



Response inhibition in a subclinical obsessive-compulsive sample



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ARTICLE INFO

Article history:

Received 17 April 2014

Received in revised form

1 September 2014

Accepted 2 September 2014

Available online 10 September 2014

Keywords:

OCD

Obsessive-compulsive disorder

Executive function

Analogue sample

Endophenotype

Neuropsychology

ABSTRACT

Background and objectives: Inconsistent findings across studies challenge the viability of response inhibition (RI) as an endophenotype of obsessive-compulsive disorder (OCD). Contemporary conceptualization of endophenotypes in psychiatric disorders suggests that these markers vary continuously in the general population, highlighting the importance of analogue sample research. Although neuropsychological functions have been studied in subclinical obsessive-compulsive (OC) samples, no study to date had examined RI in the context of the go/no-go paradigm.

Methods: A subclinical OC sample (HOC; $n = 27$) and a low OC symptoms control sample (LOC; $n = 25$), as determined by the Obsessive-Compulsive Inventory-Revised, completed a go/no-go task and clinical questionnaires.

Results: The groups did not differ on age, gender, or state anxiety. Controlling for depressive severity, the HOC group made significantly more commission errors and exhibited larger response time variability on the go/no-go task. However, standardized scores produced using population norms revealed that the HOC group performed within normative range.

Limitations: This study used a non-clinical sample and no structured clinical screening was performed. **Conclusions:** Compared to LOC participants, a psychometrically-defined subclinical OC sample exhibited deficient RI and sustained attention. However, when raw scores were converted to age and education adjusted standardized scores according to the test's population norms, the HOC group task performance was in the normative range. These results, are in line with findings in OCD samples, suggesting that moderate degree of RI deficiencies is associated with the presence of OC symptomatology regardless of clinical status. However, the conceptualization of RI underperformance as an OCD disorder-specific impairment, remains controversial.

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1. Introduction

Obsessive-compulsive disorder (OCD) is a prevalent (2.5%; Ruscio, Stein, Chiu, & Kessler, 2010), and frequently debilitating disorder, characterized by obsessions and/or compulsions that are performed in order to reduce distress (American Psychiatric Association, 2013). Functional imaging studies have claimed to be consistent in their support of the cortico-striato-thalamo-cortical (CSTC) neurobiological model of OCD (Saxena & Rauch, 2000),

highlighting aberrant frontostriatal functioning (for a review see Pauls, Abramovitch, Rauch, & Geller, 2014). In fact, whereas some changes to this model have been recently proposed (Milad & Rauch, 2012), this body of literature is considered by many to be amongst the most robust in psychiatric literature (Chamberlain, Blackwell, Fineberg, Robbins, & Sahakian, 2005). These models predict neuropsychological impairments in OCD, especially in the domain of executive functions, which the frontostriatal circuits are presumed to subserve. Indeed, research suggests that OCD may be associated with deficit in executive functions (Bannon, Gonsalvez, Croft, & Boyce, 2002; Chamberlain et al., 2005; Kuelz, Hohagen, & Voderholzer, 2004). However, in contrast to the consistent results seen across resting-state imaging studies, the large body of neuropsychological literature in OCD is characterized by inconsistent, and statistically heterogeneous results (Abramovitch, Abramowitz, & Mittelman, 2013; Kuelz et al., 2004).

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Several attempts to account for this inconsistency have been offered. Among them: 1) the use of different neuropsychological tests to examine similar constructs (Kuelz et al., 2004); 2) inconsistent application of corrections for multiple comparisons (Purcell, Maruff, Kyrios, & Pantelis, 1998); 3) the potential confounding effects of medication (Mataix-Cols, Alonso, Pifarre, Menchon, & Vallejo, 2002); 4) depressive severity (Basso, Bornstein, Carona, & Morton, 2001); 5) age of onset (Roth, Milovan, Baribeau, & O'Connor, 2005); 6) gender (Mataix-Cols et al., 2006); 7) comorbid conditions (Aycicegi, Dinn, Harris, & Erkmen, 2003); and 8) OCD symptom dimensions (Lawrence et al., 2006). However, no single factor, or combination of factors, was found to have a significant moderating effect that may account for this heterogeneity. In fact, in a recent meta-analysis examining neuropsychological performance in OCD, a comprehensive moderator analysis yielded no significant moderating effects of clinical or demographic factors, despite findings of statistically significant heterogeneity across neuropsychological domains (Abramovitch et al., 2013). The unexplained inconsistency among neuropsychological investigations in OCD hinders the identification of disorder-specific neurocognitive markers. These inconsistencies notwithstanding, the authors found that OCD is characterized by underperformance on several neuropsychological domains, including executive function, processing speed, and nonverbal memory. The overall magnitude of the differences found between OCD and control samples, however, was of moderate size, leading to the conclusion that individuals with OCD may underperform on neuropsychological tasks, but that these deficiencies may not fit the classic neuropsychological definition of clinically significant impairments in these domains (Abramovitch et al., 2013).

Response inhibition (RI), the ability to inhibit a pre-potent motor response, is a prominent executive function that is of particular interest to OCD researchers. Based on the phenotype of repetitive rituals and intrusive obsessions, it has been initially thought that OCD may be characterized by impairments in the ability to inhibit thoughts and behaviors (e.g., Penades et al., 2007). Consequently, RI has been proposed as a candidate endophenotypic marker of OCD (Chamberlain et al., 2005). This notion received support from a number of studies reporting deficient performance on tasks of RI, as well as from findings regarding familial RI deficits in OCD (Chamberlain et al., 2005). However, research into RI in OCD has produced contradictory results. Some studies reported reduced performance on tasks of RI in OCD (e.g., Abramovitch, Dar, Hermesh, & Schweiger, 2012; Martinot et al., 1990; Menzies et al., 2007; Penades et al., 2007), and yet others reported no performance differences between OCD patients to non-psychiatric controls (e.g., Bohne, Savage, Deckersbach, Keuthen, & Wilhelm, 2008; Boone et al., 1991; Krishna et al., 2011).

Several neuropsychological tasks have been used to examine RI in OCD. These include the Stop Signal Task, the Stroop test, continuous performance tests (CPT), and go/no-go tests. In the go/no-go paradigm, the index for RI is the number of commission errors (i.e., response to a no-go stimuli). Interestingly, across measures of response inhibition, Abramovitch et al. (2013) reported an overall medium effect size of .49 for RI, with a confidence interval of .61 to .04, and an overall Cohen's *d* effect size of .33 for differences between OCD and healthy controls on commission errors (Abramovitch et al., 2013). Notably, a recent meta-analysis of response inhibition across mental disorders found similar small-to-medium effect sizes across psychiatric disorders and concluded that response inhibition deficits are insufficiently sensitive or specific to be used as a biomarker in most mental disorders (Wright, Lipszyc, Dupuis, Thayaparakajah, & Schachar, 2014).

In light of the overall unexplained inconsistency, we sought to examine the association between response inhibition and OCD

phenomena using a go/no-go task, in a subclinical obsessive-compulsive (OC) sample (i.e., a samples of high and low OC symptoms). Previous research has indicated that examining OC phenomena in non-clinical samples is a viable means of investigation, that has been consistently contributing to our understanding of OCD (Burns, Formea, Keortge, & Sternberger, 1995; Gibbs, 1996). This notion received support from a recent comprehensive review of analogue sample research in OCD, suggesting that OCD symptoms are dimensional rather than categorical (i.e., they fall on a continuum from very mild to severe), and share similar qualitative characteristics across clinical and non-clinical populations (Abramowitz et al., 2014). Moreover, the use of analogue OCD samples may be particularly advantageous in examining cognitive functions, given the absence of potentially confounding factors such as medications or heterogeneous treatments (Mataix-Cols, 2003). Finally, as suggested by Cannon and Keller (2006), endophenotypes should vary continuously in the general population. The authors noted that, "Rather than binning all nonaffected individuals into a single category, continuous measures allow for the discernment of differences (i.e., scaling of liability) in the nonaffected population" (Cannon & Keller, 2006, p. 276). The authors further suggested that research into endophenotypes of psychiatric disorders should optimally include findings from different levels of analyses, and specifically, should comprise investigations of such markers in the general population (i.e., analogue samples).

A relatively limited body of research has been published on neuropsychological functioning in analogue OCD samples, especially those examining executive functions. In general, compared to individuals characterized by lower levels of OC symptom severity (LOC), individuals with higher levels of OC symptom severity (HOC) exhibit comparable performance on tasks of verbal and non-verbal memory (Kim, Jang, & Kim, 2009; Mataix-Cols, Junque, et al., 1999). However, consistent with neuropsychological studies of OCD, subclinical OC research concerning executive functions has yielded mixed results. Some studies found comparable performance between HOC and LOC on the Stroop test, Wisconsin Card Sorting test (WCST), verbal fluency test, and the Trail Making Test (i.e., TMT; Hajcak & Simons, 2002; Kim et al., 2009; Mataix-Cols, Barrios, Sanchez-Turet, Vallejo, & Junque, 1999; Mataix-Cols, Junque, et al., 1999). In contrast, relative to LOC samples, HOC samples were found to underperform on tasks assessing planning (Tower of Hanoi task), as well as on design fluency tasks, the Delayed Alternation tests, the WCST, and on the TMT (Kim et al., 2009; Mataix-Cols, Barrios, et al., 1999; Mataix-Cols, Junque, et al., 1999; Spitznagel & Suhr, 2002). To our knowledge, no study to date has utilized the go/no-go paradigm to directly assess response inhibition in a subclinical OC sample. One study (Mataix-Cols et al., 1997), however, utilized the Identical Pairs version of the Continuous Performance test (CPT-IP), and found a significant interaction effect between group and CPT-IP subscales (i.e., verbal and spatial), but no difference on commission errors between the groups.

To address this gap in the literature, the present study was designed to examine response inhibition among HOC and LOC college students, by comparing their performance on a go/no-go task while controlling for potential confounding factors. In order to aid in distinguishing between underperformance and impairment, we utilized the NeuroTrax computerized Expended Go/No-Go test. This test (described in more detail in Section 2.2.2) produces two scores automatically for every outcome measure: a raw score and a standard score, computed using the NeuroTrax normative data. These standard scores are similar to the ones produced by the Wechsler Intelligence Scale, in which standardized scaled scores have a mean of 100 and a standard deviation (SD) of 15. In accordance with these aims, and in light of the

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