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Neuropsychological investigations in obsessive–compulsive disorder: A systematic review of methodological challenges

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ABSTRACT

The inconsistent nature of the neuropsychology literature pertaining to obsessive–compulsive disorder (OCD) has long been recognized. However, individual studies, systematic reviews, and recent meta-analytic reviews were unsuccessful in establishing a consensus regarding a disorder-specific neuropsychological profile. In an attempt to identify methodological factors that may contribute to the inconsistency that is characteristic of this body of research, a systematic review of methodological factors in studies comparing OCD patients and non-psychiatric controls on neuropsychological tests was conducted. This review covered 115 studies that included nearly 3500 patients. Results revealed a range of methodological weaknesses. Some of these weaknesses have been previously noted in the broader neuropsychological literature, while some are more specific to psychiatric disorders, and to OCD. These methodological shortcomings have the potential to hinder the identification of a specific neuropsychological profile associated with OCD as well as to obscure the association between neurocognitive dysfunctions and contemporary neurobiological models. Rectifying these weaknesses may facilitate replicability, and promote our ability to extract cogent, meaningful, and more unified inferences regarding the neuropsychology of OCD. To that end, we present a set of methodological recommendations to facilitate future neuropsychology research in psychiatric disorders in general, and in OCD in particular.

1. Introduction

Obsessive–compulsive disorder (OCD) is a prevalent and often debilitating psychiatric disorder, affecting approximately 2.5% of the population worldwide (Okasha, 2003; Ruscio et al., 2010). The hallmark symptoms of OCD are obsessive thoughts or images that cause significant distress, and/or repetitive compulsive behavioral or mental rituals that the patient performs in order to alleviate distress or to avoid feared events (American Psychiatric Association, 2013). Since the early 1990s, a progressively large body of imaging research has revealed frontostriatal pathophysiology in OCD, with a pronounced hyperactivation in the orbitofrontal cortex, anterior cingulate cortex, and caudate nucleus (Chamberlain et al., 2008; Melloni et al., 2012). These findings received support from studies reporting abnormally increased resting state functional connectivity along the cortico-striato-thalamo-cortical (CSTC) circuits (Harrison et al., 2009; Fitzgerald et al., 2011). As a whole, a positive association between increased activation and OCD symptom severity has been identified at rest (Harrison et al., 2013), during symptom provocation (Breiter et al., 1996; Nakao et al., 2005), and post-treatment (e.g., Schwartz et al., 1996; Saxena et al., 2009). Aberrant brain activity has been further associated with task performance in OCD (e.g., Roth et al., 2007). However, results from these investigations are divergent, with some studies reporting reduced (van den Heuvel et al., 2005), and others increased (Maltby et al., 2005) activation during performance on neuropsychological tasks. Nevertheless, these findings have consistently supported the prevailing CSTC/frontostriatal model of OCD (Saxena and Rauch, 2000; Pauls et al., 2014).

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The growing interest in the neuronal substrates of OCD paralleled an interest in the neuropsychology of OCD, resulting in a large body of literature. However, compared to the robust and consistent nature of results seen in resting state imaging studies, neuropsychological research in OCD has yielded divergent results (Kuelz et al., 2004). The state of the field drove our group to conduct the first systematic meta-analytic review of the entire body of neuropsychological literature in adult OCD (Abramovitch et al., 2013). The result of this meta-analysis, spanning nearly a quarter century of research, revealed an average Cohen's *d* effect size of 0.5 across 10 neuropsychological subdomains. The Random effects model that was employed revealed statistically significant heterogeneity across most subdomains. A subsequent moderator analysis revealed no significant moderators. This has been supported by a second meta-analysis of 88 studies that found only two moderators associated with performance on specific outcome measures from particular tests (Shin et al., 2014). Thus, the persistent inconsistency and between studies heterogeneity remained unexplained and may have been, at least in part, affected by methodological factors.

As a part of the systematic review of the neuropsychological literature of OCD, we recorded methodological factors. Given the scope of the review, the aim of the present investigation is to inform researchers about methodological caveats in order to facilitate replicability and future meta-analytic investigations. For this purpose, we sought to examine methodological factors across three domains: (1) general (e.g., alpha correction for multiple comparisons); (2) clinical (e.g., assessing clinical correlates of neuropsychological test performance); and (3) neuropsychological (e.g., administration of neuropsychological tests that were not validated in non-English speaking populations). We aimed to explore a wide variety of factors ranging from omission of essential information pertaining to a study's methods (e.g., age of OCD onset) – which has a relatively low potential to adversely impact the field – to factors that pose a substantial risk to biasing results (e.g., not performing multiplicity corrections). Notably, some of these factors were addressed in a critical review published a decade ago (Kuelz et al., 2004). However, the number of peer-reviewed papers assessing neuropsychological correlates of OCD has more than doubled in the last decade, justifying a systematic methodological review of the literature.

Some of the aforementioned factors hold specific importance in OCD research, and are grounded in evidence supporting their potential impact on neuropsychological test performance in this population. Other factors are not disorder-specific. Thus, this review may be relevant to researchers conducting neuropsychological investigations of psychiatric disorders in general. Nevertheless, given that these factors were systematically recorded from the body of neuropsychological literature in OCD, this comprehensive review depicts the state of the field of neuropsychological research in OCD in terms of methodological challenges. For each section pertaining to a particular challenge, we provide specific recommendations that may be useful for researchers, reviewers, and editors in this field.

2. Methods

2.1. Systematic literature search and selection criteria

A systematic literature search was conducted via MEDLINE, ISI Web of Knowledge, and PsycINFO databases, as well as by searching publication reference lists and soliciting unpublished data from investigators of the neuropsychology of OCD. Due to the small body of neuropsychological research in pediatric OCD (for a review and meta analysis see Abramovitch et al., 2012b; Abramovitch et al., In-press), this review focuses on adult studies. A total of 207 published research articles were identified through February 2012. Once identified, all studies were evaluated against several inclusion criteria. Studies were included if they: (a) included an adult sample of DSM-diagnosed OCD patients using a structured or semi-structured interview; (b) screened for the presence of psychiatric or neurological conditions; and (c) compared OCD group performance to that of a healthy control group on at least one known and validated standardized neuropsychological test. When a before/after design was employed, studies were included only when a pre-treatment comparison between an OCD and a healthy control group was available. Of the initial 207 studies, 177 studies met these criteria. Of those, 42 studies were excluded due to the use of either highly specific or non-standard neuropsychological tests (e.g., emotional Stroop), the use of tests that were significantly modified from the original version, or the use of tests that are very rarely used (i.e., used in $<1\%$ of studies). Seven excluded studies were duplicates (i.e., they contained information that appeared in studies already included in the meta-analysis). Finally, 13 studies were excluded because they did not provide sufficient information to calculate or estimate effect size. This screening process resulted in a final count of 115 studies published between 1989 and 2012. In terms of geography, the largest number of studies (23) was conducted in the United States, followed by Germany (18), South Korea (13), Spain (8), and the United Kingdom (8).

2.2. Variables recorded

A meta-analytic investigation of differences between OCD and non-psychiatric control samples on neuropsychological tests has been published elsewhere (Abramovitch et al., 2013). The present systematic review focuses on methodological issues. Accordingly, the following general information was recorded from each of the 115 studies: (a) year of publication, (b) publication status, (c) country, (d) number of neuropsychological tests, and (e) percent males in the OCD group. In addition, the following methodological information was recorded: (a) length of testing session, (b) number of sessions (for studies administering 4 or more tests[1]), (c) sample recruitment source for the OCD and control groups, (d) age of onset, and (e) education level. We also noted whether the study: (a) statistically corrected for multiple comparisons (for studies administering 4 or more tests; type of correction was noted); (b) used tests validated in the study's language; (c) controlled for depressive severity; and (d) examined the association between test performance, OCD severity, and depressive severity. The rationale underlying the selection of these factors stemmed from direct evidence reported in the OCD literature wherein these factors had been shown to have an impact on neuropsychological performance in OCD, or on statistical results and their interpretation (e.g., correction for multiple comparison).

3. Results

Fig. 1 depicts the number of studies published by year, demonstrating a steady increase in the number of studies published each year (range 1–17). Descriptive statistics of the methodological factors reviewed are presented in Table 1. With regards to sample characteristics, nearly one in every 10 studies did not report how recruitment for the OCD group was established, and 30% of studies for healthy control samples. Perhaps more importantly, only three quarters of studies reported the education level of their participants—a factor with a known impact on neuropsychological test performance. With regards to statistical corrections, among the studies administering 4 or more neuropsychological tests, only 18% employed some form of alpha correction for multiple comparisons.

In terms of methodological factors pertaining more specifically to neuropsychology research, only 62% of studies reported the number of testing sessions and only 24% reported the average length of the testing sessions. Notably, of the studies employing at least one neuropsychological test requiring understanding of written or spoken English, more than half of those conducted in non-English speaking countries did not report the use of tests validated in the respective country's native language.

Factors that may be more OCD-specific are also presented in Table 1. Among the most prominent findings were that only 54% of

[1] The choice of four tests as a cutoff number for which multiplicity corrections are required is somewhat arbitrary, given that there are no available guidelines or rule of thumb, and since in theory even two tests require adjustment of alpha. In an effort to be more conservative, we chose four. Notably, in most cases each test produces multiple outcome measures and thus 4 tests represent at least 4 comparisons.