The World Journal of Biological Psychiatry

ISSN: 1562-2975 (Print) 1814-1412 (Online) Journal homepage: http://www.tandfonline.com/loi/iwbp20

Neurocognitive function in paediatric obsessive-compulsive disorder

Daniel A. Geller, Amitai Abramovitch, Andrew Mittelman, Abigail Stark, Kesley Ramsey, Allison Cooperman, Lee Baer & S. Evelyn Stewart

To cite this article: Daniel A. Geller, Amitai Abramovitch, Andrew Mittelman, Abigail Stark, Kesley Ramsey, Allison Cooperman, Lee Baer & S. Evelyn Stewart (2018) Neurocognitive function in paediatric obsessive-compulsive disorder, The World Journal of Biological Psychiatry, 19:2, 142-151, DOI: 10.1080/15622975.2017.1282173

To link to this article: https://doi.org/10.1080/15622975.2017.1282173

THE WORLD JOURNAL OF BIOLOGICAL PSYCHIATRY, 2018
VOL. 19, NO. 2, 142–151
http://dx.doi.org/10.1080/15622975.2017.1282173

ORIGINAL INVESTIGATION

Neurocognitive function in paediatric obsessive-compulsive disorder

Daniel A. Geller[a], Amitai Abramovitch[a,b], Andrew Mittelman[a], Abigail Stark[a], Kesley Ramsey[a], Allison Cooperman[a], Lee Baer[a] and S. Evelyn Stewart[c]

[a]Department of Psychiatry Massachusetts General Hospital & Harvard Medical School, Boston, MA, USA; [b]Department of Psychology, Texas State University, San Marcos, TX, USA; [c]Department of Psychiatry, University of British Columbia, BC Children's Hospital, Vancouver, BC, Canada

ABSTRACT

Objectives: The small body of neuropsychological research in paediatric obsessive-compulsive disorder (OCD) yields inconsistent results. A recent meta-analysis found small effect sizes, concluding that paediatric OCD may not be associated with cognitive impairments, stressing the need for more research. We investigated neuropsychological performance in a large sample of youths with OCD, while assessing potential moderators.

Methods: Participants with OCD ($n = 102$) and matched controls ($n = 161$) were thoroughly screened and blindly evaluated for comorbidities, and completed a neuropsychological battery assessing processing speed, visuospatial abilities (VSA), working memory (WM), non-verbal memory (NVM), and executive functions (EF).

Results: Compared to controls, youths with OCD exhibited underperformance on tasks assessing processing speed. On tests of VSA and WM, underperformance was found only on timed tasks. There were no differences on NVM and EF tasks. Notably, the OCD group's standardised scores were in the normative range. Test performance was not associated with demographic or clinical variables.

Conclusions: Youths with OCD exhibited intact performance on memory and EF tests, but slower processing speed, and underperformance only on timed VSA and WM tasks. While the OCD group performed in the normative range, these findings reveal relative weaknesses that may be overlooked. Such an oversight may be of particular importance in clinical and school settings.

ARTICLE HISTORY
Received 23 August 2016
Revised 5 December 2016
Accepted 2 January 2017

KEYWORDS
Neuropsychological tests; executive functions; processing speed; comorbidity; children

Introduction

Obsessive-compulsive disorder (OCD) is a burdensome disorder with a worldwide prevalence rate of 1–3% (Ruscio et al. 2010). Research suggests that the onset of OCD has a bimodal distribution pattern (Geller 2006), with the first peak in pre-adolescents and a second in early adulthood. Indeed, clinically significant OCD can be traced to childhood in nearly half of adult OCD patients. A large body of imaging research reveals neurobiological abnormalities in OCD (Melloni et al. 2012), generally depicting resting-state frontostriatal hyperactivation. However, in contrast to the relative consistency observed in results from imaging studies (Chamberlain et al. 2005), neuropsychological findings are notoriously inconsistent (Abramovitch & Cooperman 2015). Indeed, in a comprehensive meta-analysis of 115 studies examining neuropsychological functioning in adult OCD patients, Abramovitch et al. (2013) found a significant heterogeneity across studies that was not accounted for by any potential moderator. In terms of effect sizes, meta-analyses of neuropsychological test performance in adults with OCD found small-to-moderate effect sizes, particularly in the domains of processing speed, non-verbal memory (NVM) and executive functions (EF) (Abramovitch et al. 2013; Shin et al. 2014; Snyder et al. 2015).

Despite the extensive research conducted in adults with OCD, far fewer investigations have examined neuropsychological test performance in paediatric OCD samples. This small corpus of research reveals even greater inconsistency than seen in the results of adult OCD research. In one of the first studies investigating neuropsychological test performance in paediatric OCD, Behar et al. (1984) compared 16 adolescents diagnosed with OCD with 16 matched non-psychiatric controls. The authors found a higher number of errors on planning tasks (i.e., Money's Road Map Test and

CONTACT Amitai Abramovitch abramovitch@txstate.edu Department of Psychology, Texas State University, San Marcos, Texas 78666, USA
Supplemental data for this article can be accessed at http://dx.doi.org/10.1080/15622975.2017.1282173.

the Stylus Maze Learning Test), but no difference on tests of verbal memory, processing speed or on the Copy and Memory sections of the Rey-Osterrieth Complex Figure test (RCFT), assessing visuospatial functions and NVM, respectively. In a later study, Beers et al. (1999) administered a comprehensive neuropsychological test battery and found no difference between the 21 paediatric OCD patients and 21 matched controls. In fact, OCD patients in this study outperformed controls on tests of verbal fluency and the Stroop word and colour trials. In a more recent study, Andres et al. (2007) administered a large battery of neuropsychological tests to 35 children and adolescents with OCD and matched controls. Children with OCD demonstrated poorer performance on tests of verbal and NVM, as well as on tests of executive function (i.e. the Stroop test and the Wisconsin Card Sorting Test – WCST). Other studies reported reduced performance on tests of EF in paediatric OCD patients compared to controls, but not on the RCFT or tests of attention (Shin et al. 2008). Similarly, Ornstein et al. (2010) reported deficient performance among paediatric OCD participants on tests of planning and cognitive flexibility, but not on tasks of response inhibition and memory. In order to systematically examine this small body of literature, Abramovitch et al. (2015) conducted a meta-analysis of 11 neuropsychological studies in paediatric OCD. The authors reported effect sizes ranging between 0.04 and 0.40 with an overall weighted small effect size of 0.27, and interpreted these small effect sizes as suggesting that paediatric OCD may not be associated with major impairments in cognitive abilities. Of note, similar to the vast majority of adult neuropsychological studies, reports regarding an association between neuropsychological functioning and symptom severity in paediatric OCD are scarce (Abramovitch et al. 2012). In fact, little is known about clinical moderators of cognitive function in paediatric OCD, presumably due to the small sample sizes ranging between $n = 14$ and 35 (Abramovitch et al. 2015).

A number of problems arise from the small sample sizes characteristic of this body of literature that may not only reduce power and limit generalizability, but also limit examination of confounds, mediators and moderators. Secondly, these studies used a large number of partially intercorrelated outcome measures, which demands correction for multiple comparisons. A number of studies that did not employ an alpha correction for multiple comparison could produce an inflated Type I error that may, in part, account for this inconsistency. Clinical factors such as medication status and age of onset may have also confounded these studies results (Andres et al. 2007; Ornstein et al. 2010). Notably, meta-analytic reviews found that these factors do not moderate neuropsychological test performance in adult OCD samples (Abramovitch et al. 2013; Shin et al. 2014). In addition, it has been hypothesised that alterations in neuromaturation processes in preadolescent youths with OCD is reflected in a different pathophysiology (Fitzgerald et al. 2011) in pre- and post-adolescent OCD, with differing neuropsychological profiles. Finally, the majority of youths with OCD are diagnosed with at least one additional DSM comorbid condition (Boileau 2011), and several prevalent comorbid conditions in OCD may be independently associated with neuropsychological deficits (e.g. attention deficit/hyperactivity disorder (ADHD), chronic tic disorder, depression), which may potentially confound findings of altered neuropsychological test performance. However, several studies investigating neuropsychological functioning in paediatric OCD either excluded patients with secondary comorbid psychiatric conditions (e.g. Andres et al. 2007) or included a sample size that did not permit comprehensive analysis of the impact of comorbid conditions on neuropsychological functioning. To our knowledge, no study to date has performed a comprehensive examination of the impact of different comorbid conditions on neuropsychological performance in paediatric OCD.

In light of the paucity of studies, their inconsistent results, and small sample sizes, the primary aim of the present study was to examine neuropsychological functioning across major domains of interest in a large sample of youths with OCD. The secondary aim was to examine several potential moderating factors (i.e., OCD severity, age of onset, medication status, depression and current age), including an examination of the potential moderating effect of comorbid diagnoses. Based on clinical experience and limited evidence from the extant and inconsistent literature, we hypothesised that the OCD group would underperform the control group on several outcome measures, particularly measures of processing speed, EF (other than inhibitory control) and visuospatial functions.

Method

Participants

The OCD group ($n = 102$; see Table 1 for demographic information) was recruited as part of a large family study (NIMH K08MH01481, PI DG) via referral to the Paediatric OCD Programme at Massachusetts General Hospital in Boston. Fifteen percent of patients were ascertained directly through advertising and direct clinician referrals to the research study and 85% were

Table 1. Demographic and clinical characteristics of the OCD and control groups.

Measure	OCD ($N = 102$)	Controls ($N = 161$)	$F(1,261)/\chi^2(1)$	P value
Age M (SD)	11.39 (3.05)	11.61 (3.03)	0.34	0.56
Gender N (% Males)	57 (55.9%)	92 (57.0%)	<0.01	0.98
Estimated IQ M (SD)[a]	110.07 (14.34)	112.18 (13.76)	1.41	0.26
CY-BOCS total score M (SD)	20.88 (5.04)	–	–	–
CY-BOCS obsessions M (SD)	10.91 (2.71)	–	–	–
CY-BOCS compulsions M (SD)	9.88 (2.66)	–	–	–

[a]Estimated IQ (based on WISC Vocabulary test score).
CY-BOCS: Children's Yale-Brown Obsessive Compulsive Scale.

patients referred to the OCD clinic. Inclusion criteria were age between 6 and 17 years, a primary diagnosis of OCD and basic proficiency in English. We excluded potential participants if they had a major sensorimotor handicap (deafness, blindness), an eating disorder, psychosis, autism, pervasive developmental disorder or full scale IQ less than 80. The control group ($n = 161$) was derived from a sample of identically designed contemporaneous case–control family studies of male and female youths with and without ADHD ascertained from psychiatric and paediatric settings. Detailed study methodology is reported elsewhere (Rosenbaum et al. 2000; Biederman et al. 2002). Briefly, these studies ascertained families on the basis of a case (ADHD) or control (non-ADHD) children aged 6–17 years at time of ascertainment and included 242 control cases with their 737 first-degree biological relatives, respectively. The same pool of trained raters interviewed them with a similar assessment battery thus avoiding a cohort effect. For this comparison a random sample of biological siblings of the *non-ADHD* control cases were selected as matched to the OCD baseline sample on age and gender. For the present study, we excluded control participants with a lifetime or current diagnosis of OCD. Other disorders were not excluded to provide a 'normal' control sample representative of community rates of disorders rather than a 'super-normal control' group with all disorders screened out that may yield results that are not generalisable due to poor ecological validity. Rates of *lifetime* DSM diagnosis in the control sample were as follows: major depressive disorder (MDD, $n = 7$, 4.3%), bipolar disorder I ($n = 1$, 0.6%), bipolar disorder II ($n = 1$, 0.6%), dysthymia ($n = 3$, 1.8%), panic disorder ($n = 2$, 1.2%), agoraphobia ($n = 6$, 3.7%), simple phobia ($n = 13$, 8%), social phobia ($n = 7$, 4.3%), anorexia nervosa ($n = 1$, 0.6%), ADHD ($n = 26$, 16%) and conduct disorder ($n = 5$, 3.1%).

Clinical and diagnostic measures

Psychiatric assessments were made using the Kiddie SADS-E (Epidemiologic Version; Orvaschel & Puig-Antich 1987) and were based on blind independent interviews with the patients' mothers and direct interviews with the patients. Identically trained raters who were blind to the clinical status of the subjects evaluated participants of both groups. A diagnostic review team blindly weighed each source of information from direct and indirect Kiddie SADS-E to yield diagnoses using a Best Estimate method described by Leckman et al. (1982) as well as clinical judgment based on the information provided in each report. Diagnoses were considered definite only if DSM-IV criteria (APA 2000) were met to a degree that would be considered clinically meaningful. Discrepancies between parents and children were resolved using both reports and a consensus algorithm that included the more severe rating from either source. Next, an experienced child psychiatrist (DAG) clinically interviewed children and adolescents of all ages, administered the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS; Scahill et al. 1997) and the Yale Global Tic Severity Scale (Leckman et al. 1989) where indicated, and resolved any discrepancies in parent and child reports in favour of the informant deemed most reliable. Thus, final Best Estimate diagnoses used data from all sources.

Age at onset was determined by the age at which symptoms were estimated to be clinically impairing. This was defined by overall daily symptom presentation greater than 1 h (indicated by a CY-BOCS score $\geq$2, items 1 & 6), subjective distress greater than mild (indicated by a CY-BOCS score $\geq$2, items 3 & 8) and functional impairment of at least moderate degree ($\geq$2 on CY-BOCS, items 2 & 7).

Neurocognitive measures

To increase validity and facilitate replicability, a battery of gold standard neuropsychological tests was selected. The tests have been validated in numerous languages and are commonly used in paediatric and adult OCD studies facilitating comparison with previous investigations. The neuropsychological domains and tests were the following.

Intellectual ability. To control for intelligence we administered the Wechsler Intelligence Scale for Children – 3rd edition, vocabulary subtest (WISC-III;

Wechsler 1991), a reliable estimate of general intellectual potential (Lezak et al. 2012).

Processing Speed. The WISC-III subtests comprising the processing speed index (i.e., Digit Symbol Coding and Symbol Search) were used to assess processing speed.

Visuospatial Abilities (VSA). To assess VSA we used the Rey-Osterrieth Complex Figure Test (RCFT; Osterrieth 1944) Copy accuracy score, and the WISC-III Block Design subtest scaled score.

Working memory (WM). The WISC-III Arithmetic and Digit Span scaled scores were selected for the assessment of WM.

Non-verbal Memory. For the assessment of NVM, the RCFT Delayed accuracy score was used.

Executive functions. The Stroop test (Stroop 1935) was used to assess response inhibition/interference control. We used the Golden (1978) administration and scoring procedures where *t* scores were calculated for each of the three Stroop trials (i.e., Colour, Word and Colour-Word) as well as for the interference index. Cognitive flexibility/set shifting were assessed using the computerised version of the WCST (Harris 1990). Finally, the RCFT Copy and Delayed organisation scores were computed using the Developmental Scoring System for the RCFT (DSS-ROCF; Bernstein & Waber 1996).

Procedure

For all participants, a parent/legal guardian signed an informed consent. As this study was part of a larger family study, each family received monetary reimbursement. The present study was approved by the Massachusetts General Hospital Institutional Review Board, in accordance with the Declaration of Helsinki. All clinical and neuropsychological measures were administered in a uniform fashion for all participants according to standard published guidelines. Raters completed training pertaining to neuropsychological administration and scoring by an experienced neuropsychologist (PhD level) and clinical ratings by an experienced child psychiatrist (DAG). In addition, quality control measures were taken to assure accurate administration, scoring and data integrity as follows. Bachelor's level test administrators observed PhD-level examiners administering a neuropsychological test battery, then administered tests under direct supervision until assessment competence and testing scores matched PhD-level supervisors' scores a minimum number of times, before being permitted to administer tests independently. All neuropsychological tests were administered in a single 2–3-h session.

All data were entered independently by two research assistants and then checked for congruence errors before analyses.

Data analysis

In order to examine differences in neuropsychological test performance between the control and OCD groups, univariate analyses of variance (ANOVA) were used. In addition, ANOVAs were used in the examination of the potential confounding impact of medication and comorbidity. Age, estimated IQ and gender were used as covariates (ANCOVA) when differences on these variables were detected. Pearson correlations were computed to assess the impact of continuous variables on neuropsychological performance. Group differences on nominal variables were analysed using Pearson's χ^2-test. In order to correct for multiple comparisons, a conservative *P* value of 0.01 was used. We chose this common method (instead of methods such as Bonferroni correction) because some tests/domains had only one outcome measure, yet others had numerous variables analysed. Using the conservative *P* value of 0.01 value across all analyses provided an equal probability threshold for multiplicity correction.

Results

No significant differences were found between the groups on age, gender and estimated IQ (Table 1). The average CY-BOCS scores (M = 20.9, Table 1) reflect a moderate degree of OCD symptom severity.

Neuropsychological test performance

Results of individual comparisons on test performance are presented in Table 2. Compared to controls, the OCD group scored significantly lower on tests assessing processing speed, namely, the Digit Symbol Coding test ($F(1,261) = 34.83$, $P < 0.001$, Cohen's $d = 0.72$), and the Symbol Search test ($F(1,166) = 9.65$, $P = 0.002$, $d = 0.50$). For visuospatial ability, the OCD group scored significantly lower on the Block Design test ($F(1,261) = 50.75$, $P < 0.001$, $d = 0.91$) but not on the RCFT Copy trial ($F(1,159) = 1.11$, $P = 0.29$, $d = 0.16$). In the domain of working memory (WM), the OCD group performed significantly worse than the control group on the Arithmetic test ($F(1,261) = 13.90$, $P < 0.001$, $d = 0.46$), but there was no significant difference on the Digit Span test ($F(1,261) = 0.59$, $P = 0.44$, $d = 0.10$). Within the domain of EF, no significant differences were found on all Stroop and WCST outcome measures (all *P* values >0.05, *d* range 0.01–0.26).

Table 2. Group comparison on neuropsychological measures.

	OCD M (SD)	Controls M (SD)	OCD *N*	Controls *N*	*F*(df)	*P* value	Cohen's *d*
Processing speed							
Coding scaled score	9.25 (3.75)	11.66 (2.87)	102	161	34.83 (1, 261)	**<0.001**	**0.72**
Symbol Search scaled score	10.23 (3.40)	11.80 (2.90)	102	66	9.65 (1, 166)	**0.001**	**0.50**
Visuospatial abilities							
RCFT copy accuracy	61.55 (4.28)	62.52 (7.36)	94	67	1.11 (1, 159)	0.29	0.16
Block Design scaled score	10.76 (3.21)	13.70 (3.27)	102	161	50.75 (1, 261)	**<0.001**	**0.91**
Working memory							
Digit Span scaled score	10.68 (3.03)	10.39 (3.00)	102	161	0.59 (1, 261)	0.44	0.10
Arithmetic scaled score	11.15 (3.36)	12.58 (2.83)	102	161	13.90 (1, 261)	**<0.001**	**0.46**
Non-verbal memory							
RCFT delay accuracy	43.09 (10.64)	46.94 (12.11)	93	68	4.58 (1, 159)	0.03	0.34
Executive functions							
Stroop Word (*t* score)	46.91 (7.11)	46.98 (7.10)	99	78	.01 (1, 175)	0.94	0.01
Stroop Colour (*t* score)	43.70 (8.25)	42.23 (7.62)	99	78	1.47 (1, 175)	0.23	0.19
Stroop Colour-Word (*t* score)	45.20 (8.51)	45.87 (9.61)	99	77	.24 (1, 174)	0.63	0.07
Stroop Interference (*t* score)	48.78 (6.36)	50.51 (7.27)	99	77	2.82 (1, 174)	0.09	0.25
WCST Categories completed	4.88 (1.69)	5.00 (1.56)	64	62	.19 (1, 124)	0.67	0.07
WCST Percent perseverative errors	14.44 (9.75)	14.00 (6.71)	63	62	.09 (1, 123)	0.77	0.05
WCST Trials to complete 1st category	24.19 (27.48)	18.66 (20.60)	64	62	1.62 (1, 124)	0.20	0.23
WCST Failure to maintain set	.98 (1.15)	1.29 (1.27)	64	62	2.01 (1, 124)	0.16	0.26
RCFT Copy organisation score	8.27 (3.47)	8.93 (3.79)	95	68	1.30 (1, 161)	0.26	0.18
RCFT Delayed organisation score	6.57 (3.76)	8.04 (3.92)	94	68	5.81 (1, 160)	0.02	0.38

OCD: obsessive-compulsive disorder; RCFT: Rey complex figure test; WCST: Wisconsin Card Sorting Test.

No significant difference was found on the RCFT Copy Organisational Score ($F(1,161) = 1.30$, $P = 0.26$, $d = 0.18$). In contrast, the OCD group scored lower on the RCFT Delayed Organisational Score ($F(1,160) = 5.81$, $P = 0.02$, $d = 0.18$). However, given the conservative significance threshold determined for the present study ($P < 0.01$), the results of this analysis did not cross significance threshold. Similarly, the OCD sample scored lower on the RCFT Delayed Recall phase ($F(1,159) = 4.59$, $P = 0.03$, $d = 0.34$), but this difference was deemed insignificant.

Analysis of potential moderators

Symptom severity

Pearson's correlation analyses were conducted between the CY-BOCS total score and neuropsychological outcome measures. A significant negative correlation was found between the CY-BOCS total score and the Arithmetic scaled score ($r = -0.27$, $P = 0.006$). The direction of this correlation implies that greater OCD severity is associated with worse test performance. No significant correlations were found between the CY-BOCS total score and any of the other neuropsychological outcome measures.

Comorbid conditions The prevalence of comorbid conditions is presented in Table 3. In order to assess the potential impact of comorbid disorders on neuropsychological test performance (for tests where a significant difference was found between the groups), we examined the impact of (1) the presence of a comorbid condition, (2) functional impairment severity of the comorbid diagnosis using the K-SADS (i.e., mild, moderate and severe) and (3) the number of comorbid conditions. In order to allow sufficient statistical power, these factors were analysed only for comorbid conditions that were identified in at least 20% of patients (i.e., major depressive disorder (MDD), simple phobia, generalised anxiety disorder, ADHD, tic disorders and Tourette's syndrome and oppositional defiant disorder, see Table 3). For the purpose of this analysis we combined the Tourette's syndrome and chronic tic disorder conditions into one group (henceforth termed TS). For all analyses, we first examined differences in gender, age and estimated IQ. In cases where the groups (e.g. OCD + MDD vs OCD-MDD) differed on

Table 3. Prevalence of lifetime comorbid disorders among 102 youths with OCD.

Disorder	*N*	%
MDD lifetime	46	45.1
MDD current	20	19.6
Bipolar disorder I	6	5.9
Bipolar disorder II	10	9.8
Dysthymia	9	8.8
Conduct disorder	0	0
Panic disorder	12	11.8
Social phobia	15	14.7
Simple phobia	27	26.5
GAD	44	43.1
Anorexia	0	0
PTSD	2	2.0
ADHD	42	41.2
TS/CTD	30	31.4
PDD	4	3.9
ODD	46	45.1

MDD: major depressive disorder; GAD: generalised anxiety disorder; PTSD: post-traumatic stress disorder; ADHD: attention deficit/hyperactivity disorder; TS: Tourette's syndrome; CTD: chronic tic disorder; PDD: pervasive developmental disorder; ODD: oppositional defiant disorder.

these factors, an ANCOVA was conducted, controlling for the relevant factors.

No significant differences were found between the OCD subgroups with versus without these comorbid disorders on all outcome measures (see Supplementary Materials available online for effect sizes of these comparisons). Similarly, comparisons between degrees of severity of functional impairment between sub-samples diagnosed with these comorbid conditions yielded no significant difference on any of the neuropsychological outcomes measures. To examine the impact of the number of comorbid conditions, Pearson's correlation analyses were conducted with neuropsychological outcome measures. These analyses yielded no significant associations between the number of comorbid conditions and any of the neuropsychological outcome measures. In light of a significant correlation we found between the number of comorbid conditions and the total CY-BOCS score ($r = 0.29$, $P = 0.003$), we conducted a subsequent Pearson's partial correlation analysis, controlling for OCD severity. The result of this analysis revealed similar null findings.

Medication status

Sixty percent of the OCD sample was receiving medication at time of testing. To assess the impact of medication status on neuropsychological functioning, we compared medicated and unmedicated participants with OCD on neuropsychological outcome measures where differences between the groups were identified. The medicated OCD group ($n = 61$, $M = 11.84$, $SD = 2.88$) was found to be older than the unmedicated OCD group ($n = 41$, $M = 10.59$, $SD = 3.2$), $F(1,100) = 4.222$, $P = 0.04$). In addition, the unmedicated group had a higher prevalence of males (75%) than the medicated group (50%; $\chi^2(1) = 6.321$, $P = 0.012$). Subsequent ANCOVAs (controlling for gender and age) yielded no significant differences between medicated and unmedicated OCD patients on all relevant neuropsychological outcome measures (all P values < 0.05).

Age of onset

Age of OCD onset was found to be significantly correlated only with the organisation score on the RCFT copy trial ($r = 0.27$, $P = 0.016$), suggesting that later onset is associated with a better organisational score. However given our correction for multiplicity (significance threshold of $P = 0.01$), this association did not reach statistical significance. Finally, research suggests that preadolescence and adolescent OCD may differ in terms of pathophysiology (Rosenberg & Keshavan 1998; Fitzgerald et al. 2011). In order to examine whether these age groups differ in terms of neuropsychological functioning, we conducted a ANCOVAs comparing neuropsychological outcome measures between patients older ($n = 66$) or younger ($n = 76$) than 12 years of age while controlling for age. This analysis yielded no significant difference between the groups.

Discussion

In light of inconsistent reports regarding neuropsychological functioning in paediatric OCD the present study aimed to compare a large, well-characterised sample of paediatric OCD patients with matched controls. A second aim of the study was to examine the potential confounding impact of comorbid conditions, and clinical and demographic correlates on neuropsychological functioning.

Our results suggest that youths with OCD demonstrate reduced neuropsychological test performance on tests measuring processing speed as well as on tasks of VSA and WM. While youths with OCD underperformed compared to the control group on the Block Design subtest assessing VSA, they did not underperform on a test of VSA in which time does not count toward scoring (i.e., RCFT copy). Thus, given that the Block Design test also assesses motor ability, and more importantly is a timed test, their slower processing speed may have contributed to reduced performance. Similarly, in the WM domain, youths with OCD underperformed compared to the control group on the Arithmetic subtest, but did not differ on the Digit Span subtest. Whereas the latter is an untimed test, the former is a timed test that requires manipulating information in WM. Therefore, this may also point to reduced performance associated with processing speed in youths with OCD when compared to controls. These results imply that processing speed may be a central point of weakness in youths with OCD that underlies underperformance on tests assessing other domains. This notion has been suggested by others (Burdick et al. 2008; Bedard et al. 2009), arguing that processing speed deficits may underlie underperformance in tests of executive function in adult OCD, but to our knowledge this is the first study to demonstrate this effect in youth with OCD. Notably, we did not find performance differences in the domain of NVM and EF between youth with OCD and controls.

Our results are in accord with previous investigations that found reduced processing speed in youths with OCD compared to controls, but no difference (or

a very small effect size) on tests of EF (Andres et al. 2007; Ornstein et al. 2010). For example Chang et al. (2007) found comparable performance on the RCFT copy and executive function tests, but reduced performance on the Digit Symbol Coding tests in youths with OCD compared to controls. Additionally, Shin et al. (2008) administered an extensive neuropsychological test battery and similar to our results, reported reduced performance in a group of 17 paediatric OCD patients on the WISC Arithmetic and Block Design but no differences on response inhibition indices (auditory and visual CPT), set shifting (Trail Making B), non-verbal memory (RCFT) and the RCFT organisational scores.

It is important to note that on the four subtests where the OCD group performed lower than controls, the WISC scaled scores were within the average range (WISC scaled scores for the OCD sample ranging from 9.25 to 11.15). Although effect sizes ranged from medium to large (Cohen's *d* ranging from 0.46 to 0.91), our patient sample performed in the normal range. These results, observed in other neuropsychological investigations of paediatric OCD (Chang et al. 2007; Taner et al. 2011), suggest that this population may underperform compared to controls, but attribution of the term 'impairments' may be unsuitable. Nevertheless, given that relatively high estimated IQ of the OCD sample (110.1; 2/3 standard deviation above population mean), these factors may indicate a within-group relative weakness in this population. This has important implications, especially in school settings. Given that youths with OCD may exhibit relative reduced processing speed, these children may not be able to fulfil their intellectual potential. More importantly, standard school or clinical assessments, where results are compared to norms, may fail to identify this weakness.

An examination of potential confounding factors (i.e. age of onset, OCD severity, depression severity, age, medication, individual comorbid diagnosis and the number of comorbid diagnosis) yielded no significant impact on neuropsychological test performance. The lack of association between neuropsychological functions and symptom severity has been reported in the majority of paediatric OCD (Behar et al. 1984; Beers et al. 1999; Andres et al. 2007; Shin et al. 2008) as well as adult OCD investigations (Kuelz et al. 2004; Abramovitch et al. 2013). However, whereas a recent study examining neuropsychological performance on tests of EF and memory in a large sample of youth with OCD found no association with symptom severity (Lewin et al. 2014), analysis of symptom dimensions in this sample suggested some specific associations between test performance and symptom dimensions (McGuire et al. 2014).

Comorbid diagnosis in paediatric OCD has been reported to result in increased functional impairments, increased OCD severity and reduced treatment response (Geller et al. 1996; Storch et al. 2010; Storch et al. 2008). Thus, it may seem logical to assume that comorbidity affects neuropsychological functioning. However, lack of such association is the rule and not the exception in the vast majority of neuropsychological investigation in youths as well as in adults with OCD (Abramovitch et al. 2013; Abramovitch & Cooperman 2015). Furthermore, the lack of association between neuropsychological test performance and symptom severity may account for our findings regarding the lack of impact of psychiatric comorbidity on neuropsychological functioning. Similar to our results, comorbid ADHD was not found to influence neuropsychological test performance in a large sample of youths with OCD (McGuire et al. 2014).

Beers et al. (1999) suggested that the lack of significant neuropsychological impairments in paediatric OCD may be due to the fact that these children are examined 'early in the illness'. Similarly, discussing their results, Ornstein et al. (2010) concluded that, 'The isolated deficits … may indicate emerging impairment that … possibly represent an ongoing process' (Ornstein et al. 2010). However, no longitudinal neuropsychological study has investigated such a progression. Neuromaturational delay in youth could mean that adults with OCD may exhibit more robust or better-defined impairments. In addition, higher-order EF, which develop after the age of 12, may continue to develop until early adulthood (Rosenberg & Keshavan 1998; McCann & Roy-Byrne 2004). Our results did not reveal any association between age and neuropsychological performance, or a difference between pre- and post-adolescents on neuropsychological measures. Only a longitudinal study can demonstrate the maturational deficit hypothesis in the transition from childhood into adulthood. This line of research is particularly important given that approximately 60% of children diagnosed with OCD remit into adulthood, but research into cognitive functioning among remitted versus persistent OCD is non-existent.

The present study has several strengths. The central strengths are the large sample size that allows for reliable analysis of the impact of comorbid conditions and a statistically sound sample size to outcome measures ratio. In addition, the present study employed a rigorous screening and diagnostic processes, including

'blind' assessors, as well as a correction for multiple comparisons. A limitation of the present study is the lack of a continuous measurement of depression severity. However, a psychometrically sound ordinal measure (K-SADS) was used to assess three degrees of depression severity. Secondly, we excluded any OCD diagnosis, but some control participants had a lifetime psychiatric diagnoses (other than OCD). While this may pose a potential limitation, the rates of lifetime diagnosis in the control sample were representative of the rates in the general population, increasing the ecological validity and facilitating generalizability of our results. Indeed, the vast majority of neuropsychological studies utilised 'healthy' controls, which do not represent the general population. Moreover, the control group's standard score across neuropsychological tests were in the normative or higher average range. Notably, although the control group's performance was within the normative range across tests, it is theoretically possible that past diagnosis of certain disorders may be associated with reduced neuropsychological test performance in some individuals (even in participants who do not meet current criteria for any DSM disorder). However, even in such a case –which theoretically reduces the probability of rejecting the null hypothesis – results pertaining to performance difference between the clinical and control groups found in this study may be more reliable and may facilitate generalizability. Finally, although medication status has been assessed and analysed in the present investigation, different classes of medications (e.g., SSRIs, neuroleptics) could have a potential differential effect on neuropsychological test performance. However, direct examinations (e.g. Mataix-Cols et al. 2002), as well as meta-analytic investigations (Abramovitch et al. 2013; Snyder et al. 2015) in adults with OCD found no significant impact of medication on cognitive performance, regardless of medication class.

Conclusion

In a large sample of youths with OCD who were compared to a matched control sample, patients exhibited reduced performance on neuropsychological tests involving processing speed, and on tasks of WM and visuospatial functioning that incorporate time as part of the tests' scores. Comparable performance was found on measures of EF, memory and visuospatial organisation (that was not timed). However, objectively, OCD patients performed within a normative range, warranting clinicians and educators to pay careful attention to these relative weaknesses that may not be identifiable in standard tests that lack a peer group comparison, and that may hinder fulfilment of the full intellectual potential in this population. Finally, consistent with findings in adult OCD, neuropsychological performance was not associated with any demographic or clinical indices, including comorbid conditions and medication status.

Disclosure statement

None to declare.

Funding

National Institute of Mental Health (NIMH) [grant number K08 MH01481].

ORCID

Amitai Abramovitch http://orcid.org/0000-0001-9640-0970

References

Abramovitch A, Abramowitz JS, Mittelman A. 2013. The neuropsychology of adult obsessive-compulsive disorder: a meta-analysis. Clin Psychol Rev. 33:1163–1171.

Abramovitch A, Abramowitz JS, Mittelman A, Stark A, Ramsey K, Geller DA. 2015. Research review: neuropsychological test performance in pediatric obsessive–compulsive disorder: a meta-analysis. J Child Psychol Psychiatr. 56:837–847.

Abramovitch A, Cooperman A. 2015. The cognitive neuropsychology of obsessive compulsive disorder: a critical review. J Obsess-Compuls Relat Disord. 5:24–36.

Abramovitch A, Mittelman A, Henin A, Geller DA. 2012. Neuroimaging and neuropsychological findings in pediatric obsessive-compulsive disorder: a review and developmental considerations. Neuropsychiatry. 2:17.

Andres S, Boget T, Lazaro L, Penades R, Morer A, Salamero M, Castro-Fornieles J. 2007. Neuropsychological performance in children and adolescents with obsessive-compulsive disorder and influence of clinical variables. Biol Psychiatry. 61:946–951.

APA. 2000. Diagnostic and statistical manual of mental disorders DSM-IV-TR Washington (DC): American Psychiatric Association.

Bedard MJ, Joyal CC, Godbout L, Chantal S. 2009. Executive functions and the obsessive-compulsive disorder: on the importance of subclinical symptoms and other concomitant factors. Arch Clin Neuropsychol. 24:585–598.

Beers SR, Rosenberg DR, Dick EL, Williams T, O'Hearn KM, Birmaher B, Ryan CM. 1999. Neuropsychological study of frontal lobe function in psychotropic-naive children with obsessive-compulsive disorder. Am J Psychiatry. 156:777–779.

Behar D, Rapoport JL, Berg CJ, Denckla MB, Mann L, Cox C, Fedio P, Zahn T, Wolfman MG. 1984. Computerized tomography and neuropsychological test measures in

adolescents with obsessive-compulsive disorder. Am J Psychiatry. 141:363–369.
Bernstein JH, Waber DP. 1996. Developmental scoring system for the rey-osterrieth complex figure (DSS Rocf). Luts (FL): Psychological Assessment Resources.
Biederman J, Mick E, Faraone SV, Braaten E, Doyle A, Spencer T, Wilens T, Frazier E, Johnson MA. 2002. Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. AJP. 159:36–42.
Boileau B. 2011. A review of obsessive-compulsive disorder in children and adolescents. Dialogues Clin Neurosci. 13:401–411.
Burdick KE, Robinson DG, Malhotra AK, Szeszko PR. 2008. Neurocognitive profile analysis in obsessive-compulsive disorder. J Int Neuropsychol Soc. 14:640–645.
Chamberlain SR, Blackwell AD, Fineberg NA, Robbins TW, Sahakian BJ. 2005. The neuropsychology of obsessive compulsive disorder: the importance of failures in cognitive and behavioural inhibition as candidate endophenotypic markers. Neurosci Biobehav Rev. 29:399–419.
Chang SW, McCracken JT, Piacentini JC. 2007. Neurocognitive correlates of child obsessive compulsive disorder and Tourette syndrome. J Clin Exp Neuropsychol. 29:724–733.
Fitzgerald KD, Welsh RC, Stern ER, Angstadt M, Hanna GL, Abelson JL, Taylor SF. 2011. Developmental alterations of frontal-striatal-thalamic connectivity in obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 50:938–948.
Geller DA. 2006. Obsessive-compulsive and spectrum disorders in children and adolescents. Psychiatr Clin North Am. 29:353–370.
Geller DA, Biederman J, Griffin S, Jones J, Lefkowitz TR. 1996. Comorbidity of juvenile obsessive-compulsive disorder with disruptive behavior disorders. J Am Acad Child Adolesc Psychiatry. 35:1637–1646.
Golden CJ. 1978. Stroop color and word test: a manual for clinical and experimental uses. Chicago (IL): Stoelting Co.
Harris ME. 1990. Wisconsin card sorting test: computer version, research edition. Odessa (FL): Psychological Assessment Resources.
Kuelz A, Hohagen F, Voderholzer U. 2004. Neuropsychological performance in obsessive-compulsive disorder: a critical review. Biol Psychol. 65:185–236.
Leckman JF, Riddle MA, Hardin MT, Ort SI, Swartz KL, Stevenson J, Cohen DJ. 1989. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry. 28:566–573.
Leckman JF, Sholomskas D, Thompson WD, Belanger A, Weissman MM. 1982. Best estimate of lifetime psychiatric diagnosis: a methodological study. Arch Gen Psychiatry. 39:879–883.
Lewin AB, Larson MJ, Park JM, McGuire JF, Murphy TK, Storch EA. 2014. Neuropsychological functioning in youth with obsessive compulsive disorder: an examination of executive function and memory impairment. Psychiatry Res. 216:108–115.
Lezak MD, Howieson DB, Bigler ED, Tranel D. 2012. Neuropsychological assessment. 5th ed. New York: Oxford University Press.
Mataix-Cols D, Alonso P, Pifarre J, Menchon JM, Vallejo J. 2002. Neuropsychological performance in medicated vs. unmedicated patients with obsessive-compulsive disorder. Psychiat Res. 109:255–264.
McCann BS, Roy-Byrne P. 2004. Screening and diagnostic utility of self-report attention deficit hyperactivity disorder scales in adults. Compr Psychiatry. 45:175–183.
McGuire JF, Crawford EA, Park JM, Storch EA, Murphy TK, Larson MJ, Lewin AB. 2014. Neuropsychological performance across symptom dimensions in pediatric obsessive compulsive disorder. Depress Anxiety. 31:988–996.
Melloni M, Urbistondo C, Sedeño L, Gelormini C, Kichic R, Ibanez A. 2012. The extended fronto-striatal model of obsessive compulsive disorder: convergence from event-related potentials, neuropsychology and neuroimaging. Front Hum Neurosci. 6:259.
Ornstein TJ, Arnold P, Manassis K, Mendlowitz S, Schachar R. 2010. Neuropsychological performance in childhood OCD: a preliminary study. Depress Anxiety. 27:372–380.
Orvaschel H, Puig-Antich J. 1987. Schedule for Affective Disorder and Schizophrenia for School-age Children: Epidemiologic Version: Kiddie-SADS-E (K-SADS-E). Philadelphia (PA): Medical College of Pensylvania.
Osterrieth PA. 1944. Le test de copie d'une figure complexe; contribution à l'étude de la perception et de la mémoire. [Test of copying a complex figure; contribution to the study of perception and memory.]. Arch Psychol (Geneve). 30:206–356.
Rosenbaum JF, Biederman J, Hirshfeld-Becker DR, Kagan J, Snidman N, Friedman D, Nineberg A, Gallery DJ, Faraone SV. 2000. A controlled study of behavioral inhibition in children of parents with panic disorder and depression. AJP. 157:2002–2010.
Rosenberg DR, Keshavan MS. 1998. A.E. Bennett Research Award. Toward a neurodevelopmental model of of obsessive: compulsive disorder. Biol Psychiatry. 43:623–640.
Ruscio AM, Stein DJ, Chiu WT, Kessler RC. 2010. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Mol Psychiatry. 15:53–63.
Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, Cicchetti D, Leckman JF. 1997. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. J Am Acad Child Adolesc Psychiatry.. 36:844–852.
Shin MS, Choi H, Kim H, Hwang JW, Kim BN, Cho SC. 2008. A study of neuropsychological deficit in children with obsessive-compulsive disorder. Eur Psychiatry. 23:512–520.
Shin NY, Lee TY, Kim E, Kwon JS. 2014. Cognitive functioning in obsessive-compulsive disorder: a meta-analysis. Psychol Med. 44:1121–1130.
Snyder HR, Kaiser RH, Warren SL, Heller W. 2015. Obsessive-compulsive disorder is associated with broad impairments in executive function: a meta-analysis. Clin Psychol Sci. 3:301–330.
Storch EA, Lewin AB, Geffken GR, Morgan JR, Murphy TK. 2010. The role of comorbid disruptive behavior in the clinical expression of pediatric obsessive-compulsive disorder. Behav Res Ther. 48:1204–1210.
Storch EA, Merlo LJ, Larson MJ, Geffken GR, Lehmkuhl HD, Jacob ML, Murphy TK, Goodman WK. 2008. Impact of

comorbidity on cognitive-behavioral therapy response in pediatric obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 47:583–592.

Stroop JR. 1935. Studies of interference in serial verbal reactions. J Exp Psychol. 18:643–662.

Taner YI, Emel EB, Oner O. 2011. Impaired executive functions in paediatric obsessive-compulsive disorder patients. Acta Neuropsychiatr. 23:272–281.

Wechsler D. 1991. The Wechsler intelligence scale for children—third edition. San Antonio (TX): The Psychological Corporation.