorrelation \( [r = -0.96, P < 0.0001] \), indicating that these variables are almost identical. Both measures correlated significantly with severity of motor symptoms, but not with age (see Table 3). The same holds true for the standardized sum of trials in the two shifting phases together.

Although the correlation between age and severity of motor symptoms was not significant \( [r = 0.13, P < 0.38] \), we calculated the partial correlations between the cognitive variables and severity of motor symptoms to rule out any bias of age. The correlation of performance IQ and duration of disease was no longer significant \( [r = -0.22; P = 0.15] \). Memory performance remained significantly correlated with severity of motor symptoms. Again there was no correlation between severity of motor symptoms and the standardized sum scores of the fluency tests. The sum of categories and the standardized sum of trials remained significantly correlated with severity of motor symptoms (see Table 4). Factor analysis yielded three factors (see Table 5). Face, speech, gait and bradykinesia had the greatest loadings on the first factor, which was therefore identified as hypokinesia. Rigidity had by far the greatest loading on the second factor, and tremor on the third factor. As can be seen in Table 6, of all cognitive functions only memory performance correlated significantly with the factor hypokinesia. The two standardized sum scores of the card sorting tests only correlated significantly with the factor rigidity. None of the cognitive scores correlated with any other factor. We compared cognitive performance of patients with scores above and below the mean of the three UPDRS factors, in order to assess whether a different way of testing provides confirmation of the correlational analyses. As can be seen in Table 7, the association between memory performance and the factor hypokinesia could not be confirmed. There was a significant difference in memory performance between patients with a tremor score above and below the mean. The association between cognitive shifting and rigidity proved to be firmly significant.

### Discussion

In the present study, we investigated the association of two executive functions with the severity of motor symptoms in PD. We performed a factor analysis of six subscales of the UPDRS and operationalized two executive functions, viz. fluency and cognitive shifting, each in a number of tests with heterogeneous materials, but with an identical format. Finally, we compared test performance of patients with factor scores above the mean with those with factor scores below the mean. The results of this study show that only cognitive shifting was consistently associated with the severity of motor symptoms in PD, in particular with rigidity. Previous studies [13, 50] also found associations between severity of motor symptoms and cognitive function, but these associations involved single and rather heterogeneous cognitive measures. In the present study, we found a firm relationship between an empirically established motor impairment and a decrease of a specific cognitive function, which has been assessed in three different modalities.

None of the fluency tests had a significant association with severity of motor symptoms. The results of the correlation analyses were confirmed by the analysis of group differences between patients with factor scores above and below the mean. These results indicate that fluency and cognitive shifting are differentially related to PD, in spite of the fact that both are executive functions and both require generation of items. The present study indicates that PD, as reflected by the severity of motor symptoms, is not associated with a general decrease in executive function. These findings suggest that the concept of executive function is too heterogeneous for empirical studies.

Age and onset of disease showed an extremely high intercorrelation \( (r = 0.96) \), indicating that in this study the two variables were nearly identical. This is in line with another correlation study [45], in which it has been found that age at onset no longer correlates with test scores after correction for age. For reasons of collinearity (see Results), this finding does not imply a dichotomy of 'young' PD patients with an early onset and 'old' patients with a late onset, which could have biased our results, because late onset is frequently associated with cognitive deterioration [2, 9, 19, 29]. Duration of disease only correlated with performance IQ, but the significance of this correlation disappeared after partialling out age. Depression did not correlate with any cognitive score.

### Table 5. Factor analysis UPDRS-scores after varimax rotation

<table>
<thead>
<tr>
<th>Eigenvalue</th>
<th>( F1 )</th>
<th>( F2 )</th>
<th>( F3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradykinesia</td>
<td>2.49</td>
<td>0.42</td>
<td>0.33</td>
</tr>
<tr>
<td>Rígidity</td>
<td>0.09</td>
<td>0.96*</td>
<td>0.04</td>
</tr>
<tr>
<td>Gait</td>
<td>0.71*</td>
<td>0.18</td>
<td>-0.32</td>
</tr>
<tr>
<td>Tremor</td>
<td>-0.09</td>
<td>0.07</td>
<td>0.95*</td>
</tr>
<tr>
<td>Face</td>
<td>0.85*</td>
<td>-0.03</td>
<td>0.02</td>
</tr>
<tr>
<td>Speech</td>
<td>0.84*</td>
<td>0.11</td>
<td>-0.06</td>
</tr>
</tbody>
</table>

Total variance explained: 76%.

*Significant at level \( P < 0.0001 \).
Table 6. Correlations and partial correlations of UPDRS factor scores with scores of card sorting tests

<table>
<thead>
<tr>
<th></th>
<th>Correlations</th>
<th>Partial correlations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$F_1$</td>
<td>$F_2$</td>
</tr>
<tr>
<td>V-IQ</td>
<td>0.02</td>
<td>-0.23</td>
</tr>
<tr>
<td>Vp-IQ</td>
<td>-0.03</td>
<td>-0.12</td>
</tr>
<tr>
<td>RAVLT</td>
<td>-0.37*</td>
<td>0.05</td>
</tr>
<tr>
<td>Stroop C-B</td>
<td>0.03</td>
<td>0.05</td>
</tr>
<tr>
<td>SS-FT</td>
<td>0.10</td>
<td>-0.07</td>
</tr>
<tr>
<td>SC-CS</td>
<td>0.00</td>
<td>-0.41†</td>
</tr>
<tr>
<td>ST-CS</td>
<td>0.03</td>
<td>0.45§</td>
</tr>
</tbody>
</table>

(The number of categories increases, and the total number of trials decreases, as test performance improves.)

* $P < 0.05; † P < 0.01; ‡ P < 0.005; § P < 0.001.


Table 7. Cognitive performance of patients with factor scores above and below the mean: means and standard deviations

<table>
<thead>
<tr>
<th></th>
<th>$F_1 &gt; 0$</th>
<th>$F_1 &lt; 0$</th>
<th>$F_2 &gt; 0$</th>
<th>$F_2 &lt; 0$</th>
<th>$F_3 &gt; 0$</th>
<th>$F_3 &lt; 0$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 23)</td>
<td>(n = 22)</td>
<td>(n = 22)</td>
<td>(n = 23)</td>
<td>(n = 22)</td>
<td>(n = 22)</td>
</tr>
<tr>
<td>Age</td>
<td>60.3(8.9)</td>
<td>54.3(11.2)</td>
<td>57.0(11.4)</td>
<td>57.7(9.8)</td>
<td>57.2(11.0)</td>
<td>57.5(10.1)</td>
</tr>
<tr>
<td>V-IQ</td>
<td>115.8(12.9)</td>
<td>114.5(14.2)</td>
<td>117.2(16.0)</td>
<td>116.7(10.2)</td>
<td>112.2(15.7)</td>
<td>118.0(10.4)</td>
</tr>
<tr>
<td>Vp-IQ</td>
<td>118.5(16.6)</td>
<td>119.4(19.9)</td>
<td>116.6(20.5)</td>
<td>121.2(15.6)</td>
<td>114.2(20.4)</td>
<td>123.5(14.7)</td>
</tr>
<tr>
<td>RAVLT</td>
<td>38.4(7.3)</td>
<td>42.7(9.7)</td>
<td>41.0(9.6)</td>
<td>40.0(8.1)</td>
<td>37.8(7.9)*</td>
<td>43.1(9.1)</td>
</tr>
<tr>
<td>Stroop</td>
<td>42.9(24.8)</td>
<td>46.2(28.9)</td>
<td>45.5(31.3)</td>
<td>43.6(21.9)</td>
<td>45.7(25.8)</td>
<td>43.3(27.8)</td>
</tr>
<tr>
<td>SS-FT</td>
<td>64.9(15.5)</td>
<td>63.8(12.6)</td>
<td>64.6(16.2)</td>
<td>64.1(12.0)</td>
<td>67.0(15.9)</td>
<td>61.8(14.0)</td>
</tr>
<tr>
<td>SC-CS</td>
<td>7.6(1.4)</td>
<td>7.5(1.7)</td>
<td>6.9(1.7)†</td>
<td>8.1(1.2)</td>
<td>7.3(1.5)</td>
<td>7.8(1.6)</td>
</tr>
<tr>
<td>ST-CS</td>
<td>57.8(31.6)</td>
<td>60.1(39.5)</td>
<td>74.6(37.7)‡</td>
<td>43.8(25.4)</td>
<td>64.4(34.7)</td>
<td>53.6(35.8)</td>
</tr>
</tbody>
</table>

* $P < 0.05; † P < 0.01; ‡ P < 0.005.

$F_1$ = Factor score hypokinesia; $F_2$ = factor score rigidity; $F_3$ = factor score tremor; SS-FT = standardized sum of Fluency Tests; SC-CS = sum categories Card Sorting Tests; ST-CS = standardized sum of trials Card Sorting Tests.

All patients were outpatients in a relatively early stage of PD and without symptoms which prevented them participating in everyday life. Indications of intellectual deterioration were absent (see Table 2). Therefore, it is not plausible that the results of the present study must be attributed to a heterogeneous composition of our group of PD patients. For reasons indicated in the Introduction, we included a number of PD patients with pharmacotherapy. In our view, it is not plausible that the pharmacotherapy of our patients explains the significant correlations and group differences which we found, since the patients receiving pharmacotherapy form a minority and patients on anticholinergic therapy, a medication known to affect cognitive shifting [55], were excluded. Moreover, the studies of Downes et al. [17], Lange et al. [34] and Owen et al. [44] have indicated that set-shifting may be ameliorated rather than deteriorated by levodopa therapy. Thus, the relationship between cognitive shifting and motor symptoms was established in spite of the inclusion of patients on levodopa therapy. Our findings are discussed in more detail below.

Reference variables

Visuoperceptual intelligence and attention (Stroop Color Word Test) showed a significant correlation with age. Visuoperceptual intelligence (Vp-IQ) was calculated from age-corrected standard scores, but nevertheless Vp-IQ showed a significant correlation with age (see Table 3). In our opinion this result was due to a decreased speed of performance in PD patients. Both block design and picture completion of the WAIS are subtests with time constraints. Besides, block design also requires manual dexterity. Probably, the correlation of Vp-IQ and age might no longer be significant, if we had measured untimed performance. The finding that memory performance correlated with age, is in line with the available literature [40]. The correlation of memory performance with severity of motor symptoms is in accordance with the frequently reported decrease in short-term memory in PD [8, 22, 29, 48, 52]. In the correlational analyses, memory performance proved to be exclusively related to hypokinesia, but we were not able to confirm this finding.
in our analysis of group differences: the tremor scores were associated with a significant difference in memory performance, but the hypokinesia scores no longer shared this association. This may indicate that the relation between memory performance and hypokinesia is not a firm one. Anyhow, the results of the present study suggest that memory and cognitive shifting are differentially affected by PD.

Attention, as reflected by the difference score on the Stroop test, correlated with age, but not with severity of motor symptoms. In contrast to our findings, Hiëtanen and Teräväinen [30], who have studied a group of de novo patients, found significant correlations between the separate sections of the Stroop Color Word Test and motor symptoms. Unfortunately, these authors did not provide the crucial score, being the difference score between part C and part B, because it rules out speed of performance [21, 32]. In a later study, the same authors [31] found no difference between treated and untreated PD patients with regard to difference scores of the Stroop Color Word Test, which, just like our findings, indicates little impact of severity of motor symptoms on attention. Some studies include the Stroop Color Word Test in tests assessing executive function. In the present study, there was a poor relation of Stroop performance with fluency performances or with card sorting, which once again indicates that the concept of executive function lacks homogeneity.

Executive functions

The standardized sum scores of the four fluency tests were significantly correlated neither with age nor with severity of motor symptoms. Since fluency performance depends partly on the ability to speak quickly, one might suppose a firm correlation between the fluency scores and the scores of the factor hypokinesia, on which the speech-ratings of the UPDRS loaded heavily. However, this correlation turned out to be low \( r = 0.15 \). Moreover, the patients with a hypokinesia score above the mean and those who scored below the mean performed almost identically on the fluency tests. This is in accordance with the study by Gurd and Ward [26], who found no relation between scores of 12 fluency tasks and the rate of speaking in PD. Although the present study did not compare PD patients and CS, our results fit those of Hanley et al. [27], who found that differences in fluency between PD and CS disappeared when differences of age and verbal ability were partialled out. Just like us, they found no association between fluency performance and depression. In contrast with other types of cognitive performance in the present study, the performance on card sorting tests proved to be associated exclusively with severity of motor symptoms. This finding is not only supported by the scores of the overall performance, as reflected in the standardized sum scores, but also by the performance on the individual tests (see Results). Our results are in partial agreement with those of Lichter et al. [37]; they studied a group of PD patients on pharmacotherapy, who were older and more disabled than ours. They found negative correlations between motor disability scores and a number of neuropsychological test scores, among them the number of categories of the WCST. Apparently, the association between reduced cognitive functioning and motor disability increases as PD progresses. Our findings differ from those of Cooper et al. [13], who found no correlation between motor disability scores and performance on the WCST. This may be due to differences between the groups of patients under study. One-third of the patients involved in the latter study were considered to be cognitively impaired (score on the Blessed Dementia Scale above 3, being more than two standard deviations below the mean score of the CS in that study and firmly below their estimated premorbid IQ). Since the motor disability in the cognitively impaired and that of the non-impaired group were fairly identical, it is plausible that the prominent difference in general intelligence has suppressed a possible correlation between motor disability and a decrease of a subtle cognitive function. In contrast, the patients of our study showed a present IQ level one standard deviation above sample mean (see Table 2). Apparently, despite an above normal intelligence, our patients were not able to compensate for the decrease of the subtle cognitive function, which is associated with the severity of motor symptoms.

Reviews of cognitive function in PD [5, 20] often report a decrease in cognitive shifting in PD patients, but are rather reluctant to assume a deficit in some superordinate process, which is also responsible for other cognitive deficits. The results of the present study do not indicate a superordinate process at a level as high as self-regulation of problem solving strategies being the definition of executive function. On the other hand, it did prove possible to reveal the association between severity of motor symptoms and cognitive shifting with a variety of tests. The materials of our card sorting tests were selected from cognitive modalities which are globally associated with separate cortical regions: the verbal modality (AST) with the left frontal cortex, the spatial modality (SST) with the right parietal cortex and the conceptual modality (WCST) with the prefrontal cortex. Nevertheless, the identical format of these tests prevailed over the heterogeneity of the materials. This indicates that cognitive shifting does not break up into separate cognitive functions, each restricted to a certain modality, but is a rather comprehensive cognitive function, which goes beyond heterogeneous cognitive modalities.

Card-sorting and fluency tests proved to be significantly interrelated (standardized sum fluency tests versus sum categories card sorting tests: \( r = 0.36; \quad P < 0.05 \)). Despite their common variance, performance of fluency and card sorting tests proved to be differentially related to the severity of motor symptoms; hence, it is plausible that PD does not affect what these tests have in common, for example the generation of items. Just like us, Downes...
et al. [18] did not find evidence for a general fluency deficit. They found that PD patients and CS only differed significantly in fluency tasks, which require the generation of items alternately from heterogeneous fluency domains. They suggest that this deficit is not related to a general attentional deficit, but to an impaired switching from one domain to another, more specifically, an impairment to inhibit and disinhibit algorithms alternately. Since both card sorting and interdomain alternating fluency tasks require interdomain switching, it would be interesting to investigate whether the significant relation between card sorting and fluency performance becomes stronger, when interdomain alternating fluency tasks are used, and further, whether, in contrast to single fluency performance, alternating fluency performance is related to the severity of motor symptoms in the same way as card sorting.

From previous research it may be concluded that the principal deficit in PD is an inability to generate plans for task achievement internally [6, 7, 10, 11, 12, 48, 50, 54]. Fluency tasks are mainly predicated upon the access to stored information and performance of single fluency tasks is not improved by clustering words, being a self-generated problem-solving strategy [18]. Such a self-generated problem solving is not required in fluency tasks, which are predicated upon access to stored information [50]. However, in card sorting tests, the instruction does not indicate how to solve the problem, but is restricted to feedback in terms of ‘correct’ or ‘not correct’ and, what is more, the feedback in consecutive phases is incompatible with the preceding feedback. Thus, the subject has to rely solely on his own problem-solving abilities. The difference between fluency and card sorting in terms of externally or internally generated problem solving fits the results of the present study fairly well.

Factor analysis provided three factors which explained 76% of the variance. Other studies sometimes revealed different factors, depending on the items and patients involved. Zetusky et al. [57] found factors which globally correspond to ours. In their study, bradykinesia also loaded on two factors: rigidity and postural instability. Recently, Richards et al. [47] found three factors: balance/instability, rigidity and tremor. The loadings of UPDRS items are comparable. In their group of patients, who were on average much older than ours, they found that cognitive changes in non-demented Parkinsonians were specifically associated with motor symptoms, especially with the factor rigidity. In the present study, both the correlational analyses and the analysis of group differences indicate an exclusive and consistent association of cognitive shifting and rigidity. Since patients with a high factor score on rigidity, being the only factor which discriminates in card sorting, and with a poor performance on card sorting have approximately the same age as patients with a low factor score on rigidity and a normal performance on card sorting (M = 57.0, SD = 11.4 versus M = 57.7, SD = 9.8), this finding is not resulting from a dichotomy between ‘young’ patients with an early onset and ‘old’ patients with a late onset [2, 8, 19, 29]. Our finding differs from that of Pillon et al. [45], who analyzed neuropsychological performance of PD patients in relation to motor symptoms as a function of their response to levodopa therapy. They found that cognitive impairment correlates poorly with levodopa-responsive symptoms such as rigidity. However, Pillon et al. [45] used the simplified version of the WCST [43].

As already mentioned (see Materials and Methods), this simplification transforms the WCST into a test in which the appeal to the spontaneous generation of efficient strategies is drastically reduced. In other words, the present study does not contradict the study of Pillon et al. [45]. This emphasizes the necessity of specifying test and scoring procedures.

To summarize, the present study shows that executive function is a concept which is too heterogeneous to assess the association of cognitive functioning and severity of motor symptoms in PD. On the other hand, it proved possible to go beyond the level of single, modality-related cognitive functions. We found a firm relationship between cognitive shifting and severity of motor symptoms, especially rigidity. This relationship prevailed over the heterogeneous cognitive modalities, viz. verbal, spatial and conceptual, which are globally associated with separate cortical regions, indicating that PD affects superordinate cognitive processes, but at a lower level than the assumed level of executive functions. Our finding that fluency and cognitive shifting are differentially associated with severity of motor symptoms fits the notion of an impaired self-generated problem solving in PD.

References


