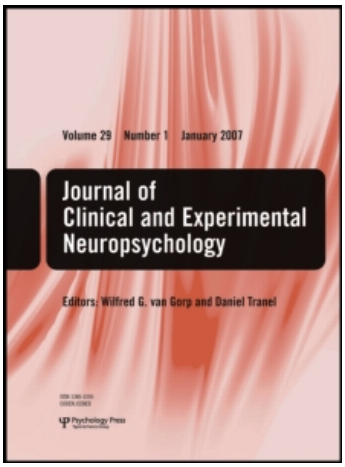

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Neurocognitive correlates of child obsessive compulsive disorder and Tourette syndrome

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Neurocognitive correlates of child obsessive compulsive disorder and Tourette syndrome

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This study investigated the neurocognitive correlates of childhood OCD and TS, which are purported to share frontal–striatal dysfunction. Neurocognitive measures tapping frontal–striatal functions such as executive, attention/memory, and visuomotor abilities were administered to three groups of participants, OCD without comorbid TS (OCD), TS without comorbid OCD (TS), and normal controls. Results suggested that OCD group demonstrated deficits in the area of spatial attention relative to healthy controls. The OCD participants demonstrated no cognitive deficits compared to the TS group. TS participants showed trends towards impairments in the areas of response inhibition, divided attention, and cognitive flexibility relative to the OCD and normal control groups. Spatial attention deficits for the OCD group are partially consistent with adult OCD studies indicating deficits in spatial memory. TS findings were less robust and may be construed tentatively as suggestive of executive function deficits. Future research is needed to delineate the influence of development on neurocognitive deficits associated with OCD and TS.

INTRODUCTION

Obsessive compulsive disorder (OCD) and Tourette syndrome (TS) are multiply linked in the clinical literature on the basis of comorbidity, family genetics, clinical phenomenology, and neurophysiology (Chang & Piacentini, 2002). TS-OCD comorbidity has long been recognized and appears to be bidirectional, with 20–60% of TS patients meeting criteria for OCD, and 20–38% of children with OCD reporting comorbid tics (King et al., 1999). Family genetic studies have suggested a familial relationship between TS and OCD, with findings indicating that some forms of OCD (e.g., child-onset) are part of the TS phenotypic spectrum (Cuker et al., 2004; Grados et al., 2001). Clinical correlates shared by the two disorders include juvenile onset, a chronic fluctuating course, familial occurrence, unintentional repetitive behaviors, stress reactivity, and overlapping sites of neuroanatomical dysfunction (Sheppard et al., 1999).

Neurocognitive investigations have provided evidence, albeit inconsistent, to indicate executive function deficits, most notably frontal–striatal dysfunction, in both disorders. Given such overlap in phenomenology, genetics, and pathophysiology, the specificity of neurobiological markers for TS and OCD still remains to be fully established. The present study attempted to address this issue in part by investigating the neurocognitive correlates specific to OCD and TS while controlling for each disorder's comorbidity with the other, with the goal of clarifying the extent to which these disorders may share a common underlying pathophysiology.

Adult imaging studies suggest that OCD and TS both involve the neuropathology of frontal–striatal pathways (Peterson et al., 1993; Schwartz et al., 1996). Functional imaging studies with OCD strongly suggest abnormalities in the orbitofrontal cortex, anterior cingulate gyrus, caudate nucleus, and thalamus; structures linked along the well-described orbitofrontal circuit (Jenike et al., 1996).

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In contrast, the sensorimotor corticostriatal circuit may be more fundamentally involved in the pathology of TS, with putamenal abnormalities signaling a more severe manifestation of the illness (Peterson et al., 2001).

Neuropsychological studies examining adult patients with frontal–striatal system dysfunction (e.g., Parkinson's and Huntington's diseases) indicate that cognitive impairments lie in the domains of visuospatial, memory, and executive functions (Rauch & Savage, 1997). There is a sizable body of literature with adult OCD patients indicating impairments in multiple cognitive domains consistent with this model of frontal–striatal dysfunction. With regard to executive deficits, adult OCD patients have shown slowed reaction time (Christensen et al., 1992), impaired motor initiation and execution (Purcell et al., 1998), deficits in word fluency, controlled attention, abstract reasoning, cognitive flexibility (Cavedini et al., 1998; Schmidtke et al., 1998), and response inhibition (Bannon et al., 2002; Hartston & Swerdlow, 1999) with response inhibition and memory deficits most consistently noted. The most notable deficits appear to be in spatial working memory and delayed nonverbal recall (Purcell et al., 1998; Savage et al., 1999), although deficits in verbal delayed recall have also been reported (Savage & Rauch, 2000). Impaired memory performance is most likely attributable to poor organization at encoding (Savage & Rauch, 2000; Savage et al., 2000a) rather than a primary memory deficit.

Only two studies examining the neurocognition of childhood OCD have been published to date. Behar et al. (1984) found spatial-perceptual deficits similar to frontal lobe lesion patients in OCD adolescents relative to controls. More recently, however, Beers et al. (1999) reported that treatment-naïve OCD children evidenced no impairments on an extensive neurocognitive battery including several measures of executive functioning. The small literature and inconsistent findings complicate drawing definitive conclusions about potential neurocognitive deficits in child OCD.

Evidence for neurocognitive deficits in uncomplicated TS is similarly limited, with the most compelling data thus far implicating difficulties in response inhibition and visual motor integration (Schultz et al., 1999). Casey et al. (2002) showed TS children to exhibit specific deficits in the inhibition of a motor response, possibly giving rise to problems overriding or suppressing inappropriate behaviors. Adults with TS have been found to exhibit impaired Stroop interference (Georgiou et al., 1995) and deficits in visuospatial priming, an experimental measure of response inhibition (Swerdlow et al., 1995). Overall, however, deficits in executive functioning as measured by constructs such as mental flexibility, tracking, and verbal fluency have been variable across studies (Channon et al., 1992; Ozonoff et al., 1994). One of the more reliable findings has been slowed reaction time on continuous performance tasks, suggesting difficulties with sustained attention (Harris et al., 1995; Shucard et al., 1997). Other studies have identified TS-related difficulties in the ability to allocate and shift attentional set (Channon et al., 1992; Silverstein et al., 1995). There is some question of whether attentional and organizational difficulties may underlie impaired visual-graphic performance in TS. Studies utilizing the Rey-Osterreith Complex Figure, a copying task influenced by organizational ability as well as visuomotor integration skills, demonstrated inconsistent results with some indicating significant difference between TS and normal controls, and others suggesting no group difference (Randolph et al., 1993; Sutherland et al., 1982).

Findings in the TS memory domain have also been variable. Stebbins and colleagues (1995) demonstrated that adult TS patients without comorbid ADHD were impaired on measures of strategic, working, and procedural memory, implicating deficits in both explicit and implicit memory systems. However, Channon et al. (2003) found no evidence of implicit or explicit memory impairment associated with TS in their study.

Although the focus of increased interest, research examining the specificities of OCD and TS neurocognition remains characterized by methodological limitations, and consequently, inconsistent findings. For example, large age effects have often confounded the direct comparison of individual OCD and TS studies. Of perhaps greater importance, most studies have failed to adequately account for OCD-TS comorbidity, thereby limiting the certainty with which observed neurocognitive impairments can be specifically attributed to one disorder or the other. This is a critical omission given a growing body of evidence suggesting that the phenomenology and/or associated cognitive status of OCD and TS can differ depending on the presence or absence of the other disorder or other comorbid conditions (Hanna et al., 2002; Ozonoff et al., 1998).

Despite inconsistencies in the emerging neurocognitive profile of OCD and TS, sufficient evidence exists currently to suggest dysfunction in the frontal–striatal circuits reflected in impairments in visuospatial, memory and executive function abilities. In order to adequately assess underlying pathology, however, studies of OCD and TS need to sample from a variety of measures tapping these relevant cognitive domains. To date, no study has directly compared participants with TS and OCD

on neurocognitive measures sensitive to frontal–striatal system dysfunction while controlling for each disorder's comorbidity with the other. We hypothesized that participants with either TS or OCD but not both would evidence poorer performance overall on measures tapping executive, memory, and visuospatial abilities relative to healthy controls. Furthermore, we proposed that the TS group would show greater impairment on visuospatial/motor abilities than the OCD group, likely reflecting greater involvement of the sensorimotor frontal–striatal circuits. The OCD group was hypothesized to evidence greater executive impairments particularly in the area of organizational strategy compared to the TS group, with implications of greater orbital frontal–striatal system involvement similar to adult OCD findings.

METHODS

Participants

Participants consisted of three groups of children: sixteen children who met Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994) criteria for primary OCD but not comorbid TS (OCD group, age range 9–17, 69% male), 15 youths who met DSM-IV criteria for primary TS but not comorbid OCD (TS group, age range 7–14, 67% male), and 15 healthy control participants (Controls, age range 8–17, 77% male). OCD and TS groups were recruited through a university psychiatric clinic specializing in the diagnosis and treatment of childhood OCD, anxiety, and tic disorders. Controls were recruited through posted notices within a major metropolitan hospital. All parents and participants provided written informed consent/assent prior to study participation and the UCLA medical institutional review board approved the study. All participants underwent standardized diagnostic evaluation based on the Anxiety Disorder Interview Schedule for DSM-IV: Child and Parent versions (ADIS-P/C; Silverman & Albano, 1997) supplemented with the Tic Disorder module from the Schedule for Affective Disorders and Schizophrenia for Children (KSADS, fifth revision; Chambers et al., 1985). Additional clinical scales included the Child Yale-Brown Obsessive Compulsive Scale (CYBOCS; Goodman et al., 1991) and the Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989). All interviews were conducted by an experienced clinical child psychologist (SC) with extensive experience in the assessment of childhood OCD and tics. Diagnoses were routinely reviewed and confirmed by a second senior psychologist (JP) or psychiatrist (JM). Diagnostic ambiguities were rare and clarified through consensus discussion.

All participants had Full Scale IQ of 80 or above (Wechsler Intelligence Scale for Children – 3rd revision, WISC-III; Wechsler, 1991). Exclusionary criteria included current substance abuse or primary diagnosis of major depression, and lifetime history of psychosis, substance dependence, head injury, pervasive developmental disorders or serious neurological condition (excluding TS). Psychiatric groups were not taking any psychotropic medications or had been on a stable regimen for at least 4 weeks prior to study participation. Control participants were not taking any psychotropic medications and were free of any psychiatric disorder (verified by the diagnostic interview), neurological disorder, or other significant medical illness.

Measures

The neurocognitive battery was administered and scored by a clinical psychologist with significant experience in child neuropsychological assessment. The battery was administered in one session and the order of the individual tests within the battery was counterbalanced. Encoding and recall conditions of the two memory tests (RCFT, CVLT) did not overlap. The battery consisted of the following instruments:

Executive function measures

The *Object Alternation Test* (Freedman, 1990) assessed response flexibility and ability to maintain cognitive set. The subject was required to guess the location of an object hidden under one of two cups. The object alternated position after each correct response, with the game continuing until 25 correct trials were achieved. Learning criterion achievement was performance of 15 consecutive correct trials. The task has been shown to be sensitive to response flexibility deficits in OCD adults (Gross-Isseroff et al., 1996).

The *Rey-Osterreith Complex Figure Test* (RCFT; Osterreith, 1944) required participants to copy an abstract detailed figure, which was evaluated for organizational strategy according to a scoring system developed by Savage et al. (1999).

The *Stroop Color-Word Test* (Golden, 1978) was used to assess cognitive response inhibition, which has been found to be impaired in adult OCD using this task (Georgiou et al., 1995). The interference score reflected the inhibition of a prepotent response after accounting for baseline processing speed.

Memory and attention measures

The *California Verbal Learning Test for Children* (CVLT-C; Delis et al., 1987) was a list-learning task of verbal memory. We examined total number of words recalled over five learning trials, short- and long-delay free recall, recognition, and semantic clustering scores.

RCFT immediate and delayed recall condition scores were used as measures of subject's nonverbal memory. Drawings were scored for accuracy according to a system developed by Taylor (1991). The focus of accuracy scoring was on construction and visual recall ability rather than organizational skill.

Digit Span from WISC-III (Wechsler, 1991) was used as a measure of immediate verbal memory span.

Finger Windows, a subtest of the Wide Range Assessment of Memory and Learning (WRAML; Adams & Sheslow, 1990), provided a measure of immediate spatial span as well as visual working memory. Participants were asked to reproduce increasingly lengthy visual patterns forwards and backwards.

Auditory Consonant Trigrams (ACT; Stuss, 1984) evaluated divided attention, an aspect of working memory. Participants were verbally presented with three consonants followed by an interference task to prevent explicit rehearsal. After varying time intervals, participants were asked to recall the trigram.

Visuospatial/motor function measures

The *Beery Test of Visual-Motor Integration* (Beery, 1989) was a measure of visual-motor integration, requiring subjects to copy an increasingly complex series of geometric figures.

Coding subtest from the WISC-III (Wechsler, 1991) served as a measure of graphomotor speed and information processing.

Statistical analyses

Group differences were examined using one-way analyses of covariance (ANCOVA), with age and medication as covariates. Significant omnibus effects were followed up with LSD posthoc tests for planned comparisons. In order to address group differences in the rates of ADHD comorbidity, analyses were rerun using a separate ANCOVA employing ADHD as an additional covariate.

Correlation coefficients were used to evaluate relationships among neurocognitive performance, psychiatric symptoms, and clinical variables such as age of illness onset and duration. Data are presented as mean ± standard deviation (SD) unless otherwise specified. All tests are two-tailed and a p value of .01 was used to indicate statistical significance in order to provide some protection against multiple comparisons. Additional efforts to mitigate potential type I errors included the testing of study hypotheses drawn a priori from the existing, primarily adult, literature and cautious interpretation of positive findings, including emphasis on the need for replication studies.

RESULTS

Demographic and clinical characteristics

The three study groups were similar on demographic and clinical characteristics with few exceptions. TS participants were more likely than OCD participants to be on psychotropic medication [46.7 vs. 6.3%; $F(1, 29)=9.76$, $p=.004$]. One OCD subject was taking a SSRI and of the seven TS subjects who were medicated, three were taking catapres, three were on guanfacine, two were on a neuroleptic (risperidone and pimozide), and three were taking a SSRI. The TS group had a significantly younger mean age of illness onset than OCD children (6.9±1.4 vs 10.1±2.5 years; $p<.001$), although the two groups did not differ in terms of illness duration. Table 1 summarizes the characteristics of the sample.

Although TS participants demonstrated slightly higher rates of diagnostic comorbidty than OCD participants (71 vs. 53%), this difference was not statistically significant ($p<.540$). The OCD and TS

TABLE 1
Demographic and clinical characteristics

Characteristic	*TS (N = 15)*	*OCD (N = 16)*	*Control (N = 15)*	*p*
Age at intake	10.6 (2.3)	12.6 (2.6)	11.9 (2.7)	.09
Gender (% Male)	67%	69%	77%	.68
Education (years)	5.4 (2.5)	7.3 (2.6)	6.7 (2.7)	.12
Age at illness onset	6.9 (1.4)	10.1 (2.5)	–	.00
Duration of illness (years)	3.7 (2.3)	2.6 (2.0)	–	.14
Current Medications	46.7% (7/15)	6.3% (1/16)	–	.004
Handedness (% right)	80%	88%	69%	.53
Verbal IQ (Vocabulary)	10.3 (2.9)	11.8 (3.3)	10.3 (1.8)	.28
Performance IQ (Block Design)	11.5 (2.9)	11.4 (2.8)	11.7 (3.8)	.72
CY-BOCS	4.07 (5.1)	20.8 (8.4)	0	.00
YGTSS	24.3 (8.2)	1.8 (3.3)	0	.00

groups did vary significantly, however, in the specific types of comorbidity characterizing each group. OCD participants had higher rates of General Anxiety Disorder (38 vs. 7%; $p = .041$) and depression (25 vs. 0%; $p = .039$), while the TS group had higher rates of ADHD (47 vs. 0%; $p < .001$).

Executive Function (EF)

A group effect was found for the Stroop [$F(2, 41) = 4.93$, $p = .01$] indicating that the TS group performed more poorly than controls on the Color-Word Interference trial of the task. No significant group differences emerged for any other EF measures (see Table 2).

Attention and memory

Significant group differences were found only on Finger Windows. The OCD group performed more poorly than controls on Finger Windows [$F(2, 41) = 7.33$, $p = .002$]. On the ACT, TS children performed more poorly than OCD and control participants [$F(2, 41) = 3.53$, $p = .04$] by recalling fewer letters after an interference task. However, this finding was not significant at $p < .01$. There were no group differences found on other measures of attention and memory including CVLT, RCFT, and Digit Span.

Visual spatial and motor function

The groups did not differ on any visuospatial/motor skill task except Coding [$F(2, 41) = 3.47$, $p = .04$] with the TS group decoding fewer numbers than controls under timed conditions. However, this finding was not significant at $p < .01$.

Repeating the above analyses with ADHD as an additional covariate yielded the same results.

Correlational analyses

There was no relationship between OCD or TS severity as assessed by the CYBOCS and YGTSS, respectively, and neurocognitive performance. However, within the OCD group a significant relationship was found between age of OCD onset and

TABLE 2
Neurocognitive measures by diagnostic group

Neurocognitive Measure	*TS Mean (SD)*	*OCD Mean (SD)*	*Control Mean (SD)*	*p**
Executive Function Measures				
Object Alternation Test				
Learning criterion achieved	1.7 (.49)	1.4 (.50)	1.1 (.35)	.09
RCFT – organization score				
Copy	1.8 (.94)	2.8 (2.0)	1.8 (1.5)	.32
Immediate recall	1.9 (1.4)	3.0 (2.0)	1.9 (1.8)	.28
Delayed recall	1.9 (1.7)	3.3 (1.8)	2.0 (1.6)	.16
Stroop Test				
Interference	27.7[a] (9.9)	34.3[a b] (5.8)	38.1[b] (9.1)	.01[c]
CVLT Semantic Clustering	1.47 (.41)	1.45 (.34)	1.41 (.48)	.56
Memory & Attention				
CVLT				
Total, list A	52.3 (8.1)	52.0 (7.1)	53.9 (4.9)	.69
Short-delay free recall	10.7 (2.1)	9.9 (3.3)	11.4 (2.7)	.32
Long-delay free recall	11.4 (2.1)	11.0 (1.4)	11.8 (2.0)	.46
Recognition	14.3 (1.6)	14.6 (.62)	14.7 (.62)	.60
RCFT - accuracy score				
Immediate recall	15.2 (8.8)	16.8 (10.1)	14.5 (9.8)	.79
Delayed recall	15.0 (9.0)	17.0 (9.2)	13.6 (8.9)	.59
ACT – total score	39.1 (11.0)	50.1 (4.6)	49.0 (11.7)	.04
Finger Windows-WRAML	9.8[a b] (3.6)	7.7[a] (2.9)	11.6[b] (2.5)	.002[c]
Digit Span – WISC-III	10.4 (3.9)	10.5 (3.5)	11.3 (3.0)	.74
Visual Spatial/Motor				
RCFT – Copy	28.7 (6.5)	30.9 (6.9)	30.7 (4.9)	.95
VMI – total scaled score	9.1 (1.8)	9.9 (2.8)	10.0 (3.0)	.29
Coding – WISC-III	8.8[a] (1.5)	9.5[a,b] (3.8)	11.5[b] (3.7)	.04

Note: Means with different superscripts [(a b)] are significantly different.
*All p values based on analyses controlling for age at intake and medication status.
[c]$p < .01$ after controlling for ADHD (in addition to age at intake and medication status).

the organization strategy scores for all three of the RCFT conditions (copy: $r=.724$, $p=.002$; immediate delay: $r=.735$, $p=.002$; long delay: $r=.795$, $p=.000$) with earlier age of OCD onset positively related to poorer RCFT organizational score. Neurocognitive status was not significantly correlated with any other demographic or clinical variables within the OCD group nor with any of these variables within the TS group.

DISCUSSION

Neither TS nor OCD participants demonstrated widespread impairments in the domains of visuospatial, memory and executive abilities relative to healthy controls which would serve to indicate frontal–striatal dysfunction. However, both groups did evidence some mild and selective neurocognitive deficits that deserve further attention and comment. The most robust finding was shown by the OCD group who demonstrated a select impairment in visual attention relative to controls but no other comparative deficits with either group. In addition, TS participants were relatively less able to inhibit erroneous but prepotent responses (Stroop interference) than control children. TS children also evidenced a trend towards poorer divided attention (ACT) than both participants with OCD and healthy controls. In addition, given the number of multiple comparisons conducted, the possibility of type I error cannot be excluded.

The relative lack of OCD findings is largely consistent with those of Beers et al. (1999) who found no differences between OCD and healthy children across a variety of cognitive domains. Neither Beers et al. (1999) nor this study replicated Behar et al. (1984) who uncovered spatial-perceptual deficits in OCD adolescents. However, our finding of impaired visual attention in the OCD group is partially consistent with adult studies indicating deficits in visual attention, memory, and executive functions (Christenson et al., 1992; Head et al., 1989; Purcell et al., 1998). In spite of similar memory measures, however, the present study did not replicate Savage's findings that impairments in episodic verbal and nonverbal delayed memory in adult's with OCD were mediated by deficits in organizational strategy at encoding. It has been proposed that OCD-related neurocognitive deficits may become more manifest as a child's neurodevelopment attains full maturity (Savage et al., 2000). While a significant cognitive spurt occurs around age 12, continued development of attention and memory abilities occur throughout adolescence both behaviorally and physiologically (Anderson et al., 2001; Casey et al., 2000). Executive deficits, which may become more apparent in later adolescence (e.g., organizational difficulties) may be preceded earlier on in the course of the illness by isolated deficits in attention and response inhibition, processes that typically mature earlier in the course of cognitive development. Therefore, emerging deficits in executive function may well mirror the clinical phenomenology of the OCD illness where obsessions are generally preceded by compulsions in younger children. A volumetric MRI study (Sowell et al., 1999, 2001) comparing brain maturation between normal adolescence and young adulthood lends supports for this developmental trend.

Morphometric MRI studies of pediatric OCD suggest abnormal pruning of frontostriatal structures in OCD, with reductions in striatal volumes in pediatric OCD patients indicating an exaggeration of the normal pruning process and increased anterior cingulate volumes representing a delay in pruning mechanisms (Rosenberg et al., 1997, 2000). Neurodevelopmental changes in the ventral prefrontal–striatal circuitry may be early neurobiological markers of the developmental pathogenesis of the illness, and reflect the developmentally mediated network dysplasia that may underlie OCD. The result may include the disruption of the brain functions that underlie ongoing purposive behaviors associated with the prefrontal cortex and its subcortical pathways, such as response inhibition, memory, and procedural learning (Rosenberg & Keshavan, 1998). Our initial data are not inconsistent with this developmental model, although further research with larger and more well-characterized developmental samples is needed to verify such hypotheses. Future investigations should examine whether neurocognitive deficits may reflect the different developmental symptom trajectories of each disorder. Furthermore, research is needed to better understand the relationship between cognitive deficits associated with each condition and the developmental organization and course of the specific corticostriatothalamic circuits that are differentially implicated in OCD and TS. How is the manifestation of cognitive deficits influenced by the developmental stage and maturity of the specific frontal–striatal circuit involved in TS and OCD? Such questions remain to be answered by longitudinal studies of well-characterized OCD and TS cohorts that carefully monitor and compare the development of cognitive deficits and clinical symptoms within the context of normal child development.

The existing literature is mixed in regard to the neurcognitive correlates of TS with some suggesting

little dysfunction associated with uncomplicated TS (e.g., Como, 2001) and others reporting associations with visuomotor integration skills and variable deficits in executive functioning (e.g., Schultz et al., 1991). Controlling for multiple comparisons, TS and control youngsters differed only in terms of the inhibitory deficits associated with the Stroop interference scores. We did not find robust visuomotor deficits particularly after controlling for comorbid conditions such as ADHD. Although the statistical approach used in this study calls for cautious interpretation, the neurocognitive findings revealed for the TS group are more consistent with a picture of minimal cognitive impairment, although mild deficits in executive functioning were also noted.

Researchers have speculated that attention and organizational difficulties may underlie slowed processing speed and reaction times associated with TS (Sheppard et al., 1999). Although we found no group differences in verbal or nonverbal organizational strategies, the TS group did show trends toward worse divided attention and verbal working memory performance, even after controlling for comorbid ADHD, relative to control and OCD participants. The executive and attentional deficit trends found in the present study are somewhat consistent with studies of TS adults indicating difficulties in working memory (Stebbins et al., 1995) and the ability to allocate and shift attentional set (Channon et al., 1992; Silverstein et al., 1995). Inhibitory control difficulties suggested by our TS group are also consistent with previous research (Casey et al., 2002; Georgiou et al., 1995; Swerdlow et al., 1995). Given that TS is often defined by intrusive and maladaptive sensorimotor urges and behaviors, inhibitory processes are likely to be implicated in the neurocognitive dysfunction underlying TS. However, some studies have suggested that uncomplicated TS is not associated with significant executive function impairments (Como, 2001; Mahone et al., 2001). Therefore, TS-related deficits that are uncovered need to be closely examined to ensure they are not attributable to other comorbid disorders such as ADHD.

Although neither the TS nor OCD groups demonstrated the pattern of memory deficits expected of frontal–striatal dysfunction (encoding deficits with intact recognition) and observed in the adult OCD literature (Savage et al., 1999), it is notable that participants in both groups exhibited some signs of attentional or short-term memory disturbance, which may be a precursor to more significant memory deficits in later development. Future studies may benefit from examining procedural as well as declarative memory processes given recent evidence that suggest procedural memory deficits for both TS and OCD (Deckersbach et al., 2002; Marsh et al., 2004).

Based upon the current OCD literature, it remains to be determined whether child and adult OCD are different disease processes or are developmental manifestations of the same underlying condition. It is interesting to note, however, the correlation between RCFT organization scores and age of illness onset (but not with illness duration) within our OCD group, which indicates younger age of onset is related to poorer organization scores. Such findings hint at the heterogeneous nature of OCD, suggesting that a subset of child OCD with younger illness onset may represent a more severe form of the condition. However, adult patients with childhood versus adult onset of OCD symptoms were shown not to differ on the same measures of verbal and nonverbal strategic memory (CVLT and RCFT) (Henin et al., 2001). This study acknowledged, however, that retrospective self-reports of age of onset made it difficult to gauge their accuracy. Juvenile-onset OCD has been distinguished from adult-onset OCD by stronger familial loading, male predominance, and higher rates of tics and neurological symptoms (Geller et al., 1998). Despite the demonstrated relevance of age at onset, the effects of this variable on neurocognitive functioning are still unclear, particularly within the full course of child development.

Despite notable group differences in rates of ADHD and medication treatment, neurocognitive status was not associated with illness severity, onset, duration, medication status, or comorbidity. Given multiple studies documenting executive function deficits associated with ADHD (Como, 2001; Mahone et al., 2001; Mostofsky et al., 2001), it would not have been surprising to have uncovered more robust cognitive findings in the TS group, but this was not the case. Although, the TS group had significantly higher rates of ADHD and medication usage than the OCD group, the two groups had similar levels of illness severity as measured by CYBOCS and YGTSS. Furthermore, utilizing comorbid ADHD and medication usage as covariates did not significantly change our findings, suggesting that at least in our sample, neurocognitive results were not strongly influenced by group differences on these two variables.

Limitations and future directions

Although the present study is characterized by several design strengths including the use of a well-characterized sample, controls for comorbid OCD, TS, and ADHD, and a carefully-selected neuropyschological assessment battery sensitive to

frontal–striatal dysfunction, a number of limitations must be noted. The primary limitation relates to the relatively small sample size and its constraint on statistical power. Although some steps were taken to mitigate the risk of type I error, we chose to emphasize protection against type II error given the relative dearth of comparable studies comparing OCD and TS participants uncomplicated by the other disorder. As a result, both positive and negative findings should be interpreted with caution and require replication in larger equally-well characterized samples. The study would also have benefited from the inclusion of a separate ADHD group given the high rates of ADHD comorbidity with OCD and TS in this and other samples. The lack of a separate ADHD group made it more difficult to parse out which deficits could be uniquely attributable to each of the disorders of interest. An additional limitation was that the neurocognitive examiner was not blind to patient diagnostic status. However, potential biases related to the lack of blindness were at least partially mitigated by the fact that all neurocognitive measures were administered according to standardized administration procedures.

Finally, the possibility also exists that that the study cognitive assessment battery may have also lacked sufficient sensitivity and specificity to detect subtle deficits associated with early expression of OCD. For example, measures such as the CVLT and RCFT may be too complex and require too broad an array of cognitive skills to adequately assess what precise cognitive processes are implicated in the performance of a developing child. Tests that are not only sensitive to adult–child differences, but also to the important developmental leaps that occur over the entire course of childhood may be needed to accurately assess the full progression of these disorders. It may be worthwhile to investigate the relationship between neurocognitive deficits and each disorder's symptom trajectory in the context of the developmental course and organization of the frontal–striatal circuits implicated in OCD and TS. Such questions remain to be addressed by longitudinal studies of well-characterized OCD and TS cohorts that will carefully monitor and compare the development of cognitive deficits and clinical symptoms within the context of normal child development.

Although requiring replication, the present study adds to a small, yet growing literature regarding the specific neurocognitive correlates of OCD and TS. Continued work in this area has the potential to enhance our understanding of the etiology and developmental course of these disorders. Furthermore, ongoing efforts to establish characteristic neurocognitive profiles for OCD and TS will continue to provide the basis for increasingly sophisticated translational trials examining the neurocognitive mechanisms and predictors of treatment response, and serve to advance ongoing endophenotypic approaches to understanding the genetics of these disorders.

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