Published in final edited form as:
J Child Psychol Psychiatry. 2011 September ; 52(9): 974–983. doi:10.1111/j.1469-7610.2010.02366.x.

Poor Fine-Motor and Visuospatial Skills Predict Persistence of Pediatric-Onset Obsessive-Compulsive Disorder into Adulthood

Michael H. Bloch, MD, MS[*], **Denis G. Sukhodolsky, PhD**[*], **Philip A. Dombrowski, BA**[*], **Kaitlyn E. Panza, BA**[*], **Brittany G. Craiglow, BA**[*], **Angeli Landeros-Weisenberger, MD**[*], **James F. Leckman, MD**, **Bradley S. Peterson, MD**[#,*], and **Robert T. Schultz, PhD**[^,*]

[*]Yale Child Study Center, Yale University School of Medicine, New Haven, CT

[#]Department of Psychiatry, Columbia University College of Physicians and Surgeons and New York State Psychiatric Institute, New York, NY

[^]Department of Pediatrics, University of Pennsylvania, Philadelphia, PA

Abstract

Background—Half of pediatric-onset OCD cases remit by adulthood. Studies have demonstrated that initial response to pharmacotherapy, age of onset, prominent hoarding symptoms, and the presence of comorbid tic disorders are associated with long-term outcome. Our goal was to examine the association between childhood performance on neuropsychological testing and persistence of OCD into adulthood.

Methods—Twenty-four children with OCD were followed for an average of 7.5 years into early adulthood. Neuropsychological performance in childhood (<16 years) was measured. The battery included the Wechsler Intelligence Scale for Children (WISC-III), the Purdue pegboard test, the Rey-Osterreith Complex Figure Task (RCFT) and the Beery-Buktenica test of Visual Motor Integration (VMI). We hypothesized that deficits in fine-motor skills, visuospatial skills, and nonverbal memory as well as overall intelligence would be associated with adulthood outcome. We used a Cox Proportional Hazard model of survival analysis in which time to remission of OCD symptoms was the main outcome variable.

Results—Poor childhood performance on the Purdue pegboard task and the block design subscale of WISC-III was associated with persistence of OCD symptoms into adulthood. IQ, VMI, and nonverbal memory performance did not predict significantly the persistence of OCD.

Conclusions—These results suggest that visuospatial and fine-motor skill deficits are predictive of poor long-term outcome in pediatric-onset OCD. Future longitudinal studies are needed to chart the course of these deficits relative to the course of symptoms in OCD and to determine whether the association of these neuropsychiatric deficits with long-term outcome is specific to pediatric-onset OCD or generalizes to other psychiatric disorders.

Keywords

Obsessive-compulsive disorder; longitudinal study; neuropsychological tests; fine-motor skills and visuospatial skills

Correspondence: Michael H. Bloch, MD, MS, Child Study Center, Yale University School of Medicine, PO Box 2070900, New Haven, CT 06520 or michael.bloch@yale.edu.

Prior Presentation: Portions of the data in this manuscript have been presented at the following meetings: American Academy of Child and Adolescent Psychiatry October 31, 2009, and American College of Neuropsychopharmacology December 6-10, 2007 and December 7-11, 2008.

Disclosures: The authors have no conflicts of interest to disclose

Introduction

Obsessive-compulsive disorder (OCD) is a psychiatric disorder characterized by obsessions that are recurrent thoughts, images, and impulses that are experienced as intrusive and unwanted, and compulsions, which are mental or physical rituals designed to relieve anxiety associated with obsessions(DSM-IV-TR, 2000). Many cases of OCD arise during childhood (Zohar, 1999). A meta-analysis of previous long-term outcome studies (greater than 1 year duration) in pediatric-onset OCD suggested that as many as 40% to 59% of cases remit with proper treatment (Stewart et al., 2004). We recently reported that the presence of comorbid tic symptoms in children with OCD was associated with remission of OCD symptoms. We also reported that the presence of prominent hoarding symptoms is associated with the persistence of OCD symptoms into adulthood (Bloch et al., 2009). Other studies have also reported that poor initial response to pharmacotherapy, a history of inpatient treatment for OCD, a family history of psychiatric illness, and an earlier age of onset of OCD, are associated with poor long-term outcome (Leonard et al., 1993, Stewart et al., 2004).

Although several studies have assessed whether clinical measures predict long-term outcome in pediatric-onset OCD, none, to our knowledge, have examined childhood neuropsychological test performance as a predictor of adulthood outcome. Cross-sectional studies have demonstrated significant deficits in visuospatial skills, nonverbal memory, and executive functioning tasks, such as response inhibition and set-shifting in adults with OCD compared to unaffected controls (Menzies et al., 2008, Chamberlain et al., 2006, Bohne et al., 2005, Anderson and Savage, 2004, Mataix-Cols et al., 2003, Savage et al., 1999, Simpson et al., 2006, Greisberg and McKay, 2003). One study comparing 35 children with OCD compared to age and gender matched controls demonstrated deficits in visuospatial skills, set-shifting and velocity taks in children with OCD (Andres et al., 2007) . However, many other studies have failed to demonstrate differences in neuropsychological testing between children with OCD and unaffected controls (Behar et al., 1984, Beers et al., 1999, Chang et al., 2007). Small sample sizes, inadequate accounting for comorbid illnesses and the heterogeneity in sympotom presentation of OCD may contribnte to the discrepant findings of previous studies (Flessner et al., 2010).

A recent study examined neuropsychological testing as a moderator of treatment effects (either Cognitive Behavior Therapy (CBT), sertraline or combination) in the Pediatric OCD Treatment Study (Flessner et al., 2010). This study demonstrated that poor performance on Rey-Osterreith Complex Figure Task (RCFT) long-term recall was associated with poor treatment response (especially to the CBT condition) over the 12-week study (Flessner et al., 2010). Another study has failed to demonstrate an association between pretreatment neurological soft sign and motor coordination measures and response to treatment with CBT (Bolton et al., 2000).

Few studies have similarly examined the association between childhood neuropsychological performance and long-term outcome in children with OCD. In a cohort of children with Tourette syndrome, who are at high risk of developing OCD, we previously demonstrated that higher childhood IQ was associated with the severity of OCD symptoms in early adulthood (Bloch et al., 2006a). A recent study examined premorbid childhood neuropsychological testing performance in OCD cases, subsequently diagnosed in adulthood, and controls who never developed psychiatric illness. This latter study found that adults with OCD had significantly worse premorbid performance in childhood on tasks measuring visuospatial skill, nonverbal memory, and fine-motor skill, but did not differ on overall IQ (Grisham et al., 2009). Adults with OCD had significantly worse childhood performance on the RCFT copying and delayed recall, grooved pegboard and the perceptual

organization factor of the WISC-R (Grisham et al., 2009). This study suggests these neuropsychological deficits are trait-related deficits of OCD. However, the findings of this study were exploratory in nature and require replication. Furthermore, neither of these two studies examined neuropsychological findings that are associated with persistence of OCD symptoms in children who already have the disorder (Bloch et al., 2006a, Grisham et al., 2009). .

The goal of our current study is to determine whether childhood neuropsychological deficits predict adulthood outcome in children with OCD. We hypothesized that childhood deficits in (1) fine-motor skills (measured by bimanual Purdue Pegboard performance), (2) visuospatial skills (measured by the Block-Design task of Wechsler Intelligence Scale for Children-III (WISC-III), (3) nonverbal memory (measured by delayed recall on the RCFT), and (4) higher overall IQ, would be associated with the persistence of OCD into adulthood.

Patients and Methods

Subjects

All participants were initially recruited through the Yale TS/OCD Clinic from 1993-1998. Eligible participants were required to (1) have a primary diagnosis of OCD, (2) participate in neuropsychological testing prior to 16 years of age and (3) were older than 16 years at the time of the potential follow-up interview. Adulthood follow-up interviews took place on average 7.5 years after initial childhood evaluation. Exclusionary criteria for receiving a childhood neuropsychological testing included: a history of seizure, head trauma with loss of consciousness, ongoing or past substance abuse, or an IQ lower than 80. Parental written informed consent and subject assent were performed at childhood baseline assessment and subject informed consent at follow-up. Compensation for participation was provided at both time points under the guidelines of the Human Investigations Committee.

From an eligible sample of 32 subjects who received focused neuropsychological testing during childhood, 24 (75%) elected to participate in adulthood follow-up interviews. Reasons for nonparticipation included subject refusal to participate in a follow-up interview (n = 1) or inability to locate subjects (n = 7). Demographic data, as assessed at childhood baseline, did not differ significantly between eligible participants and non-participants (Table 1).There were an additional 20 subjects who participated in the adulthood follow-up assessments who did not receive childhood neuropsychological testing. Participants in childhood neurpsychological testing had significantly higher rates of comorbid tic disorders at childhood assessment than non-participants. There was an additional 8 subjects who did not participate in the follow-up sample who also did not receive childhood neuropsychological testing in childhood.

Interview Procedure at Childhood Baseline Assessment

Childhood baseline assessment occurred prior to age 16 years and included current and worst-ever measures, using the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) and theYale Global Tic Severity Scale (YGTSS) (Leckman et al., 1989, Scahill et al., 1997). The Schedule for Tourette and Other Behavioral Syndromes was used to survey other comorbid psychiatric illnesses (Pauls et al., 1995). Neuropsychiatric diagnoses were established through a best-estimate consensus procedure performed by two child psychiatrists following a review of all available data (Leckman et al., 1982). Available information typically included (1) a clinical interview performed by an attending physician in the TS/OCD clinic and (2) a structured clinical interview performed by a trained research assistant. Participants were then classified based on these diagnoses on their diagnosis status

(yes/no) for Tourette's syndrome (TS), chronic tic disorder (CTD), and Attention-Deficit Hyperactivity Disorder (ADHD) in addition to a diagnosis of OCD.

Neuropsychological Testing Procedure at Childhood Baseline

Focused neuropsychological testing was performed in a uniform battery over the course of two sessions lasting, on average, two hours each. Intelligence testing was performed based on four subscale tests in the Wechsler Intelligence Scale for Children-III (WISC-III). (Wechsler, 1991) The Information and Similarity tests of the WISC-III were used to measure verbal intelligence and the Picture completion and Block Design subtests used to measure performance intelligence. Visual Motor Integration was assessed with the Beery-Buktenica Visual Motor Integration Test (VMI) (Beery, 1989). Nonverbal memory was tested with the RCFT, using the Taylor Scoring System (Rey, 1941, Osterrieth, 1944). The copying and long-term delayed recall paradigms of the RCFT were specifically examined. Fine motor skill was tested using a timed peg-placing test, the Purdue Pegboard, using the procedures described previously (Tiffen, 1968, Schultz et al., 1998). No participants in this current sample had tics involving their hands that interfered with performance on this measure. Dominant, non-dominant, and bimanual handed test conditions were administered to all subjects. A detailed description of the neuropsychological battery used in this study has been described elsewhere (Schultz et al., 1998). During these evaluation procedures, medicated children were on their usual dose and type of medication, with the exception of psychostimulants. In the case of psychostimulants, parents were asked to refrain from giving their child their daily dose(s) of psychostimulants on the day of neuropsychological testing. The administration of neuropsychological tests was counterbalanced to rule out possible effects of fatigue on the tests.

Interview Procedure at Adulthood Follow-up

Evaluations during follow-up in early adulthood included current and worst-ever ratings on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the YGTSS (Leckman et al., 1989, Goodman et al., 1989). Screening for comorbid psychiatric conditions was conducted with the *Structured Clinical Interview for* DSM-IV *Axis I Disorder*, and a standardized medication history was obtained (First et al., 1995). We asked all subjects who had improved significantly, the age that their OC symptoms “remitted,” which was defined by interviews as, “the age your OC symptoms improved substantially.”

Data Analysis

All statistical analyses were performed using SAS version 9.1 (SAS_Institute_Inc., 2008). Our primary outcome variable for the analysis was time to remission of OC symptoms from the initial childhood assessment. A participant was considered remitted if the Y-BOCS was less than 8 at follow-up. A Y-BOCS score of <8 was chosen as our criteria for remission because the anchor point of 8 demarcates subclinical (YBOCS 0-7) from clinical OCD symptoms (YBOCS≥8) (Goodman et al., 1989). Age of OCD remission was determined by a patient self-report at follow-up. Time to remission was calculated by subtracting the age of baseline childhood assessment from the age of remission.

A Cox Proportional Hazards model of survival analysis (proc phreg command in SAS) was used to test the association between neuropsychological variables of interest and persistence of OCD symptoms. In the Cox Proportional Hazards model, remission status (0-no/1-yes) and time to remission or follow-up (depending on which were applicable) were the dependent variables. We tested models with t sets of covariates. In our primary model we adjusted for age at childhood neuropsychological testing, gender, baseline OCD severity (to control for decreased likelihood of remission), important comorbid disorders (such as

comorbid tics and ADHD) and prominent hoarding symptoms in childhood. We have previously shown that chronic tics and primary hoarding symptoms clinical measures were significantly associated with persistence of OCD symptoms (Bloch et al., 2009). These association were still significant when including only the subset of children who participated in childhood neuropsychological testing. We, additionally, added ADHD as a covariate because ADHD has been associated with significant neuropsychological deficits in previous samples (Willcutt et al., 2005, Flessner et al., 2010). Findings, using this model, would demonstrate that neuropsychological test results are significantly associated with persistence of OCD into adulthood, after accounting for significant clinical predictors of outcome. We also examined two secondary models. In the first model, we adjusted only for traditional covariates -- age at childhood neuropsychological testing, gender and baseline OCD severity. This model did not adjust for known childhood clinical predictors of outcome and clinical comorbidites. In the second model, we adjusted for -- age at childhood neuropsychological testing, gender, baseline OCD severity and the presence of important comorbidities (ADHD and chronic tics) at baseline. This model was similar to the primary model but did not include prominent hoarding symptoms as a covariate.

Neuropsychological testing results were additionally entered into the Cox proportional hazard model. When appropriate, neuropsychological testing results are presented as z-scores. Z-scores were used in presenting the results of Purdue pegboard testing, block design subscale, VMI and RCFT. IQ results were presented on a traditional scale with a score of 100 representing the mean and the standard deviation being 15 points.

Based on the results of previous neuropsychological testing studies in OCD, we hypothesized that bimanual Purdue pegboard performance, block design performance on WISC-III, IQ and long-term recall on the RCFT would be associated with persistence of OCD symptoms into adulthood. We used a Bonferroni correction to set the threshold for statistical significance at $p<0.012$ for *a priori* hypothesis testing. We used the model that included significant childhood clinical predictors (comorbid tics, ADHD and primary hoarding symptoms) since we were interested in whether neuropsychological testing variables would be additionally informative about persistence of OCD symptoms in adulthood.

Additionally, for exploratory analyses, we ran Cox proportional hazard models, which tested the effects of dominant and non-dominant handed Purdue pegboard performance, VMI, RCFT copying performance and block design subscale of WISC-III. The threshold of significance for exploratory analyses was set at $p = 0.05$ to maximize the hypothesis generation. We conducted 24 non-independent statistical tests (3 models × 8 neuropsychological tests) during the course of data analysis.

To examine the effects of neuropsychological tests on persistence of symptoms in children with OCD with and without primary hoarding symptoms or comorbid tics, an interaction term of (tics × neuropsychological test performance) or (hoarder × neuropsychological test performance) was added to the primary model. Given our limited power to detect a significant interaction effect, we planned on reporting any interaction effect of $p<0.1$. We were unable to test our original Cox proportional hazard models in children with and without hoarding or tics, due to overfitting of the model (there were too few hoarders who remitted and too few tic-related OCD patients who failed to improve).

Results

The childhood baseline interview took place when children were age 11.5 ± 2.4 (mean ± standard deviation) years. The average age at early adulthood follow-up was 19.0 ± .1.9

years. The average duration between initial and follow-up interviews was 7.5 ± 1.9 years. Subjects reported marked to severe worst-ever OCD symptoms at the childhood neuropsychological testing, with a worst-ever CY-BOCS score of 27.9 ± 7.5. OCD symptoms were less severe on average at the time of adulthood follow-up (Y-BOCS 9.7 ± 9.8). At follow-up in adulthood, 14 subjects (58%) had OCD that remitted (Y-BOCS<8). A comparison of baseline demographics among eligible participants who did and did not participate in the follow-up clinical assessment in young adulthood is depicted in Table 1.

Among the 24 pediatric OCD subjects at childhood baseline, 18 (75%) had a comorbid tic disorder, 10 (42%) had Attention-Deficit Hyperactivity Disorder, 8 (33%) had a history of comorbid depression and 10 (42%) reported symptoms consistent with an anxiety disorder other than OCD (social phobia, separation anxiety, specific phobia, panic disorder or generalized anxiety disorder). Ninety percent of subjects were prescribed serotonin reuptake inhibitors at the time of childhood MRI. Thirty-eight percent of our sample (N=9) participated in previous CBT. The majority of both remitted and non-remitted subjects continued to take SRIs at adulthood follow-up. Further clinical details regarding this cohort at childhood baseline and adulthood follow-up can be found elsewhere (Bloch et al., 2009).

A Priori Hypothesis Testing

Poor performance in childhood on the bimanual Purdue pegboard test and the block design subset of WISC-III were significantly associated with the persistence of OCD into adulthood. We detected no significant association between childhood IQ or delayed recall on the RCFT and persistence of OCD symptoms into adulthood. Table 2 depicts the relationship between childhood neuropsychological testing performance and the persistence of OCD symptoms into adulthood.

Cox-Proportional Hazard Model Adjusting for Age, Gender, Childhood OCD Severity, Presence of Comorbid Tics, ADHD and Primary Hoarding Symptoms

Poor childhood performance on the Purdue pegboard test, in the dominant hand condition and the bimanual condition, were significantly associated with persistence of OCD into adulthood. There was no association between non-dominant handed Purdue pegboard performance and persistence of symptoms into adulthood. Poor performance on the block design subscale of WISC-III was also associated with the persistence of OCD symptoms into adulthood. There was no association between performance on the VMI or copying of the RCFT and persistence of OCD into adulthood. Table 2 depicts the relationship between childhood neuropsychological testing performance and the persistence of OCD symptoms into adulthood. These findings were nearly identical when the presence of prominent childhood hoarding symptoms was not included in the model (Table 2).

Cox-Proportional Hazard Model Not Adjusting for Age, Gender and Childhood OCD Severity Only

Poor bimanual Purdue pegboard performance was stillassociated with persistence of OCD into adulthood when important comorbidities and clinical subtypes of OCD were not taken into account in the Cox-proportional hazard model. The strength of the association between both dominant-handed Purdue pegboard performance and WISC-III block design performance, with persistence of OCD into adulthood, was much weaker when comorbid tic disorders, ADHD and hoarding symptoms were not included in the survival model. There remained no association between overall IQ, RCFT or VMI performance and persistence of OCD symptoms into adulthood.

Discussion

We found a significant association between poor fine-motor skills and visuospatial skills in childhood and the persistence of OCD symptoms into adulthood. These results are consistent with previous cross-sectional studies that have reported similar neuropsychological deficits in OCD patients compared to unaffected controls. Our findings are consistent with the results of a prior study reporting that childhood performance on a very similar Grooved Pegboard Test, assessed at age 12, was associated with the development of OCD in adulthood, at age 32(Grisham et al., 2009). Taken together, these two studies indicate that specific neuropsychological deficits such as poor fine-motor skills and visuospatial skills, may be trait markers of OCD and are predictors of OCD into adulthood.

Poor Purdue Pegboard performance is a sign of deficits in complex, visually guided or coordinated movement that are likely mediated by circuits involving the basal ganglia. (Schultz et al., 1998) Deficits on Purdue Pegboard testing have been associated with reduced putamen volumes in Parkinson's disease patients (Alegret et al., 2001) and basal ganglia hyperperfusion in 99mTc-hexamethyl propyleneamine oxime SPECT studies of patients with subclinical hepatic encephalopathy (Catafau et al., 2000). Substantial evidence suggests that abnormalities in frontal-striatal circuits are central to the pathogenesis of OCD. This finding is consistent with several cross-sectional structural neuroimaging studies of OCD that have observed larger putamen volumes in both children and adults with OCD compared to normal controls(Pujol et al., 2004, Szeszko et al., 2008, Gilbert et al., 2008, Radua and Mataix-Cols, 2009). FDG PET studies in patients with OCD has consistently demonstrated hypermetabolism of the orbitofrontal cortex and basal ganglia under resting state and symptom provocation conditions compared to unaffected controls (Menzies et al., 2008, Saxena and Rauch, 2000, Baxter et al., 1988). This hypermetabolism has been shown to normalize after successful treatment with pharmacological or behavioral therapy(Saxena and Rauch, 2000).

Fine-motor skills are also part of a series of neuropsychological deficits termed neurological soft signs. Soft signs are motor, sensory, or integrative abnormalities found on neurological exams in individuals with no neurological lesion. Soft signs are thought to reflect complex patterns of deficits involving several systems (Anderson and Savage, 2004, Shaffer et al., 1985). Although increased neurological soft signs have been reported in children with OCD and associated with obsessive slowness, these neuropsychological deficits may be associated with development and persistence of psychological illness in general (Hymas et al., 1991, Bihari et al., 1991, Hollander et al., 1990). Previous reports have also associated increased neurological soft signs with poor medication response in adults with OCD (Hollander et al., 2005) but not response to behavioral therapy in children with OCD (Bolton et al., 2000). Increased neurological soft signs are associated with a diagnosis of ADHD, learning disorders, bipolar disorder, schizophrenia, chronic post-traumatic stress disorder, borderline personality disorders and even, externalizing and internalizing disorders in general (Chan et al., 2009, Pine et al., 1997, Dickstein et al., 2005, De la Fuente et al., 2006, Negash et al., 2004, Dazzan and Murray, 2002, Foodman and McPhillips, 1996, Gurvits et al., 2000). We have previously reported that poor Purdue pegboard performance in childhood was associated with the adulthood severity of tic symptoms in children with Tourette syndrome (Bloch et al., 2006b). Other studies have associated the presence of neuropsychological soft signs with the persistence of schizophrenia and both internalizing and externalizing disorders in children (Mayoral et al., 2008, Wilson et al., 2003, Pine et al., 1997, Prikryl et al., 2007). The presence of neurological soft signs is also correlated with the severity of visuospatial skill and nonverbal memory deficits in OCD patients (Mataix-Cols et al., 2003). Further research is needed to determine the predictive validity of neurological soft signs in

the persistence of OCD and psychiatric illness in general and to determine environmental risk factors associated with these deficits (Boks et al., 2007, Hertzig, 1981).

Visuospatial skills are the mental capacity to perceive and manipulate objects in two or three dimensional space (Rauch and Savage, 1997). Several previous studies have reported deficits in visuospatial skills in OCD patients compared to unaffected controls (Mataix-Cols et al., 2003, Anderson and Savage, 2004, Hollander et al., 1990, Savage et al., 1999, Savage and Rauch, 2000). Visuospatial deficits typically reflect right temporal-parietal dysfunction, because this is the part of the brain responsible for spatial reasoning (Anderson and Savage, 2004). In OCD, it has been hypothesized that these deficits may instead be secondary to other deficits in executive functioning (Savage and Rauch, 2000). Executive function is the cognitive system in psychology that controls and manages other cognitive processes and typically localizes to the prefrontal cortex. Executive function is responsible for planning, cognitive flexibility, abstract thinking, rule acquisition, initiating appropriate actions, and inhibiting inappropriate actions. The most elegant illustration of this hypothesis is with the RCFT. Children and adults with OCD have shown deficits in copying and especially delayed recall compared to unaffected controls (Savage and Rauch, 2000, Savage et al., 1999, Andres et al., 2007). This deficit has been correlated with OCD patient's inability to recognize the core organizational elements of this complex figure – an executive functioning trait (Savage et al., 1999, Cabrera et al., 2001). These same investigators went on to further show that these deficits in recalling complex figures could be reversed if subjects were cognitively retrained to recognize the core organizational elements of similar complex figures (Buhlmann et al., 2006). Further research needs to determine the core neuropsychological dysfunction underlying the visuospatial deficits seen in OCD patients. Regardless of the core neuropsychological deficits responsible for the association, it appears that visuospatial deficits evident in childhood, and measured by tasks like the Block Design subset of WISC-III, are likely trait-deficits of OCD associated with both the future development of OCD in unaffected cases and the persistence of symptoms into adulthood of children who have OCD. Deficits on long-term recall on the RCFT has been associated with poor treatment response in children with OCD, further suggesting that visuospatial deficits are an important moderator of treatment effects in pediatric OCD(Flessner et al., 2010).

Limitations

Our study had several limitations. The study population was clinically referred to our TS/OCD specialty clinic, and thus the study sample had a higher rate of comorbid illness (especially tic disorders and ADHD) and more severe pathology than does the general population of individuals with OCD. No children in our sample had OCD without any other comorbid disorders. Our method of analysis, however, allowed us to statistically covary for important comorbidities and illness severity. Seventy-five percent of the eligible study sample participated in follow-up interviews. Although clinical characteristics of nonparticipating subjects did not differ significantly at the time of neuropsychological testing, these measures may have differed at the time of adulthood follow-up. Also, over 90% of the study sample was taking psychotropic medications at the time of neuropsychological testing and 75% at adulthood follow-up. Given our small sample size, the few number of subjects who were unmedicated and the non-random use of medication at follow-up, we were unable to control for medication effects in the sample. Lastly, several neuropsychological deficits in OCD, such as response inhibition and cognitive flexibility, have been demonstrated to correlate strongly with OCD, since the initiation of our neuropsychological battery over a decade ago (Chamberlain et al., 2006). Future longitudinal studies should also examine the predictive validity of these tests vis a vis long term outcome.

Conclusions

Despite these limitations, our study had several important findings. We replicated recent findings in suggesting that poor fine-motor skills and visuospatial skill deficits are trait-related deficits in OCD (Grisham et al., 2009). We also extend upon their findings in reporting that fine-motor and visuospatial deficits are a risk factor for persistence of pediatric OCD into adulthood. Future longitudinal studies, examining neuropsychological testing performance in pediatric-onset OCD cases and in high risk samples, will be particularly useful in tracing the course of these deficits with disease course and quantifying the predictive value of these measures. Equally important, will be future studies examining neuropsychological testing studies examining several of these measures as potential moderators of the effects of both psychological and pharmacological treatments for OCD. Understanding neuropsychological testing deficits as moderators of both short-term treatment effects and long-term adulthood in pediatric OCD has the potential to be informative for both treatment selection and prognosis. These future studies should compare OCD patients, not only to unaffected controls, but also to children with other psychiatric disorders. This could help determine whether the association of these neuropsychiatric deficits with long-term outcome is specific to pediatric-onset OCD or can be generalized to other psychiatric disorders. Understanding distinct neuropsychological deficits associated with OCD has the potential to provide endophenotypes for genetic and imaging studies of OCD.

Acknowledgments

The authors acknowledge the National Institute of Mental Health support of the Yale Child Study Center Research Training Program (MHB, JFL), K05MH076273 (JFL), K02MH074677 (BSP), K01MH079130 (DGS), R01MH068318 (BSP), R01MH073084 (RTS), the National Science Foundation (SBE-0542013)(RTS), the National Institutes of Health Loan Repayment Program (MHB), P50HD055726 (RTS) and RO1HD055741 (RTS), the support of the Pennsylvania Department of Health (SAP#410042728)(RTS), the support of the Tourette's Syndrome Association Inc. (JFL, MHB), the APIRE/Eli Lilly Psychiatric Research Fellowship (MHB), the AACAP/Eli Lilly Pilot Research Award (MHB), the Trichotillomania Learning Center (MHB), NARSAD (MHB) and the APA/NIMH PMRTP Program (ALW).

References

Alegret M, Junque C, Pueyo R, Valldeoriola F, Vendrell P, Tolosa E, Mercader JM. MRI atrophy parameters related to cognitive and motor impairment in Parkinson's disease. Neurologia. 2001; 16:63–69. [PubMed: 11257931]

Anderson KE, Savage CR. Cognitive and neurobiological findings in obsessive-compulsive disorder. Psychiatr Clin North Am. 2004; 27:37–47. viii. [PubMed: 15062629]

Andres S, Boget T, Lazaro L, Penades R, Morer A, Salamero M, Castro-Fornieles J. Neuropsychological performance in children and adolescents with obsessive-compulsive disorder and influence of clinical variables. Biol Psychiatry. 2007; 61:946–951. [PubMed: 17157271]

Baxter LR Jr, Schwartz JM, Mazziotta JC, Phelps ME, Pahl JJ, Guze BH, Fairbanks L. Cerebral glucose metabolic rates in nondepressed patients with obsessive-compulsive disorder. Am J Psychiatry. 1988; 145:1560–1563. [PubMed: 3264118]

Beers SR, Rosenberg DR, Dick EL, Williams T, O'hearn KM, Birmaher B, Ryan CM. Neuropsychological study of frontal lobe function in psychotropic-naive children with obsessive-compulsive disorder. Am J Psychiatry. 1999; 156:777–779. [PubMed: 10327915]

Beery, KE. Developmental test of visual motor integration: Administration, scoring and teaching manual. Cleveland, OH: Modern Ciriculuum Press; 1989.

Behar D, Rapoport JL, Berg CJ, Denckla MB, Mann L, Cox C, Fedio P, Zahn T, Wolfman MG. Computerized tomography and neuropsychological test measures in adolescents with obsessive-compulsive disorder. Am J Psychiatry. 1984; 141:363–369. [PubMed: 6703099]

Bihari K, Pato MT, Hill JL, Murphy DL. Neurologic soft signs in obsessive-compulsive disorder. Arch Gen Psychiatry. 1991; 48:278–279. [PubMed: 2036127]

Bloch MH, Craiglow BG, Landeros-Weisenberger A, Dombrowski PA, Panza KE, Peterson BS, Leckman JF. Predictors of early adult outcomes in pediatric-onset obsessive-compulsive disorder. Pediatrics. 2009; 124:1085–1093. [PubMed: 19786445]

Bloch MH, Peterson BS, Scahill L, Otka J, Katsovich L, Zhang H, Leckman JF. Adulthood outcome of tic and obsessive-compulsive symptom severity in children with Tourette syndrome. Arch Pediatr Adolesc Med. 2006a; 160:65–69. [PubMed: 16389213]

Bloch MH, Sukhodolsky DG, Leckman JF, Schultz RT. Fine-motor skill deficits in childhood predict adulthood tic severity and global psychosocial functioning in Tourette's syndrome. J Child Psychol Psychiatry. 2006b; 47:551–559. [PubMed: 16712631]

Bohne A, Savage CR, Deckersbach T, Keuthen NJ, Jenike MA, Tuschen-Caffier B, Wilhelm S. Visuospatial abilities, memory, and executive functioning in trichotillomania and obsessive-compulsive disorder. J Clin Exp Neuropsychol. 2005; 27:385–399. [PubMed: 15962686]

Boks MP, Selten JP, Leask S, Castelein S, Van Den Bosch RJ. Negative association between a history of obstetric complications and the number of neurological soft signs in first-episode schizophrenic disorder. Psychiatry Res. 2007; 149:273–277. [PubMed: 17189652]

Bolton D, Raven P, Madronal-Luque R, Marks IM. Neurological and neuropsychological signs in obsessive compulsive disorder: interaction with behavioural treatment. Behav Res Ther. 2000; 38:695–708. [PubMed: 10875191]

Buhlmann U, Deckersbach T, Engelhard I, Cook LM, Rauch SL, Kathmann N, Wilhelm S, Savage CR. Cognitive retraining for organizational impairment in obsessive-compulsive disorder. Psychiatry Res. 2006; 144:109–116. [PubMed: 17007938]

Cabrera AR, Mcnally RJ, Savage CR. Missing the forest for the trees? Deficient memory for linguistic gist in obsessive-compulsive disorder. Psychol Med. 2001; 31:1089–1094. [PubMed: 11513376]

Catafau AM, Kulisevsky J, Berna L, Pujol J, Martin JC, Otermin P, Balanzo J, Carrio I. Relationship between cerebral perfusion in frontal-limbic-basal ganglia circuits and neuropsychologic impairment in patients with subclinical hepatic encephalopathy. J Nucl Med. 2000; 41:405–410. [PubMed: 10716310]

Chamberlain SR, Fineberg NA, Blackwell AD, Robbins TW, Sahakian BJ. Motor inhibition and cognitive flexibility in obsessive-compulsive disorder and trichotillomania. Am J Psychiatry. 2006; 163:1282–1284. [PubMed: 16816237]

Chan RC, Xu T, Heinrichs RW, Yu Y, Wang Y. Neurological Soft Signs in Schizophrenia: A Meta-analysis. Schizophr Bull. 2009

Chang SW, Mccracken JT, Piacentini JC. Neurocognitive correlates of child obsessive compulsive disorder and Tourette syndrome. J Clin Exp Neuropsychol. 2007; 29:724–733. [PubMed: 17896198]

Dazzan P, Murray RM. Neurological soft signs in first-episode psychosis: a systematic review. Br J Psychiatry Suppl. 2002; 43:s50–57. [PubMed: 12271801]

De La Fuente JM, Bobes J, Vizuete C, Bascaran MT, Morlan I, Mendlewicz J. Neurologic soft signs in borderline personality disorder. J Clin Psychiatry. 2006; 67:541–546. [PubMed: 16669718]

Dickstein DP, Garvey M, Pradella AG, Greenstein DK, Sharp WS, Castellanos FX, Pine DS, Leibenluft E. Neurologic examination abnormalities in children with bipolar disorder or attention-deficit/hyperactivity disorder. Biol Psychiatry. 2005; 58:517–524. [PubMed: 16239160]

Dsm-Iv-Tr. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. Washington DC: American Psychiatric Association; 2000.

First, M.; Spitzer, R.; Gibbon, M.; Williams, J. Structured clinical interview for DSM-IV axis I disorders-Patient edition (SCID-I/P). New York: Biometric Research Department, New York Psychiatric Institute; 1995.

Flessner CA, Allgair A, Garcia A, Freeman J, Sapyta J, Franklin ME, Foa E, March J. The impact of neuropsychological functioning on treatment outcome in pediatric obsessive-compulsive disorder. Depress Anxiety. 2010; 27:365–371. [PubMed: 19842168]

Foodman A, Mcphillips K. ADD and soft signs. J Am Acad Child Adolesc Psychiatry. 1996; 35:841–842. [PubMed: 8768341]

Gilbert AR, Keshavan MS, Diwadkar V, Nutche J, Macmaster F, Easter PC, Buhagiar CJ, Rosenberg DR. Gray matter differences between pediatric obsessive-compulsive disorder patients and high-risk siblings: a preliminary voxel-based morphometry study. Neurosci Lett. 2008; 435:45–50. [PubMed: 18314272]

Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, Heninger GR, Charney DS. The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch Gen Psychiatry. 1989; 46:1006–1011. [PubMed: 2684084]

Greisberg S, Mckay D. Neuropsychology of obsessive-compulsive disorder: a review and treatment implications. Clin Psychol Rev. 2003; 23:95–117. [PubMed: 12559996]

Grisham JR, Anderson TM, Poulton R, Moffitt TE, Andrews G. Childhood neuropsychological deficits associated with adult obsessive-compulsive disorder. Br J Psychiatry. 2009; 195:138–141. [PubMed: 19648544]

Gurvits TV, Gilbertson MW, Lasko NB, Tarhan AS, Simeon D, Macklin ML, Orr SP, Pitman RK. Neurologic soft signs in chronic posttraumatic stress disorder. Arch Gen Psychiatry. 2000; 57:181–186. [PubMed: 10665621]

Hertzig ME. Neurological ‘soft’ signs in low-birthweight children. Dev Med Child Neurol. 1981; 23:778–791. [PubMed: 7198596]

Hollander E, Kaplan A, Schmeidler J, Yang H, Li D, Koran LM, Barbato LM. Neurological soft signs as predictors of treatment response to selective serotonin reuptake inhibitors in obsessive-compulsive disorder. J Neuropsychiatry Clin Neurosci. 2005; 17:472–477. [PubMed: 16387985]

Hollander E, Schiffman E, Cohen B, Rivera-Stein MA, Rosen W, Gorman JM, Fyer AJ, Papp L, Liebowitz MR. Signs of central nervous system dysfunction in obsessive-compulsive disorder. Arch Gen Psychiatry. 1990; 47:27–32. [PubMed: 2294853]

Hymas N, Lees A, Bolton D, Epps K, Head D. The neurology of obsessional slowness. Brain. 1991; 114(Pt 5):2203–2233. [PubMed: 1933242]

Leckman JF, Riddle MA, Hardin MT, Ort SI, Swartz KL, Stevenson J, Cohen DJ. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry. 1989; 28:566–573. [PubMed: 2768151]

Leckman JF, Sholomskas D, Thompson WD, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis: a methodological study. Arch Gen Psychiatry. 1982; 39:879–883. [PubMed: 7103676]

Leonard HL, Swedo SE, Lenane MC, Rettew DC, Hamburger SD, Bartko JJ, Rapoport JL. A 2- to 7-year follow-up study of 54 obsessive-compulsive children and adolescents. Arch Gen Psychiatry. 1993; 50:429–439. [PubMed: 8498877]

Mataix-Cols D, Alonso P, Hernandez R, Deckersbach T, Savage CR, Manuel Menchon J, Vallejo J. Relation of neurological soft signs to nonverbal memory performance in obsessive-compulsive disorder. J Clin Exp Neuropsychol. 2003; 25:842–851. [PubMed: 13680461]

Mayoral M, Bombin I, Zabala A, Robles O, Moreno D, Parellada M, Ruiz-Sancho A, Arango C. Neurological soft signs in adolescents with first episode psychosis: two-year followup. Psychiatry Res. 2008; 161:344–348. [PubMed: 18990454]

Menzies L, Chamberlain SR, Laird AR, Thelen SM, Sahakian BJ, Bullmore ET. Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: the orbitofronto-striatal model revisited. Neurosci Biobehav Rev. 2008; 32:525–549. [PubMed: 18061263]

Negash A, Kebede D, Alem A, Melaku Z, Deyessa N, Shibire T, Fekadu A, Fekadu D, Jacobsson L, Kullgren G. Neurological soft signs in bipolar I disorder patients. J Affect Disord. 2004; 80:221–230. [PubMed: 15207935]

Osterrieth PA. Filetest de copie d'une figure complex: Contribution a l'etude de la perception et de la memoire. Archives de Psychologie. 1944; 30:286–356.

Pauls DL, Alsobrook JP 2nd, Goodman W, Rasmussen S, Leckman JF. A family study of obsessive-compulsive disorder. Am J Psychiatry. 1995; 152:76–84. [PubMed: 7802125]

Pine DS, Wasserman GA, Fried JE, Parides M, Shaffer D. Neurological soft signs: one-year stability and relationship to psychiatric symptoms in boys. J Am Acad Child Adolesc Psychiatry. 1997; 36:1579–1586. [PubMed: 9394943]

Prikryl R, Ceskova E, Kasparek T, Kucerova H. Neurological soft signs and their relationship to 1-year outcome in first-episode schizophrenia. Eur Psychiatry. 2007; 22:499–504. [PubMed: 17614262]

Pujol J, Soriano-Mas C, Alonso P, Cardoner N, Menchon JM, Deus J, Vallejo J. Mapping structural brain alterations in obsessive-compulsive disorder. Arch Gen Psychiatry. 2004; 61:720–730. [PubMed: 15237084]

Radua J, Mataix-Cols D. Voxel-wise meta-analysis of grey matter changes in obsessive-compulsive disorder. Br J Psychiatry. 2009; 195:393–402. [PubMed: 19880927]

Rauch SL, Savage CR. Neuroimaging and neuropsychology of the striatum. Bridging basic science and clinical practice. Psychiatr Clin North Am. 1997; 20:741–768. [PubMed: 9443348]

Rey A. L'examen psychologique dans les cas d'encephalopathie traumatique. Archives de Psychologie. 1941; 28:215–285.

Sas_Institute_Inc. SAS version 9.2. Cary, NC: SAS Institute Inc.; 2008.

Savage CR, Baer L, Keuthen NJ, Brown HD, Rauch SL, Jenike MA. Organizational strategies mediate nonverbal memory impairment in obsessive-compulsive disorder. Biol Psychiatry. 1999; 45:905–916. [PubMed: 10202579]

Savage CR, Rauch SL. Cognitive deficits in obsessive-compulsive disorder. Am J Psychiatry. 2000; 157:1182–1183. [PubMed: 10873941]

Saxena S, Rauch SL. Functional neuroimaging and the neuroanatomy of obsessive-compulsive disorder. Psychiatr Clin North Am. 2000; 23:563–586. [PubMed: 10986728]

Scahill L, Riddle MA, Mcswiggin-Hardin M, Ort SI, King RA, Goodman WK, Cicchetti D, Leckman JF. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. J Am Acad Child Adolesc Psychiatry. 1997; 36:844–852. [PubMed: 9183141]

Schultz RT, Carter AS, Gladstone M, Scahill L, Leckman JF, Peterson BS, Zhang H, Cohen DJ, Pauls D. Visual-motor integration functioning in children with Tourette syndrome. Neuropsychology. 1998; 12:134–145. [PubMed: 9460741]

Shaffer D, Schonfeld I, O'connor PA, Stokman C, Trautman P, Shafer S, Ng S. Neurological soft signs. Their relationship to psychiatric disorder and intelligence in childhood and adolescence. Arch Gen Psychiatry. 1985; 42:342–351. [PubMed: 3977551]

Simpson HB, Rosen W, Huppert JD, Lin SH, Foa EB, Liebowitz MR. Are there reliable neuropsychological deficits in obsessive-compulsive disorder? J Psychiatr Res. 2006; 40:247–257. [PubMed: 15950242]

Stewart SE, Geller DA, Jenike M, Pauls D, Shaw D, Mullin B, Faraone SV. Long-term outcome of pediatric obsessive-compulsive disorder: a meta-analysis and qualitative review of the literature. Acta Psychiatr Scand. 2004; 110:4–13. [PubMed: 15180774]

Szeszko PR, Christian C, Macmaster F, Lencz T, Mirza Y, Taormina SP, Easter P, Rose M, Michalopoulou GA, Rosenberg DR. Gray matter structural alterations in psychotropic drug-naive pediatric obsessive-compulsive disorder: an optimized voxel-based morphometry study. Am J Psychiatry. 2008; 165:1299–1307. [PubMed: 18413702]

Tiffen, J. Purdue Pegboard Test. Chicago: Scientific Research Associates; 1968.

Wechsler, D. Wechsler Intelligence Scale for Children, 3rd edition (WISC-III). San Antonio, TX: The Psychological Corporation; 1991.

Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. Biol Psychiatry. 2005; 57:1336–1346. [PubMed: 15950006]

Wilson JJ, Pine DS, Cargan A, Goldstein RB, Nunes EV, Weissman MM. Neurological soft signs and disruptive behavior among children of opiate dependent parents. Child Psychiatry Hum Dev. 2003; 34:19–34. [PubMed: 14518621]

Zohar AH. The epidemiology of obsessive-compulsive disorder in children and adolescents. Child Adolesc Psychiatr Clin N Am. 1999; 8:445–460. [PubMed: 10442225]

Key Points

- Roughly half of children with OCD remit by adulthood with evidence-based treatments.
- We demonstrated that poor fine-motor and visuospatial skills in childhood are associated with the persistence of OCD into adulthood
- Previous research has demonstrated that poor fine-motor and visuospatial skills in childhood are risk factors for the future development of OCD in adulthood.
- Poor fine-motor skills are hypothesized to be a marker for dysfunction in cortico-striatal circuits and have been previously associated with the persistence of a variety of childhood psychopathologies.

Table 1

Demographic Characteristics inParticipants and Non-participants at Childhood Baseline and Adulthood Follow-up.

Demographic	Included Sample	Non-Participants at Adulthood Follow-Up	Non-Participants in Childhood Neuropsychological Testing
N	24	8	20
Gender (% male)	22 (92%)	8 (100%)	12 (60%)
Baseline Childhood Assessment			
Age	11.5 +/- 2.4	10.9 +/- 1.9	12.7 +/- 1.4
OCD Severity	11.4 +/-8.9	15.4 +/- 11.6	11.9 +/- 7.4
Worst-Ever OCD Severity	27.9 +/- 7.5	24.9 +/- 8.9	23.6 +/- 6.7
Tics	18 (75%)	5 (63%)	8 (40%)
ADHD	10 (42%)	3 (37%)	8 (40%)
Primary Hoarding	5 (21%)	1 (13%)	5 (25%)
SRI	22 (92%)	6 (75%)	18 (90%)
Neuroleptics	15 (63%)	5 (63%)	8 (40%)
Alpha-2 Agonists	10 (42%)	2 (25%)	3 (15%)
Psychostimulants	10 (42%)	1 (13%)	5 (25%)
Adulthood Follow-Up Assessment			
Age	19.0 +/- 1.9		23.5 +/- 2.5
OCD Severity	9.7 +/- 9.8		10.6 +/- 7.2
SRI	16 (67%)		10 (50%)
Neuroleptics	4 (17%)		3 (15%)
Alpha-2 Agonists	2 (8%)		0
Psychostimulants	1 (4%)		1 (5%)

Seventy-five percent of eligible participants participated in adulthood follow-up interview. Participants and non-participants in adulthood follow-up assessment did not differ significantly in any demographic characteristics at baseline. Children who did not participate in neuropsychological testing at childhood baseline had a lower rate of comorbid tic disorders than those children who participated (χ^2=5.2, df=1, p=0.02).

Table 2

Association between Childhood Neuropsychological Test Performance and Persistence of OCD Symptoms into Adulthood

	Adjusting for Gender, Age and OCD Severity at Childhood Neuropsychological Testing				Adjusting for Significant Childhood Comorbidities (ADHD and tic disorder)				Additionally Adjusting for Comorbidities and Primary Hoarding Symptoms			
		95% CI				95% CI				95% CI		
Test	**HR**	**Lower**	**Upper**	**p**	**HR**	**Lower**	**Upper**	**p**	**HR**	**Lower**	**Upper**	**p**
Fine-Motor Skill												
Purdue Pegboard Dominant Hand	1.82	0.97	3.41	NS	3.78	1.30	11.02	0.015	3.94	1.28	12.15	0.017
Purdue Pegboard Non-dominant Hand	1.37	0.80	2.33	NS	1.39	0.79	2.44	NS	1.52	0.87	2.65	NS
Purdue Pegboard Bimanual	2.58	1.36	4.91	0.004	4.06	1.71	9.61	0.001	3.67	1.50	8.99	0.005
Visuospaital Skill												
WISC-III Block Design Subscale*	1.25	0.89	1.77	NS	2.05	1.13	3.72	0.019	2.77	1.17	6.60	0.021
RCFT-Copy	0.87	0.47	1.59	NS	0.74	0.33	1.67	NS	0.42	0.11	1.59	NS
Nonverbal Memory												
RCFT- Long-Term Recall	1.47	0.52	4.17	NS	1.10	0.38	3.17	NS	0.89	0.30	2.65	NS
Intelligence												
WISC-III IQ	0.99	0.93	1.04	NS	1.05	0.98	1.13	NS	0.97	0.92	1.03	NS
Visual-Motor Integration												
Beery Visual-Motor Integration Test	1.02	0.97	1.07	NS	1.01	0.96	1.06	NS	1.04	0.96	1.12	NS

This table presents a summary of the association between performance on childhood neuropsychological testing and the persistence of OCD Symptoms into adulthood. Neuropsychological tests in which significant associations were detected in exploratory analyses (p values < 0.05) are shaded in light gray and significant findings for a priori analyses (p values < 0.012) are shaded in dark gray. Hazard Ratios (HR) for each neuropsychological test are presented for Cox proportional hazard models with time to remission as the outcome measure and adjusting for covariates as indicated in the table. HR>1 indicate that poor performance is associated with greater persistence of symptoms into adulthood and HR<1 indicate that good performance is associated with persistence into adulthood.