Executive Functions and the Obsessive-Compulsive Disorder: On the Importance of Subclinical Symptoms and Other Concomitant Factors

Marie-Josée Bédard a,*, Christian C. Joyal a, Lucie Godbout a, Sophie Chantal b

a Department of Psychology, Université du Québec à Trois-Rivières, Trois-Rivières, Quebec, Canada
b Hôpital de l’Enfant-Jésus du CHA de Québec, Québec, Canada

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Abstract

Although reviews concerning the neuropsychology of obsessive-compulsive disorder (OCD) put great emphasis on impaired executive functioning, the overall conclusions are notoriously divergent. The main goal of the present study was to use a battery of neuropsychological tasks to assess nine cognitive domains with a special focus on executive functions in 40 patients with OCD. A secondary objective was to examine the relationships between clinical or demographic variables and neuropsychological performances. The third goal was to separate executive functions in more homogeneous components to verify whether specific impairment might be found in persons with OCD. Confirming the main hypothesis, few neuropsychological differences emerged between the OCD and healthy participants when concomitant factors were controlled. Moreover, subclinical symptoms appeared to play a different and independent role on the cognitive results. Future studies should include more specific tasks of lower-order executive functions among persons with OCD to confirm this possibility.

Keywords: Obsessive-compulsive disorder; Neuropsychology; Executive functions; Confounding factors; Depression; Anxiety

Introduction

Obsessive-compulsive disorder (OCD) is a disabling condition characterized by recurrent intrusive thoughts or impulses (obsessions) and by repetitive, irresistible, ritualized behaviors (compulsions) performed to neutralize anxiety and obsessions (American Psychiatric Association, 1994). The neurobiological correlates of OCD have been extensively studied during the past decade and structural, functional, and behavioral signs of cerebral fronto-striatal anomalies, involving particularly (but not exclusively) the orbitofrontal cortex, the basal ganglia, and the anterior cingulum are repeatedly reported (e.g., Saxena and Rauch, 2000; Whiteside, Port, & Abramowitz, 2004; Menzies et al., 2008; for reviews, Szeszko et al., 2008). These conclusions prompted the search of a neuropsychological profile of persons with OCD, and the results are notoriously mixed (e.g., Kuelz, Hohagen, & Voderholzer, 2004, for a critical review). On one hand, a wide array of cognitive impairments have been associated with OCD (including such diverse capacities as decision-making, planning, learning strategies, set-shifting, response inhibition, memory, visuospatial abilities, and psychomotor functions; see Aouizerate et al., 2004; Greisberg & McKay, 2003; Kuelz et al., 2004; Tallis, 1997, for reviews) and additional non-frontal cerebral anomalies are increasingly underlined (see Menzies et al., 2008, for a review). On the other hand, however, recent neurocognitive conclusions tended to be moderate (e.g., Moritz et al., 2007; Moritz, Jelinek, Hottenrott, Klinge, & Randjbar, 2009), as impairments might in fact be limited to basic functions such as motor execution and speed of processing (e.g., Burdick, Robinson, Malhotra, & Szeszko, 2008). The main goal of this study was to consider potential factors underlying this divergence of neuropsychological
results among persons with OCD and verify whether the elusive “cognitive endophenotype” might be unveiled with the use of a comprehensive assessment.

These mixed findings of neuropsychological assessments among OCD patients might be explained by several factors. First, possible confounding variables such as age, sex, educational level, and intellectual quotient (IQ) of the participants were not systematically considered by earlier studies of OCD (see Kuelz et al., 2004). When comparison groups began to be matched for such variables, motor deficits were still found (both for initiation and execution), but cognitive impairments were less prevalent and severe than previously believed (e.g., Purcell, Maruff, Kyrios, & Pantelis, 1998; Jurado, Junqué, Vallejo, & Salgado, 2001). Similarly, after it was realized that severity of OCD symptoms and levels of depression and anxiety might have important and independent influences upon neuropsychological results (e.g., Basso, Bornstein, Carona, & Morton, 2001; Basso et al., 2007; Moritz et al., 2001; Moritz, Kloss, Jahn, Schick, & Hand, 2003; Nielen, Veltman, de Jong, Mulder, & den Boer, 2002), findings began to be tempered (e.g., Ayiciego, Dinn, Harris, & Erkmen, 2003; Bannon, Gonsalvez, Croft, & Boyle, 2006; Burdick et al., 2008; Kivircik, Yener, Alptekin, & Aydin, 2003; Moritz, Kuelz, Jacobsen, Kloss, & Fricke, 2006; Moritz et al., 2007, 2008).

Statistical analyses represent a second potential factor for divergence of results among neuropsychological studies with OCD. As underlined elsewhere (Menzies et al., 2008), many statistical pitfalls are present in this field, including the use of parametric analyses with typical non-normal distributions, the inclusion of several dependent variables with small numbers of participants and the use of multiple uncorrected univariate comparisons, which all might lead to false-positive results. For instance, Chamberlain, Fineberg, Blackwell, Robbins, and Sahakian (2006) recently reported impairments in motor inhibition and set shifting with 20 OCD patients. The same group of researchers, however, subsequently reported other impairments in diverse cognitive domains with the same participants (Chamberlain et al., 2007). Overall, 10 neuropsychological tests were given to 20 patients with OCD without correction for multiple assessments. Although the authors acknowledged the situation in the second publication (although only the number of intra-task comparisons, not the number of group comparisons, was considered; Chamberlain et al., 2007), it was not the case in the first report, in which the set-shifting impairment would not have been statistically significant (Chamberlain et al., 2006). For this reason, a growing number of neuropsychological studies, especially in the field of schizophrenia, use comprehensive assessments and regroup the variables into cognitive domains instead of reporting single results (e.g., Bilder et al., 2000; Milev, Ho, Arndt, & Andreasen, 2005; Nuechterlein et al., 2004). In doing so, the likelihood of finding spurious differences between groups due to chance associations are significantly reduced (Milev et al., 2005). This approach also helps to reveal a profile, if any, of the participants.

The third factor to consider is the type of neuropsychological task involved. Although deficits of implicit learning, closely associated with subcortical anomalies (e.g., striatal and cerebellar), are reported with a fair consistency in OCD (Kathmann, Rupertseder, Hauke, & Zaudig, 2005; Rauch et al., 2007), neuropsychological hypotheses of OCD commonly involve frontal-related executive functions (e.g., Penadés, Catalan, Andres, & Salamero, 2005; Menzies et al., 2008). However, assessments of executive functions encompass numerous and vastly different capacities and, consequently, generate mixed results (including positive findings, e.g., Cavedini, Ferri, Scarone, & Bellodi, 1998; Fenger et al., 2005; Schmidtko, Schorb, Winkelmann, & Hohagen, 1998; and negative or partially positive results, e.g., de Geus, Denys, Sitskoorn, & Westenberg, 2007; Jurado et al., 2001; Simpson et al., 2006; Veale, Sahakian, Owen, & Marks, 1996). Thus, neuropsychological studies of OCD should attempt to consider different aspects of executive function assessments, such as inhibition, set shifting, working memory, planning, problem solving, and reasoning separately. This approach may be helpful in identifying more specific problems. More particularly, defects in set shifting and inhibition, two basic executive functions, are more commonly reported among persons with OCD, and they might represent core deficits. For instance, a lack of planning measured at the Tower of London task or a low score at the Wisconsin card sorting task, classically associated with dorsolateral frontal lesions (e.g., Milner, 1963), might in fact reflect low motor inhibition or poor set-shifting capacities, respectively, more closely associated with frontal ventral or caudate involvement (Monchi, Petrides, Petre, Worsley, & Dagher, 2001). Thus, considering different executive processes might help disentangle the neuropsychological reports in OCD.

Another example of basic executive function is self-organizational strategies, which are traditionally overlooked in neuropsychological assessment (e.g., Lezak, Howieson, Loring, & Hannay, 2004). A growing number of studies stressed that OCD might be associated with poor self-organization, which might lead to apparent defects of other cognitive processes (e.g., Roth, Baribeau, Milovan, & O’Connor, 2004), especially memory (Deckersbach, Otto, Savage, Baer, & Jenike, 2000; Savage et al., 1999, 2000; Penadés et al., 2005). Thus, it is important to consider separately different types of executive functions and their components.

Still another aspect to consider in neuropsychological assessments of OCD is fundamental functions, such as speed of information processing and motor execution. According to Moritz and colleagues (2006), subjective complaints from the patients concern psychomotor slowness much more than higher cognitive dysfunctions (especially memory; Moritz et al., 2006). As for motor slowing, it is a well-known characteristic of OCD patients (e.g., Gross-Isseroff, Sasson, Voet, Hendler,
& Luca-Haimovici, 1996; Purcell et al., 1998) and, importantly, it is frequently observed in conjunction with normal neuropsychological accuracy (Christensen, Kim, Dysken, & Hoover, 1992; Galderisi, Mucci, Catapano, Damato, & Maj, 1995; Martin, Wiggs, Altemus, Rubenstein, & Murphy, 1995; Veale et al., 1996). It might also be stated that Basso and colleagues (2001), in their seminal paper, not only suggested that impairments on several executive tasks are rather linked with depression than OCD symptoms, but also that OCD by itself is simply a good predictor of basic sensory-motor deficits. Thus, the impact of motor speed and speed of processing (or lack of thereof) on neuropsychological results should be considered in assessment of persons with OCD. This suggestion is in direct line with the recent short communication of Burdick and colleagues (2008), which deserves further attention.

In this well-designed study, Burdick and colleagues (2008) used 22 neuropsychological variables to generate six cognitive domains based on the z-scores of 26 patients OCD and 38 healthy controls (matched for age, education, sex, handedness, and race). While the patients presented with a significant global neuropsychological deficit, multivariate and profile analyses revealed that it was mainly due to two domains: Speed of processing and motor functions (Burdick et al., 2008). Scores on the verbal memory, the reasoning/problem solving, and the language domains did not differ significantly between the groups. These authors concluded that specific neuropsychological impairments of OCD were related to motor speed and processing speed capacities (Burdick et al., 2008). It should be noted, however, that lower-order executive functions such as attentional set shifting were not evaluated in that study, and certain effect sizes for domains with negative results were relatively strong. Focusing on executive function tasks and recruiting a higher number of participants might help confirm these conclusions.

The main goal of this study was to evaluate a relatively high number of OCD participants with a comprehensive neuropsychological battery to assess nine selected cognitive domains. A secondary objective was to determine whether a cognitive profile of OCD would emerge compared with healthy controls matched for gender, age, education, and IQ. A third objective was to consider the potential influence of the severity of OCD, depression, and anxiety symptoms on the neuropsychological results, and the last goal was to separate the broad category of executive functions in more homogeneous subcategory of measures.

On the basis of the preliminary study of Burdick and colleagues (2008), it was first hypothesized that motor skills and speed of information processing would differentiate the groups when concomitant variables are controlled. The second hypothesis was that clinical variables (e.g., OCD symptom severity, co-morbid symptoms, IQ estimate) would significantly influence the performances in the cognitive domains. The third hypothesis was that among executive functions, set shifting and inhibition would differentiate the groups.

**Materials and Methods**

**Participants**

Forty persons diagnosed with OCD and 22 healthy controls participated in the study. The patients were recruited at two outpatient clinics in Quebec City. All participants were French-speaking and all testing was performed in French. Two psychiatrists independently confirmed primary and, when necessary, secondary diagnoses based on the DSM-IV criteria (American Psychiatric Association, 1994). In a few cases, where only one psychiatrist evaluated the patient, diagnosis confirmation was obtained from a licensed psychologist using the French version of the anxiety disorders interview schedule for DSM-IV (ADIS-IV: Boivin & Marchand, 1996; Brown, Di Nardo, & Barlow, 1994). In these cases, a difference of at least two points was required to differentiate primary from secondary diagnoses. Reliability of the English and French versions of the ADIS-IV scale has been demonstrated in previous studies (e.g., Brown, Di Nardo, Lehman, & Campbell, 2001; Marchand, Roberge, Reinhart, & Cloutier, 2000). Exclusion criteria included brain injury or any neurological condition, psychosis, primary personality disorder, mental retardation, and a history of alcohol or substance abuse. Patients with other co-morbid diagnoses were not excluded provided that OCD was the main diagnosis. Of the OCD participants, 11 (27.5%) had co-morbid axis I disorder (three had a depressive disorder, i.e., major depressive episode or dysthymia; seven had another anxiety disorder, i.e., social phobia, generalized anxiety disorder, specific phobia; and one had anorexia). The majority of OCD participants (n = 31; 77.5%) were on medication at the time of the study (mostly a selective serotonin reuptake inhibitor, SSRI) with the criterion of receiving a stable dose for at least 3 months. Illness duration was 8.92 years on average (SD = 8.07; range = 1–35, from the day of first diagnosis). The mean Y-BOCS score was 27.65 (SD = 6.8), representing moderate-to-severe disease severity (obsessions: M = 13.23, SD = 3.4; compulsions: M = 14.23, SD = 3.9, see Table 1).

The volunteer healthy participants were recruited through advertisements in a local newspaper. They were screened with ADIS-IV to exclude any significant present or past psychiatric illness and reported no history of neurological illness, head injury resulting in a loss of consciousness, substance abuse, or systemic illness with potential effects on cognitive functioning.
None received psychotropic medication during the time of study. Both groups had similar mean age, sex ratio, education level, and IQ estimates (Table I). All participants provided written informed consent after the nature and requirements of the study were explained to them. The study was approved by the ethics committees of the Université du Québec à Trois-Rivières and both clinics where OCD patients were recruited.

**Measures of Symptoms**

All clinical scales (French-language versions) were administered on the day of testing. The severity of OCD symptoms was assessed with the Yale–Brown obsessive-compulsive scale (Y-BOCS; Goodman, Price, & Rasmussen, 1989; French version, Mollard, Cottraux, & Bouvard, 1989). In both groups, depressive symptoms and anxiety levels were assessed with the Beck depression inventory (BDI-II: Beck, Steer, & Brown, 1994; French version, Éditions du centre de psychologie appliquée, 1996) and the Beck anxiety inventory, respectively (BAI; Beck, Epstein, Brown, & Steer, 1988; French version, Freeston et al., 1994). Reliability and validity of the French-language versions of the three scales are well established (e.g., Bouvard et al., 1992; Éditions du centre de psychologie appliquée, 1996; Freeston et al., 1994).

**Neuropsychological Tests**

All neuropsychological tests were administered within two 90-min sessions by licensed neuropsychologists trained for standardized assessment and scoring procedures. Testing took place in a quiet room, rest periods were allowed, and the test order was counterbalanced to control for fatigue effects. Fourteen neuropsychological tasks assessing different cognitive domains with well-known psychometric properties were selected on the basis of previous investigations with OCD patients (see Kuelz et al., 2004, for a review; and Lezak et al., 2004, for a complete description of the tests). These tasks were: The Purdue pegboard test (Tiffin & Asher, 1948); the Rey-complex figure test, (RCFT; procedure of Meyers & Meyers, 1995); the Brown–Peterson task (Stuss, Stethem, & Pelchat, 1988); the trail making, color-word interference, verbal fluency, and 20 question subtests of the D-KEFS battery (Delis–Kaplan executive function system; Delis, Kaplan, & Kramer, 2001); the California verbal-learning test second edition, (CVLT-II; Delis & Fridlund, 2000); the Spatial span of the Wechsler memory scale third edition (WMS-III; Wechsler, 1991); the block design, digit span, vocabulary, and arithmetic subtests of the Wechsler adult intelligence scale third edition (WAIS-III; Wechsler, 1997); and the Mesulam and Weintraub cancellation test (MWCT; Mesulam, 1985). These assessments generated more than 60 neuropsychological variables, which were grouped into broad cognitive domains to limit the number of comparisons.

**Cognitive Domains**

On the basis of past research in this field (e.g., cognitive functions typically assessed and more likely to be impaired with OCD persons; e.g., Burdick et al., 2008; see also Kuelz et al., 2004; Menzies et al., 2008, for reviews) and theoretical constructs in neuropsychology (Lezak et al., 2004; Spreen and Strauss, 1998), the dependant variables were grouped into nine domains (see Appendix for a detailed list of their constituents): (1) motor skills; (2) speed of processing; (3) visuospatial analyses; (4) verbal memory (encoding and retrieval); (5) visual memory (encoding and retrieval); (6) executive functions I (Inhibition/switching); (7) executive functions II (working memory); (8) executive functions III (reasoning, planning, and problem solving); (9) executive functions IV (composite score of errors). Because the number of participants was not sufficient to

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**Table 1.** Demographic and clinical characteristics of OCD (n = 40) and healthy control samples (n = 22)

<table>
<thead>
<tr>
<th>Variable</th>
<th>OCD</th>
<th>Controls</th>
<th>Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>χ² = 0.41</td>
<td>.52</td>
</tr>
<tr>
<td>Men</td>
<td>16 (40%)</td>
<td>7 (32%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>24 (60%)</td>
<td>15 (68%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>41.15 (11.42)</td>
<td>42.50 (12.17)</td>
<td>t = 0.44</td>
<td>.67</td>
</tr>
<tr>
<td>Education (years)</td>
<td>13.98 (3.25)</td>
<td>13.89 (2.77)</td>
<td>t = 0.11</td>
<td>.91</td>
</tr>
<tr>
<td>Estimated IQ</td>
<td>102.43 (14.11)</td>
<td>103.55 (10.62)</td>
<td>t = 0.32</td>
<td>.75</td>
</tr>
<tr>
<td>BDI-II</td>
<td>23.90 (6.41)</td>
<td>6.41 (6.92)</td>
<td>t = 6.60</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>BAI</td>
<td>16.23 (11.09)</td>
<td>3.55 (3.99)</td>
<td>t = 6.51</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

**Notes:** Means (SD) except for gender (absolute numbers and ratios). BDI-II = Beck depression inventory II; BAI = Beck anxiety inventory; OCD = obsessive-compulsive disorder.
perform a factorial analysis (less than 300 participants; Tabachnick and Fidell, 2007), and the grouping of neuropsychological tasks is inevitably subjective (for instance, the WAIS-III arithmetic subtest can be viewed as measuring both working memory and problem solving), the internal consistency of each domain was assessed with alpha coefficients of Cronbach (\(\alpha\)). The minimum criterion was set at .70 (see Appendix). Following this criterion, the domain of “storage abilities for verbal and visual memory,” created with recognition conditions of the CVLT and RCFT tasks was removed because of a lack of internal consistency. Because no previous studies suggested that recognition might be impaired in persons with OCD, this domain was discarded and no additional comparisons were performed with its individual variables. Thus, the final analyses were based on nine cognitive domains.

These cognitive domains were computed after transforming the raw scores of the neuropsychological variables in standardized z-scores with the results of the control group (mean of 0 and SD of 1). This procedure sets all results on the same scale. Standardized scores were reversed when necessary, so that positive scores reflect better performances. Thus, each cognitive domain score represents the mean of its component neuropsychological test variable standardized scores (Appendix). In order to assess whether the reliability of each cognitive domain could further be improved, the correlation between each constituent variable and the entire cognitive domain was calculated. Since all variables were significantly correlated with the total (\(r > 0.40\) in all cases), all were kept in the analyses.

IQ estimates were based on the arithmetic, block design, and vocabulary subtests (Sattler & Ryan, 1999). The reliability and validity coefficients of this approach were, respectively, 0.95 and 0.91, as calculated with the standardization data of the WAIS-III and the Tellegen and Briggs (1967) procedure.

Secondary Indexes

Three additional measures were computed during the course of study to explore. They were not included in the primary analyses because they were not part of the hypotheses and they were not selected a priori as constituents of the cognitive domains. The first two measures were derived from the CVLT-II data as indexes of self-ordering capacities. Scores of semantic clustering (efficacious self-ordering) and serial clustering (poor self-ordering) were used. These scores were obtained with the CVLT-II comprehensive scoring system of Delis and Fridlund (2000). The third index was obtained with the random number generation task (RNG; Evans, 1978), which was introduced during the data collection. Because performance at this task was associated with anterior cingulate activation (Artiges et al., 2000), which is hypothesized to underlie the cognitive deficits observed in OCD (e.g., De Geus et al., 2007), a subgroup of 10 patients and 10 healthy controls performed that task. They were asked to verbally produce a sequence of 100 numbers between 1 and 10, as close as possible to a random series. They were told to imagine that they were drawing numbers from a hat one at a time, calling them out, then replacing them, so that on any draw any of the 10 numbers were equally likely to be selected. To avoid possible effects of speed difference, the number generation was paced with a metronome set at 1 beat·s⁻¹. The randomization index is a \(\chi^2\)-like measure that evaluates the frequency with which any number follows any other number, compared with chance expectations and appropriately modified by an adjustment based on the marginal frequency of use of each of the 10 digits in the series of 100 numbers (Evans, 1978).

Statistical Analyses

The first step was to compare the average scores of both groups on the nine cognitive domains. Because most of the neuropsychological variables were not normally distributed in the patient group (which is typical of psychiatric samples, e.g., Milev et al., 2005), and the effects of logarithmic transformations was not successful in every domain, non-parametric Mann–Whitney tests were used to compare the means. The Bonferroni method (0.05/number of comparisons) was applied to verify whether any difference would remain statistically significant after correcting for multiple comparisons. Because it is commonly argued that the Bonferroni method is too conservative in clinical context, especially when comparisons are not independent (e.g., Purcell et al., 1998) or based on unambiguous hypotheses of performance difference (e.g., Moritz et al., 2007), an alternative approach was also used (e.g., \(\alpha\) of 0.01; Purcell et al., 1998). Effect sizes were also calculated to detect any potential difference that was not significant because of insufficient statistical power related to the sample sizes. The formula of effect sizes for Mann–Whitney tests was applied (\(r = Z/N^2;\) Rosenthal, 1991) and the convention of Cohen (1992; small effect size, \(r = 0.1\); medium, \(r = 0.3\); large, \(r = 0.5\)) was used to evaluate their magnitude.

The second step was to explore the association between sociodemographic or clinical variables and the neuropsychological performance within the OCD group. A multiple regression model was computed with age, gender, IQ estimate, symptom severity (Y-BOCS), and levels of depression (BDI-II) and anxiety (BAI) as independent variables, and the cognitive domains and the clustering scores as dependent factors. Colinearity between independent variables was evaluated by examination of the
variance inflation factor (VIF). VIF was lower than five in all cases, suggesting that there were no colinearity problems. Residual scatter plots, normal probability plots, and partial residual plots were used to determine if regression assumptions were satisfied. When necessary, data were log(x + 1) or square-root transformed to normalize the residuals. If these procedures were not successful, regressions were conducted on rank-transformed data (Quinn and Keough, 2002).

The randomization index of the RNG task was not entered into the regression model because the sample that completed this task was too small (10 OCD participants and 10 healthy controls). Spearman correlations were used to examine any relationships between the sociodemographic or clinical and variables the randomization index.

Results

Comparisons Between OCD and Healthy Control Participants on the Cognitive Domains

Among the nine cognitive domains, only two differed significantly between OCD and healthy participants: Motor skills (median z-scores = −0.152 and 0.344, respectively, \( U = 236.5, p < 0.01 \), with an effect size \( r = 0.38 \), between medium and large) and speed of information processing (median z-scores = −0.0013 and 0.347, respectively, \( U = 276.0, p < 0.05 \), \( r = 0.32 \), medium effect size; Table 2), in favor of the control group. When the Bonferroni procedure for multiple comparisons (0.05/9 = 0.006) or the more stringent \( \alpha (0.01) \) are applied, only the difference for motor skills remains significant.

Relationships Between OCD Clinical Variables and Neuropsychological Data

The multiple regression analysis first revealed that none of the clinical or demographic variables were significantly associated with performances in the domains of motor skills and speed of information among participants with OCD (Table 3). Furthermore, no significant relationship was found between symptom severity of OCD and any neuropsychological data. However, the depression score was significantly and negatively associated with performances in the working memory domain (\( r^2_{\text{adj}} = 0.60; \beta = -0.02, p < 0.05 \)) and the executive function errors (\( r^2_{\text{adj}} = 0.52; \beta = -0.76, p < 0.01 \); Table 3). The anxiety score was also negatively associated with the executive function errors (\( r^2_{\text{adj}} = 0.52; \beta = -0.55, p < 0.05 \)). The estimated IQ was positively associated with the scores in the domains of visuospatial analyses (\( r^2_{\text{adj}} = 0.74; \beta = 0.92, p < 0.0001 \)), working memory (\( r^2_{\text{adj}} = 0.60; \beta = 0.04, p < 0.01 \)), and problem solving (\( r^2_{\text{adj}} = 0.47; \beta = 0.60, p < 0.05 \)).

Comparisons Between OCD and Healthy Control Participants on the Secondary Indexes

First, OCD participants obtained a significantly lower mean randomization index than healthy volunteers (\( M = 0.35 \pm 0.06 \) vs. \( M = 0.30 \pm 0.04 \), respectively; \( U = 23.0, p < 0.05 \); effect size of 0.46; Table 4). Second, there was no significant difference between OCD patients and healthy controls for either the semantic (\( M = 1.46 \pm 1.7 \) and \( M = 1.7 \pm 1.7 \), respectively; \( U = 330.0, p > 0.1 \); effect size of 0.05) or the serial clustering (\( M = 0.93 \pm 1.1 \) and \( M = 0.51 \pm 0.8 \); \( U = 411.5, p > 0.1 \); effect size of 0.21) in the CVLT-II task (Table 4). The randomization index was not significantly associated with any clinical or sociodemographic variable (data not shown; all rho values of <0.46, and all p-values >0.18).

Table 2. Mann–Whitney comparisons between OCD (n = 40) and healthy control (n = 22) participants on the nine cognitive domains

<table>
<thead>
<tr>
<th>Cognitive domains</th>
<th>OCD median*</th>
<th>Controls median</th>
<th>U</th>
<th>p-value</th>
<th>Effect size (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor skills</td>
<td>−0.152</td>
<td>0.344</td>
<td>236.5</td>
<td>.0027</td>
<td>0.38</td>
</tr>
<tr>
<td>Speed of information processing</td>
<td>−0.0013</td>
<td>0.347</td>
<td>276.0</td>
<td>.0158</td>
<td>0.32</td>
</tr>
<tr>
<td>Visuospatial analyses</td>
<td>0.0046</td>
<td>0.17</td>
<td>388.0</td>
<td>.44</td>
<td>0.10</td>
</tr>
<tr>
<td>Encoding and retrieval in verbal memory</td>
<td>0.0269</td>
<td>0.1365</td>
<td>387.5</td>
<td>.43</td>
<td>0.10</td>
</tr>
<tr>
<td>Encoding and retrieval in visual memory</td>
<td>−0.0623</td>
<td>0.267</td>
<td>417.5</td>
<td>.74</td>
<td>0.05</td>
</tr>
<tr>
<td>Inhibition/switching</td>
<td>0.111</td>
<td>0.33</td>
<td>340.0</td>
<td>.14</td>
<td>0.19</td>
</tr>
<tr>
<td>Working memory</td>
<td>−0.0187</td>
<td>−0.0005</td>
<td>438.5</td>
<td>.39</td>
<td>0.11</td>
</tr>
<tr>
<td>Problem solving</td>
<td>0.13</td>
<td>0.153</td>
<td>399.0</td>
<td>.55</td>
<td>0.08</td>
</tr>
<tr>
<td>Errors in executive tasks</td>
<td>−0.15</td>
<td>−0.0799</td>
<td>409.0</td>
<td>.65</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*Since non-parametric tests are based on ranking, the median z-scores of the groups are more informative than their means. Negative scores indicate performance below average. Effect sizes for ranked Mann–Whitney tests are derived from the formula: \( r = ZN \). OCD = obsessive-compulsive disorder.
A Posteriori Statistical Analyses

Because psychomotor speed represents an important part of the processing speed domain (affecting five of its seven neuropsychological variables; Appendix), it might explain some of the difference observed in this study between OCD patients and healthy controls in the speed of information processing. In order to address this issue, the processing speed domain was split into two composite scores, one involving motor execution (completion times of the trail making, conditions 1–3 and completion times of the MWCT, structured and unstructured arrays); and the other without a motor involvement (completion time, color-word interference, conditions 1 and 2). The speed of processing domain differed significantly between the groups when a motor component was present ($M = 20.22 \pm 1.03$ and $M = 0.40 \pm 0.47$, respectively; $U = 242.0$, $p < 0.01$) but not without motor involvement ($M = 20.09 \pm 0.99$ and $M = 0.15 \pm 0.58$, respectively, $U = 321.5$, $p = 0.30$).

Discussion

The main goal of this study was to determine whether a cognitive profile could be associated with OCD when a comprehensive neuropsychological battery is used and age, sex, education, and IQ are controlled. In accordance with the first hypothesis, the domains of motor skills and speed of information processing were significantly different between persons with OCD and healthy volunteers before application of Bonferroni procedure. No difference emerged between the groups for the domains of visuospatial analyses, memory (visual and verbal), set shifting/inhibition, working memory, planning/reasoning, and executive errors, with or without control for multiple comparisons. The second goal of this study was to further investigate the possible influence of clinical variables upon neuropsychological results. As postulated, depressive symptoms, anxiety symptoms, and IQ estimates (but not OCD symptom severity) were significantly associated with the results of certain cognitive domains, including executive functions (e.g., working memory, problem solving, and executive errors). These findings support the notion that previous conflicting reports of cognitive characteristic associated with OCD might in part result from concomitant,

Table 3. Associations between demographic or clinical variables and the neuropsychological performances of OCD participants ($n = 40$): A multiple regression analysis

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Age (years)</th>
<th>Education (years)</th>
<th>Estimated IQ</th>
<th>Depression$^a$</th>
<th>Anxiety$^b$</th>
<th>Symptom severity$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor skills$^d$</td>
<td>−0.25</td>
<td>1.13</td>
<td>0.20</td>
<td>−0.36</td>
<td>0.04</td>
<td>0.02</td>
</tr>
<tr>
<td>Speed of information processing$^d$</td>
<td>−0.27</td>
<td>1.73</td>
<td>0.28</td>
<td>−0.22</td>
<td>−0.21</td>
<td>−0.21</td>
</tr>
<tr>
<td>Visuospatial analyses$^d$</td>
<td>−0.36$^i$</td>
<td>0.73</td>
<td>0.92$^{***}$</td>
<td>0.03</td>
<td>0.01</td>
<td>0.30</td>
</tr>
<tr>
<td>Encoding and retrieval, verbal memory</td>
<td>−0.02</td>
<td>0.03</td>
<td>0.02</td>
<td>−0.01</td>
<td>0.01</td>
<td>−0.03</td>
</tr>
<tr>
<td>Encoding and retrieval, visual memory</td>
<td>−0.01</td>
<td>0.07</td>
<td>0.03$^i$</td>
<td>0.01</td>
<td>−0.02</td>
<td>−0.01</td>
</tr>
<tr>
<td>Inhibition/switching$^g$</td>
<td>−0.20</td>
<td>1.72</td>
<td>0.32</td>
<td>0.03</td>
<td>−0.18</td>
<td>0.14</td>
</tr>
<tr>
<td>Working memory</td>
<td>−0.01</td>
<td>0.01</td>
<td>0.04$^{**}$</td>
<td>−0.02$^*$</td>
<td>−0.01</td>
<td>0.03$^i$</td>
</tr>
<tr>
<td>Problem solving$^g$</td>
<td>0.08</td>
<td>1.49</td>
<td>0.60$^*$</td>
<td>−0.36</td>
<td>−0.37</td>
<td>0.36</td>
</tr>
<tr>
<td>Executive function errors$^d$</td>
<td>−0.50$^i$</td>
<td>1.08</td>
<td>0.39</td>
<td>−0.76$^{**}$</td>
<td>−0.55$^{**}$</td>
<td>−0.36</td>
</tr>
<tr>
<td>Semantic clustering</td>
<td>−0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>−0.02</td>
</tr>
<tr>
<td>Serial clustering</td>
<td>−0.03</td>
<td>−0.08</td>
<td>0.05</td>
<td>−0.02</td>
<td>0.02</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Notes: OCD = obsessive-compulsive disorder.
$^a$Beck depression inventory II.
$^b$Beck anxiety inventory.
$^c$Yale–Brown obsessive-compulsive scale.
$^d$These regressions were conducted on rank-transformed data.
$^i$p < .06 (statistical trend).
$^*p < .05.$
$^{**}p < .01.$
$^{***}p < .0001.$

Table 4. Secondary Mann–Whitney comparisons between OCD ($n = 40$) and healthy controls ($n = 22$)

<table>
<thead>
<tr>
<th>Cognitive domain</th>
<th>OCD (mean ± SD)</th>
<th>Controls (mean ± SD)</th>
<th>$U$</th>
<th>$p$-value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomization index (RNG)$^a$</td>
<td>0.35 ± 0.06</td>
<td>0.30 ± 0.04</td>
<td>23.0</td>
<td>.04</td>
<td>0.46</td>
</tr>
<tr>
<td>Semantic clustering (CVLT-II)</td>
<td>1.46 ± 1.71</td>
<td>1.71 ± 1.72</td>
<td>330.0</td>
<td>.67</td>
<td>0.05</td>
</tr>
<tr>
<td>Serial clustering (CVLT-II)</td>
<td>0.93 ± 1.14</td>
<td>0.51 ± 0.84</td>
<td>411.5</td>
<td>.11</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Notes: RNG = random number generation task; CVLT = California verbal learning task; OCD = obsessive-compulsive disorder.
$^a$Only 10 OCD and 10 controls completed this test.
uncontrolled variables such as symptom severity, IQ, and educational attainment. The third hypothesis of specific set-shifting deficits was not confirmed, however, although effect sizes were intriguing and the dichotomy between higher- and lower-order executive functions might be crucial in neuropsychological assessment of OCD. These points are discussed later.

The first conclusion of this study is that slow motor execution and/or processing of information might represent core neuropsychological deficits of OCD, as it was recently suggested by Burdick and colleagues (2008). These domains were not related to the depression or the anxiety scores in the present study, which is also in accordance with the proposition that sensory-motor functions are reliably associated with OCD (Basso et al., 2001). Moreover, generalized slowness is well-documented among OCD patients (Galdersi et al., 1995; Gross-Isseroff et al., 1996; Martin et al., 1995; Sawle, Hymas, Lees, & Frackowiak, 1991). However, the origin of this processing and/or motor slowness is less clear. Significance of impairments for the information processing speed domain was lost in this study, both by removal of measures with motor involvement and Bonferroni procedures. Because assessments of speed of information processing typically involve motor execution (see for instance the trio of letter cancellation time, trail making time, and digit symbol in Burdick et al., 2008), future neuropsychological studies of persons with OCD should consider the motor component of the processing speed task (and that of other cognitive measures). Importantly, Burdick and colleagues (2008) suggested that low psychomotor speed among OCD patients might be secondary to medication administration. In view of this report, analyses were performed a posteriori between the 31 medicated and the 9 unmedicated OCD participants on the psychomotor speed domain score. Although not significant, the difference between medicated \( (M = 0.34, SD = 0.98) \) and unmedicated \( (M = 0.05, SD = 0.76) \) participants \( (p = 0.21) \) was in the proposed direction. It should also be kept in mind that psychiatric patients in general, especially under medication, tend to be slower. However, this study was not designed to examine the relationship between medication and neuropsychological performance, and data are needed to confirm the possibility with a larger sample of unmedicated participants.

The second finding of this study was the absence of difference between the groups in the cognitive domains when age, gender, educational level, and IQ are similar. Also, the severity of illness (OCD) was not statistically related to the scores of any cognitive domains, which is consistent with prior reports (e.g., Bolton, Raven, Madronal-Luque, & Marks, 2000; Cavedini et al., 1998; Schmidtke et al., 1998). These results might help explaining, in part, the notorious divergence of neuropsychological conclusions with OCD patients (Kuelz et al., 2004; Menzies et al., 2008). When concomitant variables are controlled, cognitive deficits are less important (e.g., Burdick et al., 2008; Moritz et al., 2007, 2008).

Interestingly, however, the dichotomy between higher- and lower-order executive functions might prove to be crucial among persons with OCD. Lower-order executive functions are more basic abilities, such as inhibitory control, attentional set shifting, and decision-making, associated with regionally lower and older parts of the prefrontal cortex, especially the orbital and ventral regions (e.g., Happaney, Zelazo, & Stuss, 2004). Higher-order executive functions refer to phylogenetically and ontogenetically newer capacities, including reasoning, judging, and planning, and more closely associated with dorsal and lateral parts of the prefrontal cortex (e.g., Stuss & Knight, 2002; see also the “hot” vs. “cool” dichotomy in children literature, e.g., Hongwanishkul, Happaney, Lee, & Zelazo, 2005). Among persons with OCD, there are substantially more signs of lower-order executive function deficits than higher-order executive impairment functions (e.g., Ayiccegi et al., 2003; Bannon et al., 2006; Chamberlain et al., 2006, 2007, 2008; Hartston & Swerdlow, 1999; Lawrence et al., 2006; Penadés et al., 2007; Veale et al., 1996). In this study, it is worth noting that the effect size for the inhibition/set-shifting domain approached the medium range (see the Results section), so that a type-II error is plausible. Although the goal of this investigation was not to specifically compare lower- (or “hot”) versus higher-order (or “cool”) executive functions, future studies (including meta-analyses) should attempt to verify the hypothesis that the former are more likely to be impaired than the latter in OCD. Inclusion of specific lower-order executive tasks such as the continuous performance task, the stop-signal task, the Iowa gambling task, the balloon analogue task, and the Cambridge risk-taking task might help clarify the picture. Overall, it seems that when executive functions impairments are found among persons with OCD, it typically concerns such lower-order executive capacities as inhibitory control, set shifting (including efficacious search of alternative strategies), and operant conditioning (including advantageous decision-making; e.g., Menzies et al., 2008). Demonstrating impaired lower-order executive functions with relatively preserved higher-order executive functions in OCD would have important clinical implications, especially for occupational and psychological therapies.

Still, it should be noted that even among recent studies of lower-order executive functions findings are divergent including, for instance, significant results for reversal learning (e.g., Chamberlain et al., 2008) and negative results for object alternation (e.g., Moritz et al., 2008). As for the results of this study (see also Burdick et al., 2008), it remains possible that simple motor/information processing slowing affect measures of lower-order capacities. For instance, several reports of inhibition defects measured with the stop-signal task are not based on commission errors with OCD patients (a direct measure of inhibitory control), but instead on the mean latency required by the participants to inhibit a response (e.g., Chamberlain et al., 2006; Menzies et al., 2007). Since this latency measure of the stop-signal is also elevated by a deficit in speed of information processing (e.g., Badcock, Michie, Johnson, & Combrinck, 2002), it is difficult to separate such a deficit from a true defect of
inhibitory control. Thus, future neuropsychological investigations in OCD should focus on (and consider separately) motor execution, speed of processing, and lower- and higher-order executive functions.

Secondary analyses performed in the present study also deserve further attention. First, although indexes of self-ordering capacities (derived from the CVLT-II) failed to discriminate the groups, the effect size for the serial clustering index (suggesting poor capacities) is noteworthy (0.42). Serial clustering is an ineffective learning strategy that correlates with poor performance on many of the CVLT-II parameters (Delis, Freeland, Kramer, & Kaplan, 1988). It often reflects a “stimulus-bound” style of recall in which the individual, by adhering rigidly to the temporal order of the list, fails to reorganize the words semantically. Further investigation of self-ordering capacities among persons with OCD should be encouraged. Second, the randomization index was significantly different between the groups, which might indicate an abnormal activation of the anterior cingulate in OCD (Artiges et al., 2000). Several authors theorized that an overactive action-monitoring system, associated with cingulate anomalies, lead to feelings of erroneous performance, doubts, and checking behaviors associated with OCD (de Geus et al., 2007; Gehring, Himle, & Nisenson, 2000). The present preliminary data (only 10 participants per group) with the randomization index task tentatively support the proposition of anterior cingulate cortex alteration. Using this paradigm with OCD persons in brain imaging protocols would help confirm this possibility.

Finally, it should be noted that a growing number of authors stress the importance of considering more homogeneous subgroups of OCD patients in neuropsychological assessments. For instance, it is increasingly realized that the presence of hoarding might be significant since it is associated with a poorer prognosis, lower global functioning, and more social deficits among persons with OCD (e.g., Hartl et al., 2004; Leckman and Bloch, 2008). In the present study, only two participants (5%) presented hoarding symptoms, which might explain the relatively good results.

Potential limitations of this study should be underlined. First, participants on and off medication were included because no differences were reported between medicated and unmedicated OCD participants in prior neuropsychological investigations with a wide range of tasks (Mataix-Cols, Alonso, Pifarre’, Menchón, & Vallejo, 2002; Purcell et al., 1998; Savage et al., 2000). Moreover, most OCD participants on medication were receiving an SSRI alone, which is not known to significantly impair attention, visuospatial skills, verbal and non-verbal memory, and executive functioning among persons with OCD (Mataix-Cols et al., 2002). However, in regard to the present results with motor skill deficits (see Burdick et al., 2008), recruitment of unmedicated participants is warranted to verify whether it is genuinely linked with OCD or not. Second, this study was not performed to specifically investigate lower- versus higher-order executive functions, so future assessments should focus on this dichotomy, as reports of set-shifting and inhibition deficits seem to be more consistent with OCD patients. Third, this study did not consider clinical aspects such as schizotypal personality features (e.g., Aycicegi et al., 2003; Harris & Dinn, 2003) and OCD symptom dimensions (e.g., Mataix-Cols, Rosario-Campos, & Leckman, 2005; Mataix-Cols et al., 2004) that could also influence the neuropsychological profile. These clinical aspects, especially the presence of hoarding (e.g., Leckman and Bloch, 2008), might be taken into account in future neuropsychological profiling of OCD patients. Finally, it should be noted that confirmations of diagnoses were not obtained with a research instrument as the structured clinical interview for the DSM (SCID).

In summary, few differences were found between performance of a relatively large clinical sample of OCD participants and that of healthy controls on a relatively high number of tasks. Future studies with OCD patients should consider psychomotor speed and assess at least three different cognitive domains using tasks sensitive to three distinct parts of the frontal cortex: (1) higher-order executive functions and the dorsolateral prefrontal cortex, (2) complex attention and the medial prefrontal cortex (including the anterior cingulate gyrus), and (3) lower-order executive functions (including behavioral inhibition) and the ventro-orbitofrontal cortex. From the present results, it could be hypothesized that common measures of executive function (higher-order), which depend more closely on frontal dorsolateral cortex functioning, are less affected by OCD than by co-morbid depressive and anxiety symptomatology. It seems that OCD patients present few reliable neuropsychological deficits specific to the illness and that psychomotor slowness could represent a core deficit, if not related to SSRI medication, with a possible basic attentional dysfunction. Divergent results from previous studies might be explained by the fact that OCD is a complex disorder with many symptoms and variants. Co-morbid conditions associated with the illness appear to play a different and independent role on the cognitive profile of a person with OCD and appear to be central in understanding this disorder.

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Conflict of Interest

None declared.
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Appendix

The Nine Cognitive Domains and their Components

1) Motor skills (n = 61) α = 0.91
   Purdue pegboard—preferred hand
   Purdue pegboard—other hand
   Purdue pegboard—both hands
   Trail making—condition 5, time
2) Speed of information processing (n = 57) α = 0.93
   Trail making—condition 1, time
   Trail making—condition 2, time
   Trail making—condition 3, time
   Stroop color-word interference—condition 1, time
   Stroop color-word interference—condition 2, time
   MWCT—structured arrays, time
   MWCT—unstructured arrays, time
3) Visuospatial analyses (n = 62) α = 0.70
   WAIS-III—block design
   RCFT—copy
4) Encoding and retrieval, verbal memory (n = 62) α = 0.91
   CVLT-II—correct recall on list A trial 1
   CVLT-II—total correct recall on list A trials 1–5
   CVLT-II—correct recall on list B
   CVLT-II—short-delay free-recall trial
   CVLT-II—percentage recall, trial 5 to short delay a
   CVLT-II—long-delay free-recall trial
5) Encoding and retrieval, visual memory (n = 62) α = 0.97
   RCFT—immediate recall
   RCFT—delayed recall
   RCFT—percentage recall, copy to immediate recall b
6) Inhibition/switching (n = 55) α = 0.86
   Verbal fluency—category switching, total switching accuracy
   Trail making—switching score c
   Color-word interference—inhibition score d
   Color-word interference—inhibition/switching score e
7) Working memory (n = 62) α = 0.70
   Brown–Peterson technique
   WMS-III—digit span (backward)
   WMS-III—spatial span (backward)
   WAIS-III—arithmetic
8) Reasoning, planning, and problem solving (n = 55) α = 0.85
   Twenty questions—initial abstraction score
   Twenty questions—total weighted achievement score
   Twenty questions—total questions asked
   TOL—total time scores
   TOL—total time violations
   TOL—total move score
   WAIS-III—arithmetic

(continued on next page)
Appendix Continued

9) Errors in executive tasks (n = 56) α = 0.72
   Color-word interference—total uncorrected errors, conditions 3 and 4
   Color-word interference—total corrected errors, conditions 3 and 4
   TOL—total rule violations
   Verbal fluency—number of repetition errors
   Twenty questions—number of repeated questions

Notes: α = Cronbach’s alpha; WAIS-III = Wechsler adult intelligence scale third edition; CVLT-II = California verbal learning test second edition; RCF-T = Rey–Osterrieth complex figure test; WMS-III = Wechsler memory scale third edition; MWCT = Mesulam and Weintraub cancellation test; D-KEFS = Delis–Kaplan executive function system; TOL = The Tower of London-Drexel University.

*Percentage recall, Trial 5 to short delay = short delay/Trial 5 × 100.
  *RCFT—percentage recall, copy to immediate recall = immediate recall/copy × 100.
  *D-KEFS—trail making, switching score = completion time for condition 4 – ([completion time for condition 2 + completion time for condition 3]/2).
  *D-KEFS—color-word interference, inhibition score = completion time for condition 3 – ([completion time for condition 1 + completion time for condition 2]/2).
  *D-KEFS—color-word interference, inhibition/switching score = completion time for condition 4 – ([completion time for condition 1 + completion time for condition 2]/2).

References


