The relationship between executive functions and fluid intelligence in Parkinson’s disease

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Background. We recently demonstrated that decline in fluid intelligence is a substantial contributor to frontal deficits. For some classical ‘executive’ tasks, such as the Wisconsin Card Sorting Test (WCST) and Verbal Fluency, frontal deficits were entirely explained by fluid intelligence. However, on a second set of frontal tasks, deficits remained even after statistically controlling for this factor. These tasks included tests of theory of mind and multitasking. As frontal dysfunction is the most frequent cognitive deficit observed in early Parkinson’s disease (PD), the present study aimed to determine the role of fluid intelligence in such deficits.

Method. We assessed patients with PD (n=32) and control subjects (n=22) with the aforementioned frontal tests and with a test of fluid intelligence. Group performance was compared and fluid intelligence was introduced as a covariate to determine its role in frontal deficits shown by PD patients.

Results. In line with our previous results, scores on the WCST and Verbal Fluency were closely linked to fluid intelligence. Significant patient-control differences were eliminated or at least substantially reduced once fluid intelligence was introduced as a covariate. However, for tasks of theory of mind and multitasking, deficits remained even after fluid intelligence was statistically controlled.

Conclusions. The present results suggest that clinical assessment of neuropsychological deficits in PD should include tests of fluid intelligence, together with one or more specific tasks that allow for the assessment of residual frontal deficits associated with theory of mind and multitasking.

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Introduction

In 1904, Charles Spearman proposed the existence of a general factor that contributes to all cognitive activities (Spearman 1904, 1927). Spearman’s general factor (g) was proposed to explain one of the strongest findings in the study of human intelligence – the universal positive correlations typically found between different cognitive tests. The best measures of g are generally tests of so-called fluid intelligence, involving novel problem-solving (Carroll, 1993). The cognitive functions reflected in g are still under active study. Positive g correlations for all manner of cognitive tasks, including tests of working memory, especially working memory for novel task rules (Duncan et al., in press), tests of processing speed (e.g. Nettelbeck, 1987), and many more, suggest that g reflects cognitive functions of importance in any form of organized behavior. Obvious candidates are the broad organizational functions of the frontal lobe, and indeed, performance in fluid intelligence tests is impaired after frontal lobe lesions, in particular lesions in lateral and dorsomedial frontal regions (Duncan et al. 1995; Woolgar et al. 2010). Similar regions are active in functional imaging studies of fluid intelligence test performance (Prabhakaran et al. 1997; Esposito et al. 1999; Duncan et al. 2000; Bishop et al. 2008).

Many clinical and experimental tests are known to be sensitive to frontal impairment, even if they are also known to recruit other cognitive functions and brain areas. The Wisconsin Card Sorting Test (WCST) and Verbal Fluency, for example, are often used to measure frontal ‘executive’ impairment, even though both certainly also involve a variety of posterior
cortical functions. Recent attention has also been given
to tests of multitasking (e.g. Manly et al. 2002) and
theory of mind (e.g. Stone et al. 1998), although again,
it is likely that individual tests have contributions
from both frontal and posterior functions.

The importance of the frontal lobe in fluid intelli-
gence and in a diversity of specific cognitive tests
raises the question of how much a loss of fluid intelli-
gence contributes to other frontal deficits. In a recent
study (Roca et al. 2010a), we showed that, in a group
of patients with frontal lesions, fluid intelligence (g)
was a substantial contributor to many frontal deficits.

For some classical ‘executive’ tasks, such as the WCST
and Verbal Fluency, frontal deficits were entirely
explained by individual scores of g. Once fluid intelli-
gence was partialled out, there was no remaining
difference between patients and normal controls.
However, on a second set of frontal tasks, performance
deficits remained even after fluid intelligence was
statistically controlled. Such tasks were associated
particularly with anterior frontal damage [Brodmann
area (BA) 10] and included tests of theory of mind
(Faux Pas) and multitasking (Hotel Task), among
others.

Although Parkinson’s disease (PD) is characterized
by its motor symptoms, it is now widely accepted
that cognitive changes can also be present, even dur-
ing the early stages of the disease. Most frequently,
cognitive deficits exhibited by PD patients resemble
those produced after frontal-lobe damage, with par-
ticular difficulties on executive functioning (Foltynie
et al. 2004; Lewis et al. 2005; Muslimovic et al. 2005;
Williams-Gray et al. 2007), theory of mind (Saltzman
et al. 2000; Mengelberg & Siegert, 2003; Mimura et al.
2006; Perón et al. 2009; Bodden et al. 2010; Roca et al.
2010b) and multitasking (Perfetti et al. 2010).

Fluid intelligence loss has also been described in
PD, most commonly as measured by Raven’s
Colored Progressive Matrices (RCPM; Pillon et al.
1995; Bostantjopoulou et al. 2001; Basić et al. 2004;
Nagano-Saito et al. 2005). In PD patients, performance
in RCPM has been shown to correlate positively with
gray matter density within the dorsolateral prefrontal
cortex (Nagano-Saito et al. 2005).

Although both frontal deficits and fluid intelligence
loss have been described in PD, to our knowledge
no previous study has investigated the role of fluid
intelligence in frontal deficits associated with this
disease. To achieve this objective, we assessed a group
of patients with PD using tasks sensitive to frontal
dysfunction and with the RCPM as a test of fluid
intelligence. In addition to comparing PD patients
with a group of controls, we investigated how far
frontal deficits in PD were explained by fluid intelli-
gence loss.

Method

Participants

Thirty-two patients who met the UK Parkinson’s
Disease Society Brain Bank criteria, between Hoehn
and Yahr stages I–III (Hoehn & Yahr, 1967), were
recruited from the INECO Data Base in Buenos Aires,
Argentina and from the Movement Disorders Clinic
at the Institute of Neuroscience of the Favaloro
Foundation. Mean (±S.D.) age for the patient popu-
lation was 62.25 (±10.23) years. Information on dis-
ease history and drug therapy was obtained by
neurologists specialized in studying PD (A.C., G.G.A.,
O.G.). Patients with different neurological diagnoses
or presenting radiological structural brain abnormali-
ties compatible with diagnoses other than PD were
excluded from this study. Patients who scored under
24 on the Mini-Mental State Examination (Folstein
et al. 1975) were also excluded to ensure a good level of
overall cognitive functioning. Of the patients selected,
15 were under pharmacological treatment with either
levodopa or a dopamine agonist with a mean levodopa
equivalent daily dose of 318.56 (±268.48) mg. Among
those patients, assessment was conducted during the
‘on’ state of the medication. Seventeen of the patients
were not taking any medication for their motor symp-
toms. Performance between medicated and non-medi-
cated patients was compared to ensure that the results
were not influenced by medication intake. For cases in
which significant differences between medicated and
non-medicated patients were found, the levodopa
equivalent daily dose (mg) was introduced as a co-
variable in subsequent analysis. Permission for the
study was initially obtained from the local research
ethics committee and all participants gave their signed
informed consent prior to inclusion. The subjects’
consent was obtained according to the Declaration of
Helsinki.

Healthy control volunteers (n = 22) were recruited
through word of mouth and were matched to patients,
taking into account the mean and range of age and
level of education. Controls were recruited from the
same geographical area as patients. Participants were
included in the control group if they reported no his-
tory of neurological or psychiatric disorders, including
traumatic brain injury or substance abuse.

Clinical and demographical data for all participants
are shown in Table 1.

Procedure

All participants were initially assessed using a com-
plete neuropsychological battery that included cogni-
tive screening tests, tests of language, memory, praxis,
attention and executive functions and pre-morbid IQ.
Experimental tests were administered during a second session of assessment, including both theory of mind and multitasking tasks.

Neuropsychological testing

Word Accentuation Test – Buenos Aires (WAT-BA)

To estimate premorbid intelligence we used the WAT-BA (Burin et al. 2000). This test, similar to the National Adult Reading Test (Nelson & Willison, 1991), measures ability to read 44 irregularly stressed Spanish words. The score was the number of words stressed correctly.

RCPM

To assess fluid intelligence, we used the RCPM (Raven, 1995), which is a multiple-choice test of novel problem-solving comprising 36 items. In each test item, the subject is asked to identify the missing item that completes a certain pattern. The test is organized in three sets of 12 items ranging in complexity (series A, Ab and B). The score was the total number of items solved correctly.

WCST (Nelson, 1976)

For the WCST, we used Nelson’s modified version of the standard procedure. Cards varying on three basic features (color, shape and number of items) must be sorted according to each feature in turn. The participants’ first sorting choice becomes the correct feature, and once a criterion of six consecutive correct sorts is achieved, the subject is told that the rules have changed, and cards must be sorted according to a new feature. After all three features have been used as sorting criteria, subjects must cycle through them again in the same order as they did before. Each time the feature is changed, the next must be discovered by trial and error. The score was the total number of categories achieved. Data were available for 31/32 patients.

Verbal Fluency (Benton & Hamsher, 1976)

In verbal fluency tasks, the subject generates as many items as possible from a given category in a specific period of time. We used the standard Argentinean phonemic version (Butman et al. 2000), asking subjects to generate words beginning with the letter P in a 1-min block. The score was the total number of correct words generated.

Hotel Task (Manly et al. 2002; Torralva et al. 2009)

The task comprised five primary activities related to running a hotel. Individual activities are described in more detail elsewhere (Torralva et al. 2009; Roca et al. 2010a). Subjects were told to execute at least some of all five activities during a 15-min period, so that, at the end of this period, they would be able to give an estimate of how long each would take to complete. It was explained that the time available was not enough to complete any of the tasks; the goal, instead, was to ensure that every task was attempted. Subjects were also asked to remember to open and close the hotel garage doors at particular times (open at 6 min, close at 12 min), using an electronic button. The score was time allocation: for each primary task we assumed an optimal allocation of 3 min, and measured the summed total deviation (in seconds) from this optimum. Total deviation was given a negative sign, so that high scores meant better performance. Data were available for 29/32 patients.

Faux Pas (Stone et al. 1998)

On each trial of this test, the subject was read a short, one-paragraph story. To reduce working memory load, a written version of the story was also placed in front of the subject. In 10 stories, there was a faux pas, involving one person unintentionally saying something hurtful or insulting to another. In the remaining 10 stories, there was no faux pas. After each story, the subject was asked whether something inappropriate was said and, if so, why it was inappropriate. If the answer was incorrect, an additional memory question was asked to check that basic facts of the story were retained; if they were not, the story was re-examined and all questions repeated. The score was 1 point for each faux pas identified correctly, or non-faux pas rejected correctly. Data were available for 31/32 patients.

Table 1. Clinical and demographical data

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>Controls</th>
<th>Mean</th>
<th>S.D.</th>
<th>Mean</th>
<th>S.D.</th>
<th>p</th>
</tr>
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<tr>
<td>Age (years)</td>
<td>62.25</td>
<td>59.27</td>
<td>10.23</td>
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<td>1.98</td>
<td>0.57</td>
<td>0.33</td>
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<tr>
<td>Education (years)</td>
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<td>14.5</td>
<td>4.80</td>
<td>2.79</td>
<td>2.79</td>
<td>0.10</td>
<td>0.57</td>
</tr>
<tr>
<td>WAT-BA</td>
<td>36.91</td>
<td>38.68</td>
<td>4.36</td>
<td>2.93</td>
<td>2.93</td>
<td>0.010</td>
<td></td>
</tr>
<tr>
<td>Hoehn &amp; Yahr (1967)</td>
<td>1.46</td>
<td>5.82</td>
<td>5.82</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>1.47</td>
<td>1.46</td>
<td>1.46</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

PD, Parkinson’s disease; WAT-BA, Word Accentuation Test – Buenos Aires; s.d., standard deviation.
better performance on both the WCST and Verbal scores in the RCPM were strongly associated with frontal tests are shown in Fig. 1, revealing that higher values were not related to medication intake. As a covariable ($p_{\text{levodopa equivalent daily dose (mg)}}$ was introduced for the Faux Pas, on which medicated patients performed more poorly than non-medicated patients on any of the aforementioned variables, except for the Faux Pas, on which medicated patients performed more poorly than non-medicated patients ($t(29) = -2.46, p = 0.02$). However, significant differences between patients and controls persisted after the levodopa equivalent daily dose (mg) was introduced as a covariable ($p = 0.03$), suggesting that group differences were not related to medication intake.

Scatterplots relating RCPM to the two classical frontal tests are shown in Fig. 1, revealing that higher scores in the RCPM were strongly associated with better performance on both the WCST and Verbal Fluency. Analysis of covariance (ANCOVA) was used to compare patients and controls, adjusting for the difference in RCPM; regression lines in Fig. 1 come from this ANCOVA model, reflecting the average within-group association of the two variables and constrained to have the same slope across groups. As calculated from the corresponding variance terms of the ANCOVA, average within-group correlations with RCPM were 0.70 for WCST and 0.43 for Verbal Fluency. The scatterplots suggest that, at least for the WCST, PD deficits were largely or entirely explained by fluid intelligence. The group effect was to shift the RCPM distribution downward, leaving its relationship to executive task performance largely unchanged. In line with this conclusion, for the WCST, the difference between patients and controls was far from significant once RCPM was introduce as a covariate (Table 2, $p_{\text{<0.07}}$). For Verbal Fluency, ANCOVA showed a remaining but non-significant trend for a group difference ($p = 0.07$).

Scatterplots relating RCPM to the other frontal tests are shown in Fig. 2. For the Hotel Task, the results were somewhat similar to those observed in Verbal Fluency, with an average within-group correlation of 0.47. However, using ANCOVA to remove the influence of RCPM, the comparison between groups remained significant (Table 2, $p < 0.04$). On the theory-of-mind tasks, the scores were barely related to RCPM, with average within-group correlations of 0.14 for Faux Pas and 0.11 for Mind in the Eyes. Using ANCOVA to remove the influence of RCPM, significant group differences for Mind in the Eyes persisted (Table 2, $p < 0.02$), whereas for Faux Pas, the difference now fell just short of significance ($p = 0.06$).

| Table 2. Patient and control scores, average within-group correlation with Raven Colored Progressive Matrices (RCPM), and significance of group differences for each task |
|---------------------------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | Patients                        | Controls        | Patients versus controls $p$ | Average within-group correlations with RCPM | Patients versus controls after adjustment for RCPM $p$ |
|                                | Mean    | S.D. | Mean    | S.D. |                  |                  |                  |
| RCPM                            | 27.78   | 5.98 | 31.27   | 3.90 | 0.02             | 0.70             | 0.34             |
| WCST (categories achieved)      | 4.61    | 1.64 | 5.55    | 0.80 | <0.01            | 0.43             | 0.07             |
| Verbal Fluency<sup>a</sup>      | 14.31   | 4.78 | 18.09   | 5.07 | <0.01            | 0.14             | 0.06             |
| Hotel Task<sup>b</sup>          | -460.41 | 219.10 | -300.91 | 142.10 | <0.01             | 0.47             | 0.04             |
| Faux Pas (max = 20)             | 17.74   | 1.91 | 18.86   | 1.35 | 0.02             | 0.11             | 0.02             |
| Mind in the Eyes (max = 17)     | 13.42   | 1.68 | 14.64   | 1.29 | <0.01            | 0.11             | 0.02             |

WCST, Wisconsin Card Sorting Test; s.d., standard deviation.
<sup>a</sup>Total number of words generated.
<sup>b</sup>Deviation from optimum time per task.

Mind in the Eyes (Baron-Cohen et al. 1997)
This task consisted of 17 photographs of the eye region of different human faces. Participants were required to make a two-alternative forced choice that best described what the person was thinking or feeling (e.g. worried–calm). The score was the total number correct. Data were available for 31/32 patients.

Results
The results are shown in Table 2. For all cognitive tasks, two-tailed $t$ tests were used to compare patients and controls. As expected, the PD group was significantly impaired on all tests, including the RCPM ($t(52) = -2.40, p = 0.02$), the classical executive tests [WCST: $t(51) = -2.45, p < 0.01$; Verbal Fluency: $t(52) = -2.78, p < 0.01$] and the tests of multitasking and theory of mind [Hotel: $t(49) = -2.97, p < 0.01$; Mind in the Eyes: $t(51) = -2.83, p < 0.01$; Faux Pas: $t(51) = -2.35, p = 0.02$]. No significant differences were found between medicated and non-medicated patients on any of the aforementioned variables, except for the Faux Pas, on which medicated patients performed more poorly than non-medicated patients ($t(29) = -2.46, p = 0.02$). However, significant differences between patients and controls persisted after the levodopa equivalent daily dose (mg) was introduced as a covariable ($p = 0.03$), suggesting that group differences were not related to medication intake.
Discussion

In this study, we aimed to investigate the role of fluid intelligence in different frontal deficits shown in a group of patients with PD. In line with previous studies (Pillon et al. 1995; Bostantjopoulou et al. 2001; Basić et al. 2004; Nagano-Saito et al. 2005), we found a loss of fluid intelligence in PD patients relative to control subjects. In the present study, this was found even in the absence of significant differences between the groups on pre-morbid IQ. We then asked what other cognitive deficits remained after statistical control for this fluid intelligence deficit.

For the classical executive tasks, WCST and Verbal Fluency, deficits in PD patients were no longer present once $g$ was introduced as a covariate. However, for other tasks, including multitasking and theory-of-mind tests, performance deficits remained once fluid intelligence was partialled out.

These results are largely compatible with data from patients with focal frontal lesions. In a recent study (Roca et al. 2010a) we showed that for the WCST and Verbal Fluency deficits of frontal patients were entirely explained by their fluid intelligence loss. The present study extends those results to patients with PD: even if original differences emerged when the PD...
group was compared with a group of control subjects, such differences became non-significant when fluid intelligence was introduced as a covariate.

Our data also replicate previous reports of multitasking and theory-of-mind deficits in patients with PD. PD patients showed deficits in their ability to infer other people’s thoughts and feelings (theory of mind) and in their ability to hold in mind a higher-order goal while performing other subgoals (Hotel Task). Unlike the findings for the WCST and Verbal Fluency, performance deficits on the Hotel Task and Mind in the Eyes remained significant even after fluid intelligence was statistically corrected. Again, the results resemble those obtained previously in patients with focal frontal lesions (Roca et al. 2010a). In that study also, we found that deficits in multitasking and theory of mind were not fully explained by fluid intelligence, with some evidence of link to lesions in the anterior frontal cortex (BA 10). In the Roca et al. (2010a) study, the theory-of-mind test that showed these results was the Faux Pas rather than Mind in the Eyes. In the present data, by contrast, the Faux Pas deficit fell just short of significance once fluid intelligence was controlled. Nevertheless, our findings confirm that deficits on multitasking and theory of mind shown by PD patients cannot be fully explained by their loss of fluid intelligence.

Both lesion and neuroimaging studies have previously linked multitasking and theory of mind to the prefrontal cortex. For theory of mind, lesion studies have indicated the particular importance of the orbitofrontal cortex (e.g. Stone et al. 1998; Rowe et al. 2001; Stuss et al. 2001), whereas neuroimaging studies indicate the parallel importance of other regions including the anterior cingulate cortex, the superior temporal sulcus, the temporal poles and the amygdala (Baron-Cohen et al. 1999; Gallagher & Frith, 2003; Frith & Frith, 2006). Multitasking and planning deficits have also been described in patients with frontal cortex damage (e.g. Hebb & Penfield, 1940; Shallice & Burgess, 1991; Goldstein et al. 1993), and the particular importance of the anterior prefrontal cortex has been suggested by both lesion and neuroimaging studies (e.g. Burgess et al. 2007; Gilbert et al. 2007; Dreher et al. 2008; Badre & D’Esposito, 2009; Roca et al. 2011). In PD, the impairment in these functions has been explained by the progressive deterioration of frontostriatal circuits that occurs during the course of the disease (Bodden et al. 2010; Roca et al. 2010b).

Although here we have discriminated two groups of tests, distinguished by whether frontal deficits are entirely explained by fluid intelligence, a more realistic possibility may be a continuum. For the WCST, we found the strongest overlap with fluid intelligence, with the patient-control difference far from significance ($p=0.34$) once fluid intelligence was controlled. The results are very similar to those we obtained previously for patients with focal lesions ($p=0.36$). For Verbal Fluency the evidence of overlap was less, with a marginal difference ($p=0.07$) remaining after fluid intelligence was controlled. Again this resembles our previous results ($p=0.07$). For multitasking and theory of mind, overlap with fluid intelligence may be weaker, although especially for multitasking, some correlation certainly exists. For some tests, accordingly, fluid intelligence accounts for the major part of frontal deficit, whereas for others, probably with a somewhat different anatomical substrate, it does not.

Our data have strong implications for the use and interpretation of executive tests such as the WCST and Verbal Fluency in patients with PD. Although several reports have highlighted the sensitivity of such tests in the detection of cognitive dysfunction in PD (e.g. Green et al. 2002; Azuma et al. 2003; Ong et al. 2005; Muslimovic et al. 2006; Williams-Gray et al. 2007), our results reveal that the deficits detected by such tasks may not be related to their particular cognitive content and that, instead, they might solely reflect a general cognitive loss. In our view, neuropsychological assessment in PD should include both fluid intelligence tests and specifics test of multitasking and theory of mind. Further studies should investigate the contribution of fluid intelligence to other executive tests used in PD.

Our data also have powerful implications for the understanding of the relationship between fluid intelligence and frontal functions. The previously reported results in patients with focal lesions now extend to PD: whereas some frontal deficits are entirely explained by fluid intelligence, others are not. Very possibly, this dissociation reflects dependence on somewhat different frontal regions, with fluid intelligence dependent in particular on lateral and dorsomedial regions (Bishop et al. 2008; Woolgar et al. 2010), whereas more of the anterior frontal cortex is crucial for multitasking and theory of mind. Further studies should investigate such relationships in other clinical populations with frontal involvement.

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Declaration of Interest

None.
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