Obsessive-Compulsive Symptoms among Children in the Adolescent Brain and Cognitive Development Study: Clinical, Cognitive, and Brain Connectivity Correlates

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Abstract

Background.—Childhood obsessive-compulsive symptoms (OCS) are common and can be an early risk marker for Obsessive-Compulsive Disorder (OCD). The Adolescent Brain and Cognitive Development (ABCD) Study provides a unique opportunity to characterize OCS in a large, normative sample of school-age children and to explore cortico-striatal and task-control circuits implicated in pediatric OCD.

Method.—The ABCD Study acquired data from 9–10-year-olds (N=11,876). Linear mixed-effects models probed associations between OCS (Child Behavior Checklist) and cognition (NIH Toolbox), brain structure (subcortical volume, cortical thickness), white matter (diffusion tensor imaging), and resting-state functional connectivity.

Results.—OCS scores showed good psychometric properties, high prevalence, and related to familial/parental factors, including family conflict. Higher OCS related to better cognitive performance (b=0.06, t(9966.60)=6.28, p<.001, η^2_p=0.01), particularly verbal, when controlling for ADHD, which related to worse performance. OCS did not significantly relate to brain structure but did relate to lower superior cortico-striate tract fractional anisotropy (b=−0.03, t=−3.07, p=.002, η^2_p=0.02). Higher OCS related to altered functional connectivity, including weaker within dorsal attention network connectivity (b=−0.04, t(7262.87)=−3.71, p<.001, η^2_p=0.002) and weaker dorsal attention-default mode anti-correlation (b=0.04, t(7251.95)=3.94, p<.001, η^2_p=0.002). Dorsal attention-default mode connectivity predicted OCS at 1-year (b=−0.04, t(2407.61)=−2.23, p=.03, η^2_p=0.03).

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Conclusions.—OCS are common and may persist throughout childhood. Cortico-striatal and attention network connectivity are likely mechanisms in the subclinical-to-clinical spectrum of OCS. Understanding correlates and mechanisms of OCS may elucidate their role in childhood psychiatric risk and suggest potential utility of neuroimaging, e.g. dorsal attention-default mode connectivity, for identifying children at increased risk for OCD.

Keywords

OCD; MRI; DTI; dorsal attention network; children; ABCD

Introduction

Subclinical obsessive-compulsive symptoms (OCS) in childhood predict increased risk for Obsessive-Compulsive Disorder (OCD) diagnosis in adulthood (odds ratio [OR]~5–10) (1). Critically, OCS are common in children and adolescents and, even below clinical threshold, associate with impairment and comorbidity (1–7). Childhood OCS exhibit moderate stability, with some ebb and flow within-individuals over development (4, 8). Cross-sectional research generally suggests greater OCS prevalence in mid vs. early childhood, (3) whereas longitudinal work indicates weak persistence of OCS during this developmental period (4, 8). Uncovering neural and cognitive mechanisms underlying OCS and their variable course over childhood OCS could help improve early identification of children most at risk for OCD.

Few pediatric studies have examined neural or cognitive mechanisms underlying OCS or subsequent OCD risk. Several relatively small studies in healthy adults associate OCS with executive function deficits, e.g. cognitive flexibility (9, 10), spatial problem (11, 12), and response inhibition (13); c.f. (14). Likewise, few pediatric studies have related OCS to brain structure and function. Among 255 healthy 8–12-year-olds, overall OCS scores did not associate with voxel-based morphometry, whereas subscales showed differential associations, e.g. ordering symptoms vs. doubt-checking symptoms (15). Among 1,938 healthy adolescents from the IMAGEN study, compulsive behaviors (including OCD and eating disorder symptoms) associated with greater ventral striatal, orbitofrontal, and dorsolateral prefrontal cortex gray matter volume (16).

While much work suggests that disruptions in cortico-striatal-thalamo-cortical (CSTC) circuits are central to OCD pathophysiology, e.g. (17), leading to deficits in controlling obsessions and urges to perform rituals, emerging evidence highlights broader circuit alterations, e.g. (18). Particularly, meta-analytic work suggests OCD-related alterations in connectivity within and between executive, salience, and default mode networks (DMN) (19) in line with a proposed triple network model of psychopathology. (20) Furthermore, reviews examining research on pediatric OCD highlight structural, functional, and connectivity alterations in both fronto-striatal and task-control neural circuits (21–23). For example, findings from our group suggest alterations in cingulo-opercular structural connectivity (24) and functional connectivity between default mode network (DMN) and task-positive network regions in pediatric OCD (25). The ENIGMA OCD consortium noted

larger thalamic volumes (26) (*N*=201 healthy controls vs. *N*=103 unmedicated OCD) and thinner parietal cortices (27) in youth with OCD compared to healthy controls.

Large, normative studies are a critical and powerful approach to study childhood OCS in the population. The Adolescent Brain and Cognitive Development (ABCD) Study is one such study, which provides a unique opportunity to characterize OCS in 9–10-year-old children (*N*=11,876). ABCD is the largest, publicly accessible, prospective study of school-age child sampled with minimally restrictive exclusion criteria across the USA to collect harmonized neuroimaging data. This study yields several advantages in addressing our questions of interest, including sufficient power to identify even small effect sizes and to address heterogeneity in a normative population, compared to studies like the Pediatric Imaging, Neurocognition, and Genomics Study (PING) or Healthy Brain Network (HBN), both of which sample restricted geographic areas and less focal age ranges, or the ENIGMA Consortium which conducts meta-/mega-analyses on unharmonized data collected across multiple sites.

Given prior data, we expected that OCS in the ABCD sample would exhibit a ~5–10% prevalence above established cutoff scores (28, 29), minimal sex differences or a slight male preponderance (3, 4, 6, 8, 28), significant familiality (8), and greater longitudinal risk for poor psychiatric outcomes (1). We further expected that higher OCS scores would relate to lower executive functioning (9–13), smaller thalamic volumes (26) and thinner parietal cortices (27), as well as altered structural and functional connectivity within task-control circuits and between task-control networks and the DMN (21–25). In longitudinal analyses, we examined whether neural and cognitive factors associated with OCS at baseline also predicted change in OCS over development. Finally, we explored effects of comorbid ADHD on brain and behavioral correlates of OCS given the high prevalence of ADHD in the ABCD sample and data suggesting both shared and unique neural mechanisms across pediatric ADHD and OCD (30–33).

Materials and Method

Overview.

The ABCD Study is a multi-site study (21 sites across the USA) with the overall goals of: (a) assessing variability in adolescent brain and cognitive development and (b) understanding factors that influence development (34). Using a school-based recruitment strategy (public and private elementary schools), the ABCD Study has collected baseline clinical, questionnaire, behavioral, and neuroimaging data from 9–10-years-olds with ongoing longitudinal assessments (35). Exclusion criteria included lack of English fluency, major medical or neurological conditions, premature birth, MRI contraindication, history of traumatic brain injury, current diagnosis of schizophrenia, moderate/severe autism spectrum disorder, intellectual disability, or alcohol/substance use disorder. The present study examined the second public ABCD data release (version 2.0.1, released July 2019; http://dx.doi.org/10.15154/1503209), which included baseline clinical, questionnaire, cognitive, and neuroimaging data and questionnaire data from the 1-year follow-up assessment.

Assessment.

Children and their parent/guardian completed an extensive battery of clinical interviews, self- and parent-report measures, and neurocognitive tests (36). Measures examined in the current analyses are briefly summarized below (see Table 1 and Supplement). Questionnaires included parent-reported demographics, brief assessments of parent- and child-reported pubertal status (37), and parental/familial measures are summarized in the Supplement (38, 39)(40, 41)(42).

Children and their parent/guardian completed modules of a self-administered, computerized Kiddie-Schedule for Affective Disorders (K-SADS COMP; Table 2) (43–45) to assess children's lifetime (past, present, or partial remission) DSM-5 diagnoses (36). OCD was assessed solely by parent-report on the K-SADS COMP. Composite variables were created to examine lifetime diagnoses of ADHD (parent-report only), depressive disorders (parent- or child-report of major depressive disorder, dysthymia, or an unspecified depressive disorder), anxiety disorders (parent- or child-report of separation anxiety disorder, social anxiety disorder, or generalized anxiety disorder), and externalizing disorders (parent-report of conduct or oppositional defiant disorder).

OCS Measure.

Parents/guardians completed the Child Behavior Checklist (CBCL) (46) to assess their child's emotional and behavioral functioning. Age- and sex-normed T-scores were used for analyses (for high correspondence with raw scores, see Figure S1). Our primary predictor of interest was the 8-item OCS subscale (Table 3) (28, 29, 47–50), c.f. (51, 52). N=4937 participants completed the CBCL at 1-year follow-up as of the 2.0.1 release. We confirmed good psychometrics of the 8-item CBCL OCS subscale (see Supplement), including good fit of a one-factor/unidimensional model (*lavaan* package) (53, 54) and moderate/good internal consistency (*psych* package, standardized Cronbach's alpha=.71, omega=.87) (55). For item-level inter-correlation, see Figure S2. See Supplement and Figure S3 for receiver operator curve analyses (*pROC* package) (56, 57).

Cognition.

Neurocognitive performance was assessed using the NIH Toolbox (58, 59). Total Cognition age-corrected T-scores (M=100, SD=15) were examined as proxy for commonly used full-scale IQ measures (59, 60). This is derived from two verbal measures (Picture Vocabulary, Oral Reading Recognition) and six executive functioning measures (Dimensional Change Card Sort, Flanker, Picture Sequence Memory, List Sorting Working Memory, Pattern Comparison Processing Speed).

Structural Magnetic Resonance Imaging (MRI).

Children completed neuroimaging on GE, Siemens, or Phillips scanners (61). High-resolution T1- and T2-weighted structural MR images (1mm isotropic, prospective motion correction) were processed through ABCD pipelines (61) (including registration, intensity normalization, bias field correction). Structural data that did not pass quality control (QC) procedures performed by ABCD (visual inspection of T1 images and FreeSurfer outputs) (62) were excluded (see Supplement). Herein, we focused on ABCD summary of standard

FreeSurfer v5.3.0 (http://surfer.nmr.mgh.harvard.edu/) (63–66) subcortical volumes and cortical thickness from Destrieux atlas (67) regions of interest (ROI).

Diffusion Tensor Imaging (DTI).

High angular resolution diffusion imaging (1.7mm isotropic) was collected using multiband acquisition (factor=3), 96 diffusion directions, and four b-values (61). Standardized preprocessing included eddy current, head motion, and distortion correction (62). Major white matter tracts were automatically segmented using AtlasTrack (68). Participants whose DTI and structural MRI data did not pass ABCD QC (62) were excluded. Herein, we focused on tract-average factional anisotropy (FA). Supplementary analyses examined mean, longitudinal (or axial), and transverse (or radial) diffusivity (MD, LD, and TD) as well as Restriction Spectrum Imaging (RSI) model parameters (69).

Resting-State Functional Connectivity (RSFC).

Children completed resting-state acquisition during high-resolution (2.4 mm isotropic, TR=800ms) multi-band (factor=6) scanning. Standardized fMRI preprocessing included registration, distortion correction, and normalization. RSFC post-processing included regression of 24 temporally filtered motion parameters, frame-wise displacement (FD)>0.3mm outliers, as well as white matter, cerebral spinal fluid, and whole brain signal (62). Within- and between-network connectivity was extracted from the cortical ribbon parcellated using the Gordon atlas (70), i.e. averaging all connections between ROIs assigned to given networks. Participants whose resting-state and structural MRI data did not pass ABCD QC (62) were excluded. Further, per ABCD suggestions, we excluded participants with <375 frames of good data after motion/outlier regression and excluded data from Philips scanners given a preprocessing issue affecting only functional MRI (identified 12/05/2019). Given our hypotheses, we focused on 28 network-level RSFC averages within and between task-control circuits (cingulo-opercular [CO], cingulo-parietal [CP], dorsal attention network [DAN], fronto parietal [FP], salience network [SN], ventral attention network [VAN]) and the DMN.

Analysis.

Analyses were performed in R v4.0.0 (71). Sample characteristics and group differences as a function of K-SADS lifetime OCD diagnosis were summarized using the *scipub* package (72). Specifically, two-sample *t*-tests were used for continuous variables and χ^2 tests for categorical variables with Cohen's *d* or OR effect sizes, respectively. SOLAR (73) polygenic analyses estimated familiality of OCS scores (see Supplement).

Linear mixed-effects (LME) models (*lme4* package) (74) were used to examine OCS scores (or OCD diagnosis) as predictors of our outcomes of interest, similar to prior work (75). All models included random effects for family nested within acquisition site (or MRI serial number for brain analyses) and fixed-effects covariates for age, sex, race, ethnicity, family income, parental education, parental marital status, pubertal status, and Total Cognition T-scores (except when cognition was the outcome). Structural analyses additionally covaried child height (accounting for overall body size/development), T1 image signal-to-noise, and intracranial volume (ICV) in subcortical analyses. DTI analyses additionally covaried mean

FD. RSFC analyses additionally covaried number of frames retained after processing. Inter-correlations among all covariates noted in Table S1. Standardized beta coefficients and partial eta-squared (η^2_p) (76) effect sizes are presented for all models.

False discovery rate (FDR) was used to correct for multiple comparisons across measures/ROIs within each analysis. For each analysis, participants were excluded for missing data using list-wise deletion. Within the useable sample for each cognition, structural, and DTI analysis, outcome variable outliers >3SD from the mean were Winsorized to the next non-outlier value (trimmed 0.25% most extreme RSFC values instead, per ABCD; see Supplement).

Follow-up Analyses.

Follow-up tests were run to confirm significant effects and address comorbidity. LME models were conducted again with psychotropic medication status and K-SADS depressive, anxious, and ADHD diagnoses as covariates. Given the high rate of ADHD in the ABCD sample (see Results, Table 2) and potential shared/distinct neurocognitive mechanisms between OCD and ADHD (30–33), we also ran separate LME models covarying CBCL DSM-oriented ADHD T-scores. Further analyses comparing children with and without OCD and ADHD as well as propensity-matched (77, 78) groups (from full sample and an unmedicated subset) comparing children with OCD to healthy and clinical controls are detailed in the Supplement.

Longitudinal Analysis.

Longitudinal analyses examined whether cognitive or neural factors associated with baseline OCS also predicted change in OCS at 1-year follow-up. Specifically, we used similar LME models to test whether these factors significantly associated with follow-up OCS over and above baseline OCS and our standard fixed and random effects.

Results

Participants.

Table 1–2 summarize demographic and clinical characteristics of the full sample and comparing by K-SADS OCD diagnosis (see Tables S2–3 comparing by OCS 5). N=1099 (9.41%) children had a lifetime parent-reported diagnosis of OCD, including n=898 (7.68%) current and n=501 (4.29%) past. Lifetime OCD prevalence varied by site (χ^2(21)=59.29, p<.001) from 5.79–13.77%. Yet, site differences (n=10,137, F(21)=1.49, p=.07) were largely accounted for by our demographic covariates in a logistic regression. OCD was more common among children with other psychiatric diagnoses (Table 2, Table S4, OR>1.50, Supplement).

Clinical Correlates of OCS:

A full range of CBCL OCS scores was observed (Figure 1; Table 3); N=5866 (55.7%) children exhibited non-zero scores and n=807 (6.8%) surpassed the suggested 5 threshold for clinically significant symptoms (28, 29). Obsessions, perfectionism, and worries were most commonly endorsed (Table 3). Baseline and 1-year follow-up OCS T-scores were

strongly correlated (r=.61, t(4935)=53.53, 95%CI=[.59,.62], p<.001). OCS T-scores also correlated moderately with counts of current K-SADS OCD symptoms (r=0.42, 95%CI=[.40,.43], t(11851)=50.22, p<.001). See Table S5 for K-SADS OCD symptom endorsement.

As expected, OCS scores were higher among children with vs. without a lifetime OCD diagnosis (Table 1, Figure 1). Supra-threshold OCS 5 were much more common among youth with vs. without an OCD diagnosis (Table 3; N=328/1098 [29.87%] vs. N=770/10,579 [4.39%]; z=23.56, p<.001, OR=8.54), over and above our standard covariates. Similar to predictors of OCD diagnosis (Table S4), higher OCS scores were also observed among participants who were male, White, lower income, or with college-educated parents (Table S2, S6). OCS scores correlated strongly with other CBCL subscales, particularly internalizing and thought problems (all r>.70, t(11862)>106.00, p<.001) likely due to item overlap, relative to ADHD (r=.50, t(11862)=62.38, p<.001) and externalizing subscales (r=.48, t(11862)=60.25, p<.001). Analysis of OCS heritability (~70%) and associations between child OCS and elevated parent self-report OCS, parenting monitoring, and family conflict are detailed in the Supplement.

OCS and NIH Toolbox Cognition:

Higher OCS scores weakly associated with worse performance on the NIH Toolbox Flanker, Card Sort, Working Memory, and Episodic Memory tasks and better Picture Vocabulary performance (all p<.05, FDR-p<.08; Table S7–8). Analyses covarying CBCL ADHD T-scores revealed FDR-corrected associations between higher OCS and *better* Cognition Total scores (b=0.06, t(9966.60)=6.28, p<.001, η^2_p=0.01; Table S7–8), driven by Working Memory, Picture Vocabulary, and Oral Reading scores, whereas ADHD associated with worse performance (b=−0.14, t(9967.11)=−13.90, p<.001, η^2_p=0.03; Table S8). Similar results were observed when controlling for K-SADS lifetime ADHD or medication use (Tables S7–8). See Supplement for results of additional follow-up tests, including better performance among children with lifetime OCD vs. those with ADHD or ADHD and OCD.

OCS and Brain Structure:

No FDR-corrected associations emerged between OCS or lifetime OCD and subcortical volumes or cortical thickness (Tables S9–10; Figure S4; Supplementary Results). Note that effects were similarly non-significant controlling for CBCL ADHD (which was itself a non-significant predictor), though thalamic and hippocampal volumes differed between children with OCD vs. comorbid OCD + ADHD (see Supplement). Among unmedicated children, higher OCS scores related to smaller right accumbens volume (b=−0.02, t(8233.19)=−2.75, p<.001, p-FDR=.08, η^2_p=0.001) but no FDR-corrected effects of OCS or OCD diagnosis were observed on subcortical volumes or cortical thickness.

OCS and White Matter Integrity (DTI):

Examining the 35 AtlasTrack tracts, FDR-corrected results indicated higher OCS scores related to lower FA in in the left superior cortico-striatal tract (SCS; Table S11), particularly in the parietal portion of the left SCS (n=8585, b=−0.03, t(8546.23)=−3.31, p=.001, FDR-p=.03, η^2_p=0.02 Table S12), including when controlling for ADHD scores or medication

status. No significant effects of lifetime OCD were observed on FA in the full sample. However, children with lifetime OCD exhibited lower parietal SCS FA than propensity-matched healthy controls and children with current OCD exhibited higher FA than those with current ADHD (See Supplement, Figure S5).

OCS and Functional Connectivity:

Examining 28 within- and between-network RSFC averages of interest, FDR-corrected associations were detected between OCS and four connections (Figure 2; Table S13). Specifically, higher OCS scores associated with weaker/less positive within-DAN RSFC and weaker/less negative DAN-VAN and DAN-DMN connectivity (Table S11). Higher OCS also related to stronger positive CO-VAN connectivity (which averaged near zero in the full sample, Figure S6). These four FDR-corrected effects were generally robust to follow-up covariates, including ADHD T-scores or medication status (see Supplement). Weaker within-DAN RSFC was also detected in children with OCD relative to healthy and clinical control groups in follow-up analyses (see Supplement). No OCD vs. ADHD or OCD +ADHD subgroup effects were noted for these four connections.

OCS at 1-Year Longitudinal Follow-up:

NIH Toolbox cognition measures and SCS FA, which related to baseline OCS, did not significantly predict change in OCS by 1-year follow-up (p>.05; See Supplement). Of the four RSFC connections significantly associating with baseline OCS, more negative DAN-DMN connectivity predicted worsening OCS at 1-year follow-up (n=3040, b=−0.04, t(2407.61)=−2.23, p=.03, η^2_p=0.03), above and beyond baseline OCS (b=0.61, t(2946,42)=38.89, p<.001, η^2_p=0.36). Note that DAN-DMN connectivity did not significantly predict change in CBCL Internalizing, Thought, or ADHD T-scores at 1-year follow-up (|t|<1.64, p>.10, η^2_p<.001), above and beyond corresponding baseline scores.

Discussion

Herein, we leveraged the large, normative ABCD Study dataset to probe obsessive-compulsive symptoms among 9–10-year-old children across the United States. Complex associations with cognitive performance were detected, specifically higher OCS scores related to better cognitive performance, particularly verbal, only when covarying for ADHD. Though we did not detect associations with brain structure, OCS did relate to differences in structural and functional connectivity of cortico-striatal and attentional circuits implicated in the pathophysiology of OCD. Particularly, altered DAN-DMN connectivity may serve as a marker for longitudinal worsening OCS over childhood. Thus, ABCD allowed for unprecedented analysis of continuous associations between OCS and brain structure/ function in youth and our findings highlight the potential for ABCD to allow the identification of circuit-based neuroimaging markers of OCS/OCD risk.

Supporting prior work, the CBCL OCS subscale showed promising psychometrics, including internal consistency, high heritability (that can be further refined when greater genetic relatedness information is available from ABCD), convergence with K-SADS OCD symptom count, and potential longitudinal stability (8, 28, 29, 47–50). With this measure,

OCS were prevalent among 9–10-year-olds (6.80% with OCS 5; 25.6% with parent-reported obsessions), consistent with prior estimates of 2–10% of youth exhibiting CBCL OCS 5 (28, 29). We noted slightly higher OCS scores among boys than girls (~0.2 raw points, ~0.8 T-score). This has been noted in some prior pediatric work (3, 4, 6, 28) though OCS are more prevalent among females in adulthood (79, 80). As expected, OCS were elevated among children with a diagnosis of OCD, as well as other mood and anxiety disorders, similar to prior adult work (79, 80). Importantly, greater information about longitudinal stability, risk, and comorbidity can be determined when later waves of follow-up are available from ABCD. Furthermore, supplemental analyses linked OCS to familial conflict, a potential indicator of impairment and reduced quality of life that is often associated with OCS (1, 2, 81). Future longitudinal ABCD analyses could better parse parental/familial factors as potential causes or consequences of OCS.

Next, we identified associations between OCS and cognitive performance, though complicated by comorbid ADHD symptoms. ADHD severity related to worse performance on NIH Toolbox measures; given strong correlations with OCS, ADHD likely masked/confounded associations between OCS and cognition. Note that this is difficult to parse fully as ADHD-OCS correlations likely reflect both method variance (i.e. both parent-report CBCL) and actual underlying symptom comorbidity. Nonetheless, when covarying (or excluding) ADHD, OCS related to better Total Cognition scores, driven by verbal performance, though effect sizes were small. OCS was unassociated with executive function deficits, inconsistent with prior work typically examining small samples of young adults (n<40 with OCS) (9, 11–13), potentially due to differences in sample characteristics (e.g., undergraduate sampling) or the types of executive functions measured, e.g. more in-depth behavioral assessments of goal-directed behavior (two-step reinforcement learning task) related to compulsivity dimensionally in adults (82). Though the NIH Toolbox measures provide robust and reliable estimates of executive function, scores generally represent a scaled composite of accuracy and reaction time (58–60, 83). This approach may not probe differential cognitive functions with optimal specificity, e.g. examining rule-switch vs. rule-repeat trials on the Card Sort to examine cognitive inflexibility (84). Additionally, as prior young adult OCS studies generally did not control for attentional problems (9, 11–13), our findings may underscore the need for thorough evaluation of potential transdiagnostic symptoms (e.g., inattention due to ADHD vs. due to intrusive obsessions).

Significant associations between OCS and brain structure were not detected. Expected associations with thalamic volumes, given ENIGMA findings in pediatric OCD (26), did not emerge from examination of OCS continuously or OCD diagnosis categorically, perhaps due to differences in MRI acquisition or sampling as ENIGMA meta-/mega-analyzed data collected from varying protocols across 1.5T and 3T studies with different demographic and clinical inclusion/exclusion criteria. In addition, the pediatric participants included in the ENIGMA analyses were older than the 9–10-year-olds in ABCD (age means across studies=11.2–15.7 years). Thus, structural correlates of OCS should indeed be examined in the ABCD sample in future longitudinal waves as the children get older. Expected effects in parietal cortices (27) were also not replicated. Instead, we detected other significant but uncorrected cortical effects of OCS in the ABCD data, e.g. thinner ACC, thicker inferior

frontal gyrus. Effects were small in magnitude but could be examined further with vertex-wise analyses and over development when longitudinal MRI data is available.

We detected significant associations between OCS and white matter microstructure, specifically, lower FA in the left superior cortico-striatal (SCS) tract. This finding is consistent with models highlighting CSTC circuits as central to OCS pathophysiology (85, 86) and with our prior work using a streamline-based approach in youth with OCD, suggesting reduced CSTC connectivity between ACC and both the thalamus and putamen (24). DTI studies in pediatric OCD have been sparse and small (generally n<40 patients), but often suggest *greater* FA in several tracts, including the cingulum (87–89) and corpus callosum (87–91) cf. (92) and greater axial and radial diffusivity in the anterior thalamic radiations (91). Herein, the right SCS, parahippocampal cingulum, anterior thalamic radiation, and fornix showed only uncorrected, small effects towards greater FA with higher OCS. Future work could parse specificity within cortico-striatal tracts given previously suggested dissociable roles of cortico-striatal tracts in balancing habitual and goal-direction action, potentially underlying vulnerability for OCS (93).

Finally, we detected significant associations between OCS and resting-state functional connectivity. Particularly, higher OCS related to less positive within-DAN and less negative DAN-VAN and DAN-DMN connectivity, as well as more positive CO-VAN connectivity. The DAN is a network of frontal and partial regions, including the frontal eye fields and intraparietal parietal sulcus, related to top-down, goal directed processing (94) and to selective attention in children (95). Altered connectivity between DAN and DMN regions has been implicated previously in adult (96) and pediatric OCD (25) and suggests that an imbalance between task positive and negative networks may underlie OCD pathophysiology. Critically, more negative DAN-DMN connectivity predicted worsening OCS at 1-year follow-up, possibly representing a marker of OCS risk; stability and specificity of this can be further probed with later waves of ABCD.

ABCD characterizes a normative, heterogenous sample of children with acquisition harmonized across sites/scanners, all strengthening the generalizability of results. Yet, several limitations and caveats to the current analyses should be noted. First, only one measure of OCS (and OCD) was available from one parent/guardian. Parent-report of symptoms is inherently limited to observable signs (e.g., behaviors or observable expressions of emotion), whereas internal/subjective experience may be better captured by self-report, e.g. experience of intrusive thoughts. Focusing on parent-report from the computerized, self-administered K-SADS may also relate to the relatively high rates of lifetime OCD diagnosis (5.79–13.77% across sites) relative to clinician interviews in epidemiological studies; alternatively, this may reflect some aspect of study sampling. In the future, having more in-depth assessments of OCS from multiple informants would be highly informative, particularly self- and clinician-report. Having multiple measures and informants could also relieve method variance issues and help disentangle OCS and ADHD effects. Second, large sample sizes increase power to detect small effects as statistically significant (e.g. >80% power to detect r>.025 with N=11,876). Note that a partial eta-squared (η^2_p)~0.01–0.02 is considered small (97)–characterizing the variance explained by a given variable (of variance unexplained by other predictors, converging on R^2 in a one-predictor

model). For example, OCS related to higher (b=0.06, η^2_p=0.006), whereas ADHD scores related lower NIH cognition scores (b=−0.14, η^2_p=0.028), yet both were $p<5\times10^{-10}$. Though both effects were small, we can determine that cognition associated with ADHD at several times the magnitude but in the opposite direction of OCS. Whereas current effect sizes may be hard to detectable in smaller, normative samples, they may emerge more readily in clinically severe samples. Relatedly, though we focused on OCS, certain covariates had larger effects of note, e.g. age strongly related to SCS FA (η^2_p=0.130 vs. η^2_p=0.002 for OCS). A large number of covariates/other measures of interest that can potentially influence brain volume, including psychotropic medication status, which we examined herein. Finally, there is a great deal of flexibility in analyzing MRI data (98), with diverse pre-/post-processing options having a potential large effect on the outcome, e.g. (99–101). Global signal regression (GSR) is a particularly contentious issue for RSFC, e.g. (102–104), with potential benefits to confound removal and potential issues in anticorrelation induction. For reproducibility and transparency, we have focused on the released ABCD data which includes GSR. Thus, the current RSFC results must be interpreted in this context while future work could aim to replicate them without GSR.

Overall, we characterized OCS and associated clinical, cognitive, and neural correlates in a large, normative sample of 9–10-year-olds. Results highlight structural and functional connectivity of cortico-striatal and attentional circuits as potential mechanisms of interest and DAN-DMN connectivity as a potential predictor of longitudinal risk for worsening OCS. Future work can expand upon this to provide greater characterization of these circuits over development with forthcoming longitudinal ABCD data and to probe the utility of targeting these circuits in future clinical trials aimed at preventing the development of OCD in youth.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements.

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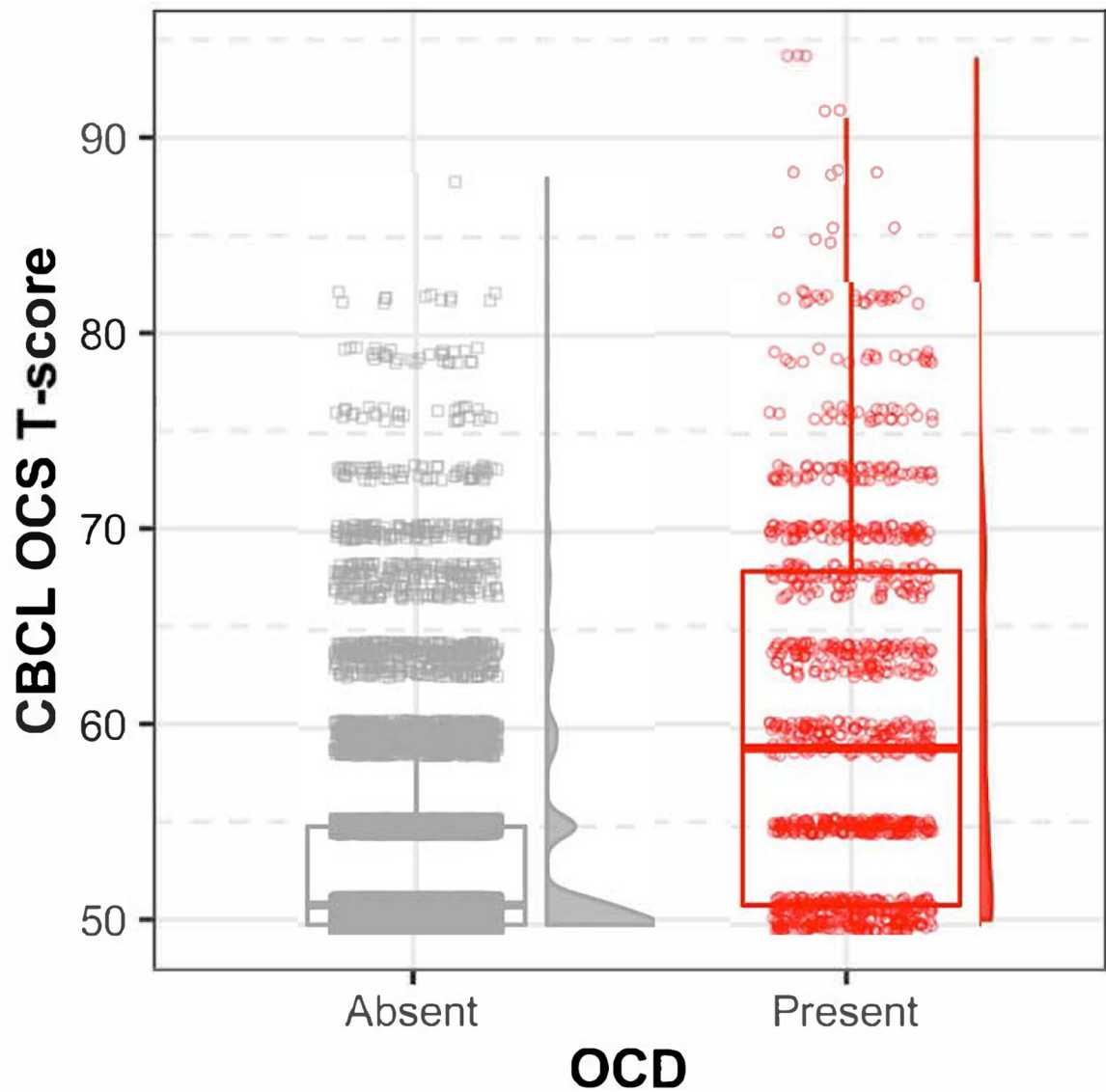
Figure 1: CBCL OCS T-scores split by the presence/absence of lifetime OCD
Scatter plot, boxplot, and histograms indicate the distribution of Child Behavior Checklist
(CBCL) obsessive-compulsive symptom (OCS) T-scores for the full ABCD study sample.
Scores are split based on the absence (gray square) or presence (red circle) of a lifetime
Obsessive-Compulsive Disorder (OCD) diagnosis.
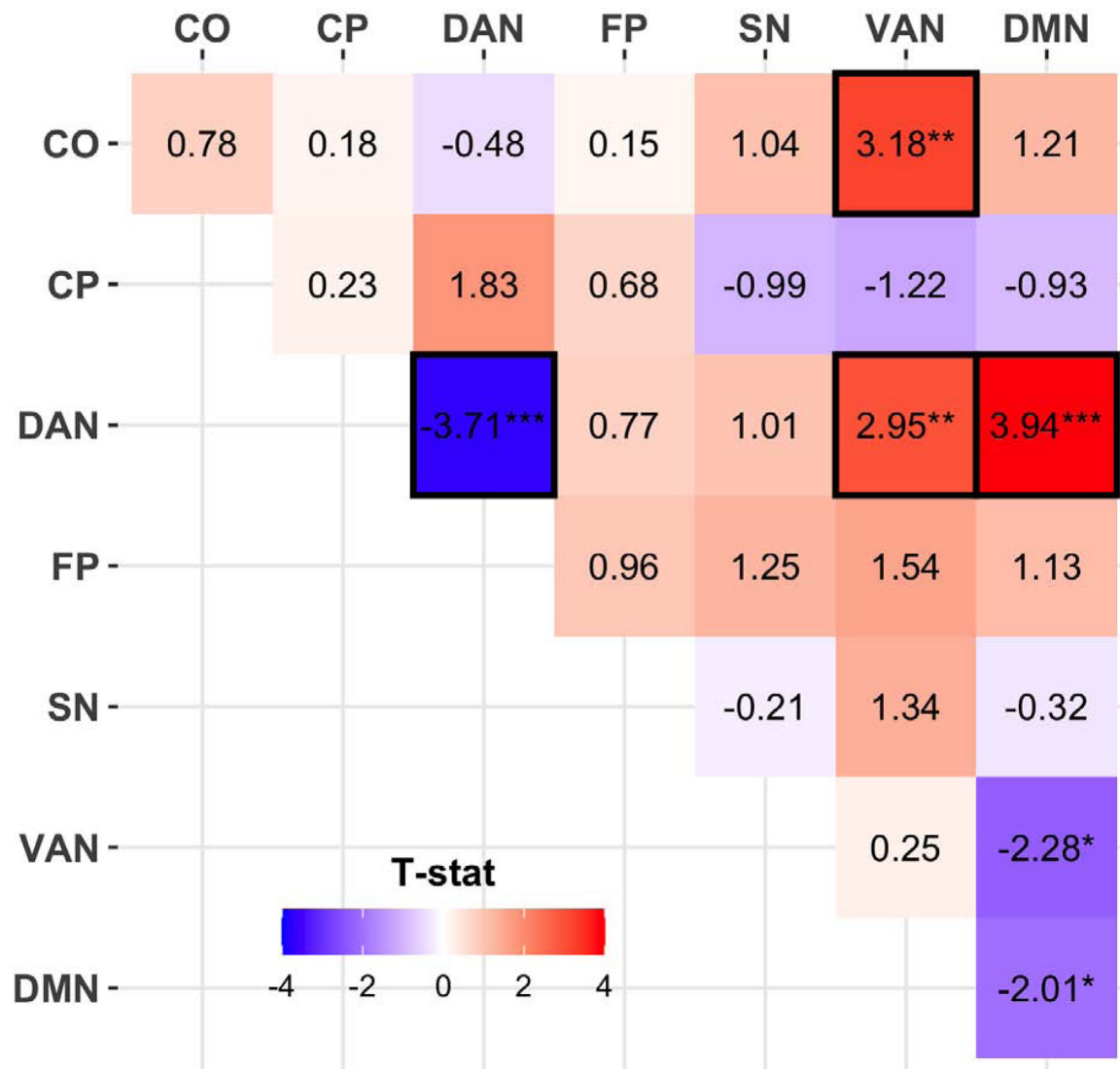
Figure 2: OCS Associations with Resting-State Functional Connectivity

Child Behavior Checklist (CBCL) obsessive-compulsive symptom (OCS) were related to resting-state functional connectivity within and between task-control and default mode networks. T-statistics from linear mixed-effects models are presented here for this association between OCS and connectivity. Red squared with positive t-statistics indicate positive associations such that greater OCS related to higher connectivity. Effects passing false discovery rate correction for multiple comparisons are outlined in black.

Networks: CO=cingulo-opercular, C*P*=cingulo-parietal, DAN=dorsal attention network, F*P*=fronto parietal, SN=salience network, VAN=ventral attention network, DMN=default mode network

* $p<.05$, ** $p<.01$, *** $p<.001$

Table 1:

Demographic Characteristics of the ABCD Sample

	Full Sample (N=11876)	OCD Absent (n=10584)	OCD Present (n=1099)	Group Difference	p	Effect Size
Age	118.94 (7.46)	118.97 (7.47)	118.61 (7.36)	t=−1.55	.12	d=−0.05
Sex (F) ***	5681 (47.86%)	5138 (48.56%)	440 (40.11%)	χ^2=28.13	<.001	OR=0.71
Pubertal Status	1.68 (0.72)	1.68 (0.72)	1.69 (0.75)	t=0.38	.70	d=0.01
Race-White	8803 (74.13%)	7879 (74.44%)	789 (71.79%)	χ^2=3.51	.06	OR=0.87
Race-Black ***	2515 (21.18%)	2186 (20.65%)	293 (26.66%)	χ^2=21.13	<.001	OR=1.40
Hispanic	9308 (79.44%)	8312 (79.59%)	863 (79.69%)	χ^2=0.00	.97	OR=1.01
Parents Marital Status (together/married) ***	8679 (73.69%)	7822 (74.5%)	732 (67.47%)	χ^2=24.79	<.001	OR=0.71
Parental Education (completed some college) ***	9812 (82.77%)	8818 (83.45%)	850 (77.55%)	χ^2=23.91	<.001	OR=0.69
Parental Income ***	7.22 (2.42)	7.31 (2.37)	6.45 (2.76)	t=−9.33	<.001	d=−0.33
NIH Toolbox - Cognition Total ***	100.37 (17.96)	100.7 (17.89)	97.3 (18.48)	t=−5.68	<.001	d=−0.19
Height (inches)	55.26 (3.22)	55.27 (3.21)	55.13 (3.36)	t=−1.31	.19	d=−0.04
Parental Monitoring ***	4.38 (0.52)	4.39 (0.51)	4.3 (0.57)	t=−5.28	<.001	d=−0.18
Parent 1 Acceptance **	2.78 (0.3)	2.78 (0.3)	2.75 (0.33)	t=−2.88	.004	d=−0.10
Parent 2 Acceptance **	2.69 (0.39)	2.69 (0.38)	2.65 (0.42)	t=−2.79	.01	d=−0.10
Family Conflict - Child Report ***	2.05 (1.95)	2.02 (1.94)	2.27 (2.03)	t=3.92	<.001	d=0.13
Family Conflict – Parent Report ***	2.54 (1.96)	2.47 (1.93)	3.12 (2.09)	t=9.93	<.001	d=0.33
Usable Structural Data	10534 (88.7%)	9405 (88.86%)	962 (87.53%)	χ^2=1.62	.20	OR=0.88
CBCL OCS sum ***	1.34 (1.82)	1.13 (1.56)	3.41 (2.66)	t=27.84	<.001	d=1.04
CBCL OCS T-score ***	53.70 (6.12)	52.97 (5.2)	60.69 (9.22)	t=27.27	<.001	d=1.03

Note. Demographic characteristics of the sample are summarized here for the full ABCD baseline sample and split by the presence/absence of a lifetime K-SADS OCD diagnosis. Continuous and categorical variables are characterized respectively by mean and (standard deviation) or *N* and (percent) with group differences based on OCD diagnosis presence are compared by t-test (Cohen's d effect size) or chi-squared test (odds ratio [OR] effect size). Pubertal status range=1–4. Income range=1–10. Conflict score range=0–9. Monitoring score range=1–5. Acceptance score range=1–3.

N=193 missing K-SADS OCD diagnosis. Additionally, *n*=1 missing Age, *n*=7 missing Sex, *n*=1 missing Pubertal Status and Race, *n*=159 missing ethnicity, *n*=99 missing Parents Marital Status, *n*=21 missing Parental Education, *n*=1019 missing Parental Income, *n*=413 missing NIH Toolbox - Cognition Total, *n*=13 missing height, *n*=24 missing parental monitoring behavior, *n*=37 missing parent 1 acceptance behavior, *n*=919 missing parent 2 acceptance behavior, *n*=27 missing family conflict - child report, *n*=6 missing family conflict - parent report, *n*=8 missing CBCL OCS sum, *n*=9 missing CBCL OCS T-score.

Group difference:

*
 p<.05,

**
 p<.01,

***
 p<.001

Table 2:

Clinical Characteristics of the ABCD Sample

	Full Sample (*N*=11876)	OCD Absent (*n*=10584)	OCD Present (*n*=1099)	Group Difference	Effect Size
CBCL T-score					
DSM Anxiety	53.49 (6.13)	52.89 (5.35)	59.21 (9.29)	t=22.16	d=0.83
DSM Depression	53.6 (5.73)	53.13 (5.21)	58.19 (8.02)	t=20.45	d=0.75
Thought Problems	53.8 (5.9)	53.13 (5.14)	60.19 (8.45)	t=27.17	d= 1.01
DSM ADHD	53.23 (5.64)	52.79 (5.13)	57.55 (8.04)	t= 19.18	d=0.71
Internalizing	48.45 (10.64)	47.46 (10.12)	57.88 (10.8)	t=30.58	d=1.00
Externalizing	45.73 (10.33)	44.98 (9.92)	52.94 (11.41)	t=22.25	d=0.75
Total	45.85 (11.34)	44.78 (10.78)	56.17 (11.4)	t=31.63	d=1.03
K-SADS lifetime diagnosis					
Any Depressive Disorder	1272 (10.9%)	1014 (9.61%)	247 (22.6%)	χ^2=171.62	OR=2.75
MDD	614 (5.27%)	475 (4.5%)	137 (12.53%)	χ^2=126.64	OR=3.04
Dysthymia	24 (0.21%)	18 (0.17%)	6 (0.55%)	χ^2=5.17	OR=3.23
Depression NOS	697 (5.97%)	570 (5.4%)	117 (10.7%)	χ^2=49.19	OR=2.10
Any Anxiety Disorder	1730 (14.83%)	1307 (12.39%)	419 (38.23%)	χ^2=523.32	OR=4.38
Separation Anxiety	1047 (8.95%)	783 (7.4%)	263 (23.93%)	χ^2=331.82	OR=3.94
Social Anxiety	619 (5.31%)	477 (4.52%)	140 (12.8%)	χ^2=133.59	OR=3.10
GAD	579 (4.96%)	382 (3.62%)	195 (17.81%)	χ^2=420.87	OR=5.76
ADHD	2428 (20.76%)	1921 (18.15%)	506 (46.04%)	χ^2=468.92	OR=3.85
ODD/CD	1782 (15.24%)	1397 (13.2%)	385 (35.03%)	χ^2=365.45	OR=3.55
PTSD	231 (1.98%)	141 (1.33%)	90 (8.19%)	χ^2=238.01	OR=6.60
No diagnoses	7348 (61.99%)	6898 (65.17%)	296 (26.93%)	χ^2=613.74	OR=0.20
Unmedicated	10739 (90.43%)	9704 (91.69%)	859 (78.16%)	χ^2=208.52	OR=0.32

Note. Clinical characteristics of the sample are summarized here for the full ABCD baseline sample and split by the presence/absence of a lifetime K-SADS OCD diagnosis. Continuous and categorical variables are characterized respectively by mean and (standard deviation) or *N* and (percent) with group differences based on OCD diagnosis presence are compared by t-test (Cohen's d effect size) or chi-squared test (odds ratio [OR] effect size). All group differences were *p*<.001 significant, except for dysthymia (*p*=.02). No diagnoses indicated that none of the listed disorders were diagnosed past or present on the K-SADS.

N=193 missing K-SADS OCD diagnosis. Additionally, *n*=10 missing CBCL T-scores, *n*=42 missing MDD and Dysthymia, *n*=40 missing Depression NOS, *n*=41 missing Social Anxiety, *n*=40 missing GAD.

Table 3:

Item-wise CBCL OCS Characterization

CBCL OCS Item	Score	Total (*N*=11876)	OCD Absent (*n*=10584)	OCD Present (*n*=1099)
9 - Can't get his/her mind off certain thoughts; obsessions	0	8830 (74.4)	8259 (78.1)	434 (39.5)
	1	2534 (21.3)	2017 (19.1)	472 (43.0)
	2	505 (4.3)	304 (2.9)	192 (17.5)
66 - Repeats certain acts over and over; compulsions	0	11050 (93.1)	10142 (95.9)	733 (66.8)
	1	687 (5.8)	393 (3.7)	282 (25.7)
	2	131 (1.1)	44 (0.4)	83 (7.6)
84 - Strange behavior	0	11374 (95.8)	10289 (97.3)	904 (82.3)
	1	456 (3.8)	270 (2.6)	177 (16.1)
	2	38 (0.3)	20 (0.2)	17 (1.5)
85 - Strange ideas	0	11054 (93.1)	10003 (94.6)	871 (79.3)
	1	770 (6.5)	549 (5.2)	210 (19.1)
	2	44 (0.4)	27 (0.3)	17 (1.5)
31 - Feels he/she might think or do something bad	0	10862 (91.5)	9834 (93.0)	857 (78.1)
	1	932 (7.9)	701 (6.6)	212 (19.3)
	2	74 (0.6)	44 (0.4)	29 (2.6)
32 - Feels he/she has to be perfect	0	8620 (72.6)	7896 (74.6)	587 (53.5)
	1	2775 (23.4)	2342 (22.1)	387 (35.2)
	2	473 (4.0)	341 (3.2)	124 (11.3)
52 - Feels too guilty	0	11093 (93.5)	10008 (94.6)	902 (82.1)
	1	708 (6.0)	527 (5.0)	173 (15.8)
	2	67 (0.6)	44 (0.4)	23 (2.1)
112 - Worries	0	7945 (66.9)	7396 (69.9)	420 (38.3)
	1	3418 (28.8)	2864 (27.1)	499 (45.4)
	2	505 (4.3)	319 (3.0)	179 (16.3)
OCS > 0		6611 (55.7%)	5539 (52.4%)	962 (87.6%)
OCS > 1		3880 (32.7%)	3010 (28.5%)	802 (73.04%)
OCS 5		807 (6.8%)	464 (4.4%)	328 (29.9%)

Note. Item-level data are presented for the CBCL OCS subscale. The number (percent) of participants endorsing each CBCL item response option (0, 1, or 2) presented for the full sample and split by the presence/absence of a K-SADS lifetime OCD diagnosis. The first four items are drawn from the Thought Problems subscale (#9, 66, 84, 85) and the latter four items are drawn from the Anxious/Depressed subscale (#31, 32, 52, 112). The number (percent) of participants with a raw sum score>0, >1, or 5 are also presented. All differences between those with and without lifetime OCD are $p<.001$ significant in this table.