Archival Report

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Direct and Indirect Associations of Widespread Individual Differences in Brain White Matter Microstructure With Executive Functioning and General and Specific Dimensions of Psychopathology in Children

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ABSTRACT

BACKGROUND: Executive functions (EFs) are important partly because they are associated with risk for psychopathology and substance use problems. Because EFs have been linked to white matter microstructure, we tested the prediction that fractional anisotropy (FA) and mean diffusivity (MD) in white matter tracts are associated with EFs and dimensions of psychopathology in children younger than the age of widespread psychoactive substance use.

METHODS: Parent symptom ratings, EF test scores, and diffusion tensor parameters from 8588 9- to 10-year-olds in the ABCD Study (Adolescent Brain Cognitive Development Study) were used.

RESULTS: A latent factor derived from EF test scores was significantly associated with specific conduct problems and attention-deficit/hyperactivity disorder problems, with dimensions defined in a bifactor model. Furthermore, EFs were associated with FA and MD in 16 of 17 bilateral white matter tracts (range: $\beta = .05$; SE = .17; through $\beta = -.31$; SE = .06). Neither FA nor MD was directly associated with psychopathology, but there were significant indirect associations via EFs of both FA (range: $\beta = .01$; SE = .01; through $\beta = -.09$; SE = .02) and MD (range: $\beta = .01$; SE = .01; through $\beta = .09$; SE = .02) with both specific conduct problems and attention-deficit/hyperactivity disorder in all tracts except the forceps minor.

CONCLUSIONS: EFs in children are inversely associated with diffusion tensor imaging measures in nearly all tracts throughout the brain. Furthermore, variance in diffusion tensor measures that is shared with EFs is indirectly shared with attention-deficit/hyperactivity disorder and conduct problems.

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Executive functions (EFs) are hypothetical cognitive control processes involved in the regulation of attention, impulse, and goal-directed behavior. Previous studies have found associations between deficient EFs and many forms of psychopathology, which suggested the hypothesis that EFs are transdiagnostically associated with internalizing and externalizing psychopathology (1–5). This gives EFs a central role in causal models of psychopathology and elevates the importance of research on its neurobiology. Additional research is needed to map the associations of EFs onto dimensions of psychopathology because most previous research did not take the ubiquitous positive correlations among every dimension of psychopathology into account (6–8). That could mean that EFs appear to be associated with both internalizing and externalizing psychopathology only because those dimensions are correlated (6,9,10).

Herein, we use a psychometric strategy that defines dimensions of psychopathology while taking into account correlations among symptoms (11). Theorists have hypothesized that the dimensions of psychopathology are organized hierarchically in the form of a bifactor model, which includes a broad general factor of psychopathology—sometimes termed the p factor—and specific factors of psychopathology (9,10,12,13). In bifactor models, every symptom loads on both the general factor and one (and only one) orthogonal specific factor (e.g., internalizing) (14–16). This partitions the variance in symptoms among the general and specific factors, distinguishing common from dissociable correlates of each dimension of psychopathology (14,15,17). Previous studies have shown the general and specific factors of psychopathology defined in bifactor models to exhibit external validity in terms of significant associations with criterion variables,

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including incarceration, poor academic progress, suicidal behavior, and self-harm (18–21). Furthermore, several studies have found that EFs are associated with the general factor of psychopathology defined in bifactor models (12,22–26).

Several studies have found variations in white matter microstructure to be associated with EFs in representative samples of children, adolescents, and adults (27–30), and in low-birthweight children (29,31–33). Additionally, three studies reported significant associations between the general factor of psychopathology in children and atypical white matter microstructure (34–36). Because two of these studies defined only the general factor without specific factors, however, it is unclear if there are associations between white matter microstructure and the specific dimensions of psychopathology (e.g., internalizing) defined in bifactor models.

These findings of brain–behavior relationships from small studies are in need of replication to assess their robustness (37). The present analyses use data from the ABCD Study (Adolescent Brain Cognitive Development Study) to test three hypotheses suggested by previous findings. First, EFs are associated with both the general and specific dimensions of psychopathology defined in bifactor models. Second, variations in white matter microstructure are associated with EFs. Third, white matter microstructure is linked with the general and specific psychopathology factors. These tests were conducted in a sample with a narrow age range (9–10 years), minimizing complications from developmental changes in brain and behavior (38). By conducting these tests before the initiation of psychoactive substance use in nearly all children, we will be in a position to distinguish neural and behavioral characteristics of children that predict substance use from those that co-occur with, and may be the results of, the use of psychoactive substances in adolescence (39).

We examine associations between individual differences in a latent factor defined by individually administered tests of EFs, dimensions of psychopathology based on parent-rated items from the Child Behavior Checklist (CBCL) (40), and putative indices of white matter microstructure in 17 white matter tracts. We do so using complementary diffusion tensor imaging (DTI) measures that are associated with variations in functional neural connectivity in the brain (41). Fractional anisotropy (FA) estimates the directional diffusivity of water molecules in white matter tracts, independent of overall diffusivity. Mean diffusivity (MD) indexes the overall magnitude of diffusion independent of anisotropy (42). For computational efficiency and to manage the number of statistical tests, we evaluated average indices in bilateral tracts.

METHODS AND MATERIALS

Sample

Analyses are based on the baseline wave of the ABCD Study, using Curated Release 2.0.1 (Study 721, https://doi.org/10.15154/1504041) from the National Institute of Mental Health Data Archive (nda.nih.gov). The sample was recruited at 22 sites across the United States at 9 to 10 years of age. The sample does not represent the country, but the same unbiased recruitment process was used within sites (43), and post-stratification weights were used to better represent population parameter (44). Parent ratings of psychopathology were collected on children (n = 11,866; 47.9% female). Most participants (n = 8142) were one child of singleton birth from different families, but 1592 singletons had a nontwin sibling in the study and 2132 participants had a twin in the study. Parents classified the children as non-Hispanic white (52.08%), Black (14.99%), Hispanic (20.29%), or other racial/ethnic groups (12.63%). Characteristics of the sample are provided in Table 1.

Measures

The CBCL (40) is a parent rating scale consisting of 119 items describing child behaviors and emotions on a scale of 0 = not true (as far as you know), 1 = somewhat or sometimes true, or 2 = very true or often true. Missing data on CBCL items were $<$0.1%. Prior to the present analyses, we conducted factor analyses of a reduced set of CBCL items, eliminating CBCL items not addressing psychopathology, such as biting fingernails, constipation, and wishing to be the opposite sex (24). Eight items referring to behaviors typical of adolescence (e.g., alcohol consumption and smoking) were eliminated because ratings above 0 were $<$0.5%, or it was not possible to estimate polychoric correlations with other items. Three pairs of items referencing similar behaviors that were correlated $>$0.85 were combined in composites by taking the mean of the ratings of these items and rounding to achieve 0, 1, or 2 scoring. Additional items were eliminated by retaining only items with loadings $>$0.40 in exploratory factor analyses, resulting in 66 items (24).

Executive Functions. Three tests of executive functioning (45) from the National Institutes of Health Toolbox Cognition Battery were administered on computer tablets monitored by an interviewer (46): Pattern Comparison Processing Speed Test (47), Dimensional Change Card Sort Task (48), and the Flanker Task (49).

Image Acquisition. Imaging procedures were described previously (50). Participant images were taken using one of five models of 3T scanners. T1-weighted, T2-weighted structural scans (0.7-mm isotropic), and diffusion magnetic resonance imaging (dMRI) scans (1.7-mm isotropic) were completed using 32-channel head coils. dMRI acquisition for the segmentation of white matter tracts and measurement of diffusion used a multiband echo-planar imaging (51,52) with slice acceleration factor 3 and included 96 diffusion directions, 7 frames of b = 0, and 4 b values (6 directions with b = 500 s/mm^2, 15 directions with b = 1000 s/mm^2, 15 directions with b = 2000 s/mm^2, and 60 directions with b = 3000 s/mm^2). Other dMRI parameters varied by 3T scanner and are available at https://abcdstudy.org/images/Protocol_Imaging_Sequences.pdf.

Preprocessing. ABCD preprocessing procedures have been described (53). Diffusion weighted images in the Curated Release 2.0.1 were corrected for head movement and eddy current distortions and were corrected for B_0 distortion (54) and for gradient nonlinearity distortion (55). T2-weighted b = 0 images were aligned to T1-weighted

Table 1. Comparison of Characteristics of Included and Excluded Children

	Included		Excluded Due to Missing Data		Excluded by MRI Quality Control				
	Mean (SD) or %	*n*	Mean (SD) or %	*n*	Mean (SD) or %	*n*	χ^2	*df*	*p* Value
Age, Mo	119.3 (7.47)	8588	118.01 (7.34)	1688	118.12 (7.37)	1596	62.62	2	<.001
Female, %	49.00	8586	46.94	1685	42.76	1595	21.66	2	<.001
Mean Highest Maternal Education Level Completed, z	0.04 (0.98)	8028	−0.18 (1.06)	1566	−0.01 (1.00)	1460	60.79	2	<.001
Mean Family Income Level, z	0.06 (0.96)	7889	−0.27 (1.14)	1508	−0.04 (1.01)	1458	145.36	2	<.001
Race/Ethnicity Categories, %		8578		1682		1594	197.74	6	<.001
Non−Hispanic White	54.90		40.31		49.31				
Black	12.91		24.38		16.31				
Hispanic	20.26		20.75		20.08				
Asian and other	11.94		14.57		14.30				
MRI Magnet, %		8588		1570		1596	875.16	8	<.001
Achieva	8.10		9.17		8.21				
Discovery	18.96		32.68		51.44				
Ingenia	4.76		5.48		2.94				
Prisma	29.89		20.19		12.03				
Prisma Fit	38.29		32.48		25.38				
Mean Fractional Anisotropy Across Tracts, z	0.03 (0.99)	8588	−0.24 (1.14)	135	−0.17 (1.03)	1596	63.04	2	<.001
Mean Diffusivity Across Tracts, z	−0.11 (0.91)	8588	−0.30 (0.82)	135	0.60 (1.23)	1596	720.47	2	<.001
Mean of All CBCL Items Used in Factor Analyses, z	−0.03 (0.97)	8588	0.12 (1.08)	1682	0.06 (1.03)	1596	39.91	2	<.001
Mean Card Sort Task, z	0.05 (0.97)	8583	−0.25 (1.07)	1531	−0.03 (1.04)	1596	117.23	2	<.001
Mean Flanker Task, z	0.05 (0.96)	8582	−0.25 (1.15)	1531	−0.02 (1.02)	1596	115.98	2	<.001
Mean Pattern Comparison Processing Speed, z	0.04 (0.99)	8570	−0.17 (1.04)	1528	−0.06 (1.00)	1593	64.84	2	<.001

Comparison of characteristics of the 8588 children included in analyses vs. those of children excluded because of either missing behavioral or diffusion tensor imaging data (n = 1688) or unacceptable quality control of imaging data (n = 1596), omitting 3 participants without poststratification weights who could not be compared. Among 11,872 children with valid identifications and poststratification weights, comparisons were made by χ^2 tests for categorical variables and t tests for continuous variables. Variations in sample sizes reflect missing data in some variables. χ^2 from χ^2 test for binary variables or 2 *df* test in generalized linear models for continuous variables.

CBCL, Child Behavior Checklist; MRI, magnetic resonance imaging.

structural images using mutual information (56) and then were resampled into a standard orientation with 1.7-mm isotropic resolution.

Mean FA and MD were calculated for white matter fiber tract regions of interest created with AtlasTrack (57), a probabilistic atlas-based method for automated segmentation of white matter fiber tracts. DTI-derived diffusion orientations for each participant were compared with the atlas fiber orientations, refining the a priori tract location probabilities, individualizing the fiber tract regions of interest, and minimizing the contribution from regions inconsistent with the atlas. Voxels containing primarily gray matter or cerebrospinal fluid identified using FreeSurfer's automated brain segmentation (58) were excluded. FreeSurfer reconstructions that did not pass post-processing quality control for motion, pial overestimation, white matter underestimation, and signal inhomogeneity were excluded. FA and MD measures were those consisting of the DTI full shell, which includes all gradient strengths/shells (6 directions at b = 500 s/mm^2, 15 directions at b = 1000 s/mm^2, 15 directions at b = 2000 s/mm^2, and 60 directions at b = 3000 s/mm^2). DTI indices measure the diffusion distribution within a voxel, which is a diffusion tensor represented by a 3-dimensional ellipsoid with major and minor axes corresponding to eigenvalues of the tensor.

Head motion was estimated by registering each frame to a corresponding image synthesized from a tensor fit, accounting for variation in image contrast across diffusion orientations (57). Overall head motion was the average of estimated frame-to-frame head motion. Dark slices, an artifact indicative of abrupt head motion, were identified as outliers in the root-mean-square difference between the original data and data synthesized from tensor fitting. The mean number of slices and frames affected by these motion artifacts were calculated for each dMRI series, using dmri_dti_meanmotion from the Curated Release, and were included as a covariate of no interest to account for variation in motion.

Exclusion From Analyses

Figure 1 shows that 8588 of the 11,872 ABCD wave 1 participants had valid CBCL and test scores and DTI data that passed quality control. A total of 3287 participants were excluded from analyses because of missing data, incidental findings, or failed quality control (described in the Supplement).

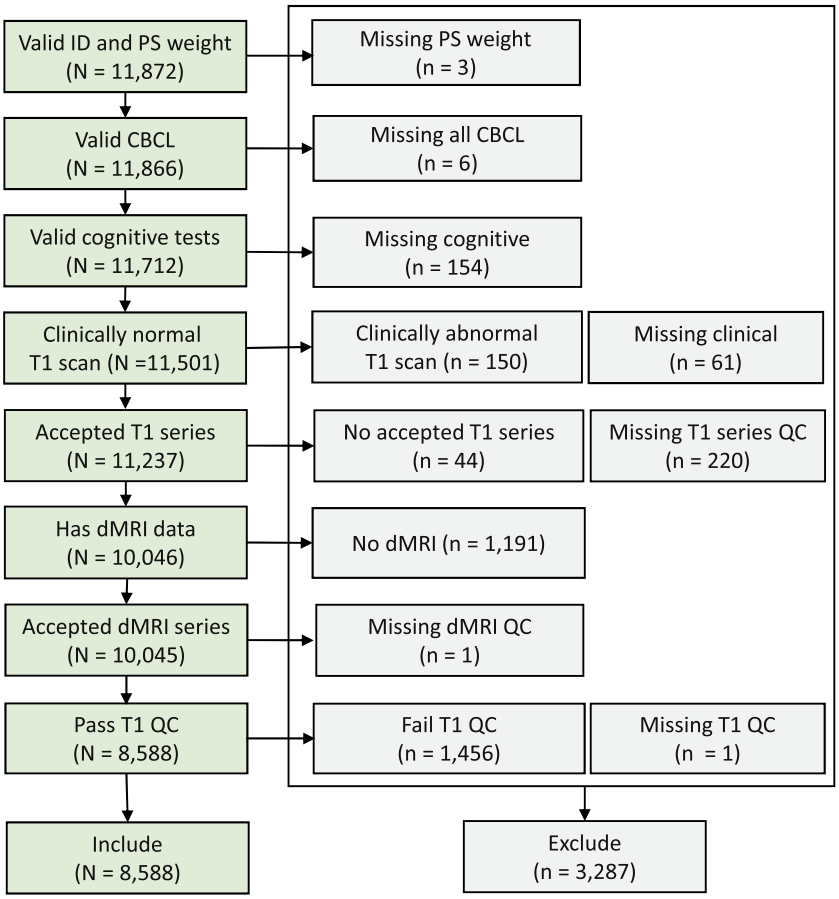

Figure 1. Exclusion of participants from wave 1 of the ABCD Study on the basis of missing data and quality control. CBCL, Child Behavior Checklist; dMRI, diffusion magnetic resonance imaging; ID, identification; PS, poststratification weight; QC, quality control.

Data Analyses

Tests of participation bias were conducted in SAS version 9.4. Structural equation modeling (SEM) was conducted in Mplus version 8.3. CBCL items were treated as ordered categorical data using the mean- and variance-adjusted weighted least squares estimator, with pairwise deletion for missing data (59). Mplus analyses not involving CBCL items used maximum likelihood estimation with robust variance estimation. All analyses accounted for the stratification of the sample in data collection sites and used poststratification weights (44). The cluster option was used to account for clustering of siblings within families.

As described in the Supplement, we dealt with collinearity among FA and MD in the 17 bilateral tracts in two ways. First, to test independent associations of FA and MD (in separate analyses) in each bilateral tract with psychopathology while avoiding interpretation difficulties caused by collinearity of predictors, we pre-regressed all predictor variables out of each other before entering them into SEMs (60). Second, we used confirmatory factor analysis to define latent factors based on the correlated tract measures. The approaches are similar, but each has advantages. Pre-regressing the predictors solves the collinearity problem without changing the core components of a model—i.e., the pre-regressed predictors combined will produce exactly the same F statistic, R^2, and predicted values as will the raw predictors combined. Examples of analyses based on these principles are very common (61–63).

Factor analysis bypasses the region-by-region comparison altogether and uses the collinearity to form factors based on regions. For example, if regions 1, 2, and 3 were collinear (even beyond the global collinearity), one could replace them with a single latent factor. If that factor related significantly to a validity criterion, we would not have the ability to parse effects of specific regions within a factor. The factor loadings would indicate how well the predictors related to the factor but would not allow comparing relationships of regions with the criterion.

Covariates of No Interest

All SEMs controlled for the same methodologic (head motion during dMRI acquisition and models of MRI magnets) and demographic covariates: sex, age in months, and race/ethnicity (contrasts of each group with non-Hispanic white).

Tests of Exclusion Bias

We compared 8588 participants with the 3287 excluded children on demographic factors and behavior to estimate bias due to exclusion.

Bifactor Structure of Psychopathology

Based on previous findings using ABCD Study data (24), a bifactor model of CBCL items was specified for the SEMs. Each item loaded on the general factor and one specific factor (i.e., internalizing, conduct problems, and attention-deficit/hyperactivity disorder [ADHD]) (15). Psychometric properties of the bifactor model exceeded guidelines (64,65) regarding construct reliability and criterion validity (24). We agree with the conclusions of another set of analyses of ABCD Study data that differences between general factors defined by bifactor models and other models are minimal (66). Nonetheless, we have argued that interpretation of lower-level factors in second-order models is ambiguous (24). They are the equivalent of factors defined in a correlated-factors model without a general factor, because the perfectly collinear general factor in second-order models cannot be controlled when examining correlates of the lower-level factors. In contrast, the specific factors in bifactor models are unambiguously interpretable (24). Nonetheless, SEMs were repeated with the psychological problems defined in the correlated-factors model.

Tests of Associations Among White Matter Indices and Behavior

As illustrated in Figure 2, SEMs were conducted separately for fractional anisotropy and mean diffusivity to test direct associations of white matter variations with latent EFs (path A, representing 17 tests for individual tracts), EFs with latent CBCL factors (4 B paths), and white matter variations with psychopathology (4 C paths, each representing 17 tests for the bilateral tracts). Additionally, indirect associations of white matter variations with psychopathology through EFs were tested. When based on cross-sectional data, the results cannot be interpreted as unbiased tests of a causal link between white matter microstructure and psychopathology that is mediated by EFs (67,68). They can, however, suggest hypotheses to test prospectively using future waves of ABCD Study data.

Sensitivity Tests

To determine if exclusion of some participants biased associations, SEMs were repeated using weights adjusting for nonparticipation. To check distributional assumptions of the SEMs, we also bootstrapped confidence intervals. To determine if the estimated associations applied to both sexes, interactions with sex were tested. As a check on our use of a latent factor of EFs, SEMs were repeated using a published executive functioning skills score identified using Bayesian principal components analysis of ABCD Study data (69).

RESULTS

FA and MD averaged across all tracts were modestly correlated, $r_{8588} = -.16$, $p < .0001$. Figures S3 and S4 present the robust correlations among the 17 bilateral tracts on FA and MD.

Associations Among White Matter Microstructure, EFs, and Psychopathology

The latent EF factor was significantly associated inversely with the general factor and each specific factor of psychopathology (Table 2). The lower 95% confidence intervals for both specific conduct problems and specific ADHD did not overlap with the confidence intervals for the other dimensions, however, suggesting stronger associations of EFs with those dimensions of psychological problems.

Accounting for correlations among the tracts and adjusting for multiple testing, higher EF factor was associated with higher FA in association fibers (temporal and parietal segments of the superior longitudinal fasciculus, inferior fronto-occipital fasciculus, inferior frontal superior frontal tract, and the parietal superior corticostriate projection), the anterior thalamic radiation, and projection fibers (corticospinal pyramidal tract, forceps minor, and corpus callosum body) (Table 3). Furthermore, greater EF factor was significantly associated with lower MD in all bilateral white matter tracts, except the forceps minor. Figure 3 represents the symmetrical associations between EFs

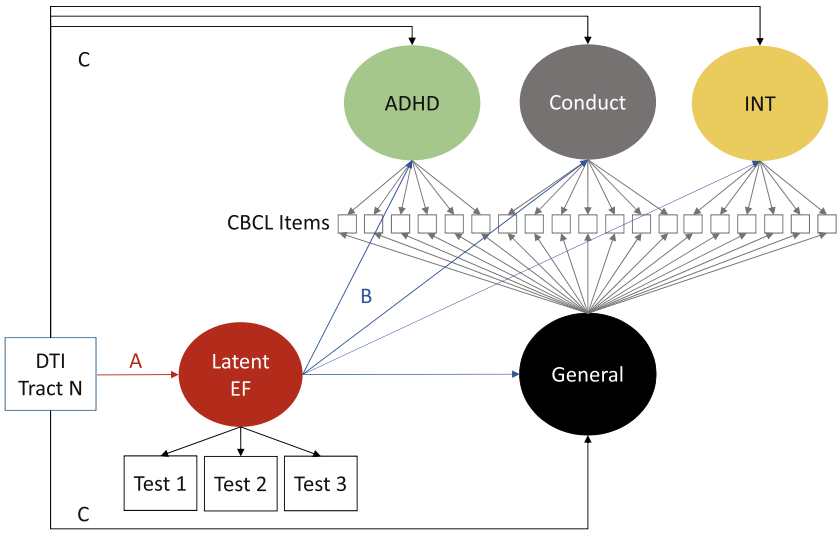

Figure 2. Illustration of structural equation models of the direct associations of diffusion tensor imaging (DTI) measures, separately for fractional anisotropy and mean diffusivity, in 17 bilateral white matter tracts (1 tract illustrated) with a latent factor of executive functions (EFs) based on 3 tests and their direct and indirect associations with orthogonal latent general and specific factors of psychopathology. Tested paths are indicated by colors and letters. ADHD, attention-deficit/hyperactivity disorder; CBCL, Child Behavior Checklist; INT, specific internalizing psychopathology.

Table 2. Standardized Path Coefficients for Direct Associations of the Latent Factor of Executive Function With Each Dimension of General and Specific Psychopathology Defined in the Bifactor Model in the Full Structural Equation Model

	General Factor				Specific Internalizing				Specific Conduct Problems				Specific ADHD			
	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]
From SEM of Fractional Anisotropy																
	−.032	.021	−.073, .009	.125	−.036	.021	−.077, .005	.086	−.194[b]	.025[b]	−.243, −.145[b]	< .001[c]	−.345[b]	.025[b]	−.394, −.296[b]	<.001[c]
From SEM of Mean Diffusivity																
	−.029	.021	−.070, .012	.163	−.039	.021	−.080, .002	.070	−.196[b]	.025[b]	−.245, −.147[b]	< .001[c]	−.353[b]	.025[b]	−.402, −.304[b]	<.001[c]

See the B paths in Figure 2.
ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; SE, standard error; SEM, structural equation model.
[a]Tabled *p* values are unadjusted.
[b]Coefficients are significant at $p < .05$ after correction for 4 tests of associations for each diffusion tensor imaging measure at a 5% false discovery rate.
[c]Significant *p* values after correction.

and FA and MD in each tract. Table S1 presents the results of the sensitivity analysis, showing essentially same results using the previously published EF component (69). When the correlated indices of microstructure were treated as latent factors, latent FA was associated with the latent factor of EFs, β = .052, SE = .013, $p < .0005$. Latent MD across tracts was associated with the latent factor of EFs, β = −.063, SE = .013, $p < .0005$.

There was no significant direct association at $p < .05$ after correction for multiple testing between FA or MD in specific white matter tracts and any general or specific dimension of child psychopathology (Tables 4 and 5). In contrast, Table 6 and Figure 3 show that both the specific conduct problems and specific ADHD dimensions were each indirectly associated through the EF factor with FA in the same 4 tracts for both dimensions of psychopathology, when controlling for the correlations among tracts and after adjustment for multiple testing: temporal and parietal segments of the superior longitudinal fasciculus, inferior fronto-occipital fasciculus, and forceps major and body of the corpus callosum (Figure 2, path D). Furthermore, Table 7 and Figure 4 show significant indirect associations of MD in every tract except the forceps minor with both specific conduct problems and specific ADHD (Figure 2,

Table 3. Standardized Coefficients for Independent Direct Associations Between a Latent Factor of Executive Functioning and Fractional Anisotropy and Mean Diffusivity in 17 Bilateral White Matter Tracts, Controlling for Correlations Among the Tracts

	Fractional Anisotropy				Mean Diffusivity			
Tract	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]
Fornix	.049[b]	.017[b]	.016, .082[b]	.004[c]	−.058[b]	.021[b]	−.099, −.017[b]	.006[c]
Cingulate Bundle	.080[b]	.019[b]	.043, .117[b]	<.001[c]	−.110[b]	.025[b]	−.159, −.061[b]	<.001[c]
Parahippocampal Cingulum	.047[b]	.017[b]	.014, .080[b]	.006[c]	−.089[b]	.019[b]	−.126, −.052[b]	<.001[c]
Anterior Thalamic Radiation	.109[b]	.024[b]	.062, .156[b]	<.001[c]	−.155[b]	.028[b]	−.210, −.100[b]	<.001[c]
Uncinate Fasciculus	.095[b]	.02[b]	.056, .134[b]	<.001[c]	−.110[b]	.026[b]	−.161, −.059[b]	<.001[c]
Inferior Longitudinal Fasciculus	.093[b]	.022[b]	.050, .136[b]	<.001[c]	−.081[b]	.025[b]	−.130, −.032[b]	<.001[c]
Inferior Fronto-occipital Fasciculus	.108[b]	.023[b]	.063, .153[b]	<.001[c]	−.185[b]	.040[b]	−.263, −.107[b]	<.001[c]
Temporal Superior Longitudinal Fasciculus	.184[b]	.028[b]	.129, .239[b]	<.001[c]	−.212[b]	.047[b]	−.304, −.120	<.001[c]
Parietal Superior Longitudinal Fasciculus	.260[b]	.034[b]	.193, .327[b]	<.001[c]	−.300[b]	.055[b]	−.408, −.192	<.001[c]
Superior Corticostriate-frontal	.270[b]	.037[b]	.197, .343[b]	<.001[c]	−.310[b]	.053[b]	−.414, −.206	<.001[c]
Superior Corticostriate-parietal	.109[b]	.030[b]	.050, .168[b]	<.001[c]	−.267[b]	.049[b]	−.363, −.171	<.001[c]
Striatal Inferior Frontal	.119[b]	.027[b]	.066, .172[b]	<.001[c]	−.249[b]	.042[b]	−.331, −.167	<.001[c]
Inferior Frontal Superior Frontal	.082[b]	.022[b]	.039, .125[b]	<.001[c]	−.099[b]	.035[b]	−.168, −.030	.004[c]
Corticospinal/Pyramidal	.133[b]	.025[b]	.084, .182[b]	<.001[c]	−.202[b]	.041[b]	−.282, −.122	<.001[c]
Forceps Major	.121[b]	.024[b]	.074, .168[b]	<.001[c]	−.099[b]	.028[b]	−.154, −.044	<.001[c]
Forceps Minor	.057[b]	.028[b]	.002, .112[b]	.039[c]	−.009	.035	−.078, .060	.798
Corpus Callosum Body	.242[b]	.042[b]	.160, .324[b]	<.001[c]	−.198[b]	.057[b]	−.310, −.086[b]	<.001[c]

See the A paths in Figure 2.
CI, confidence interval; SE, standard error.
[a]Tabled *p* values are unadjusted.
[b]Coefficients are significant at $p < .05$ after correction for 34 tests of associations for each diffusion tensor imaging measure at a 5% false discovery rate.
[c]Significant *p* values after correction.

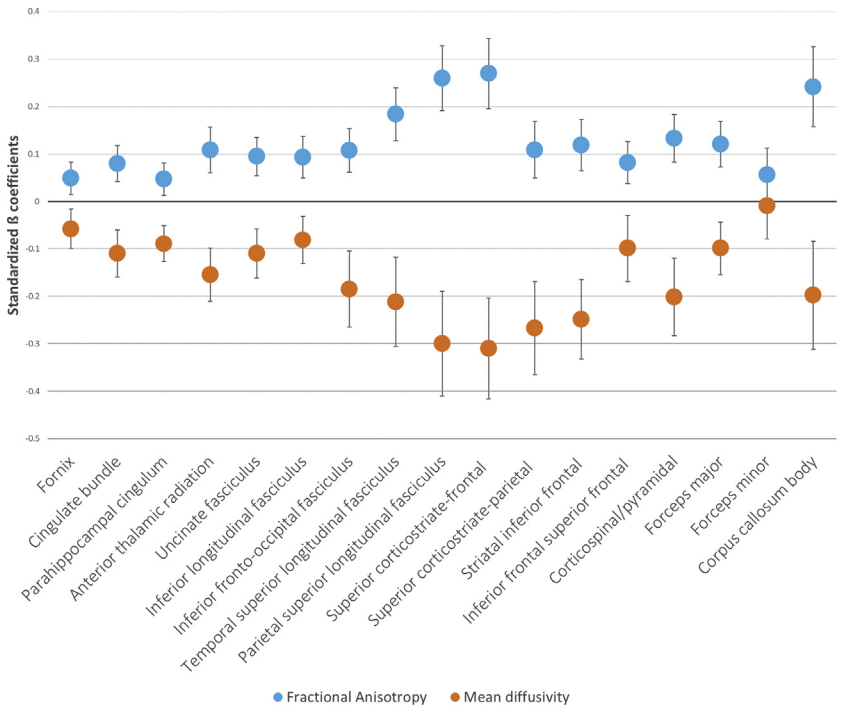

Figure 3. Standardized coefficients for independent direct associations between and the latent factor of executive functions and fractional anisotropy and mean diffusivity in 17 bilateral white matter tracts (compare with Table 2).

path D). One indirect association of MD with the general factor of psychopathology through EFs was significant, but only for the parietal segment of the superior corticostriate projection. The symmetrical patterns of indirect associations between FA and MD in each tract with these dimensions of psychopathology were in the same directions (Figure 4).

Results of Sensitivity Analyses

Table 1 shows no significant difference between the children included and excluded from the analyses in sex of participants, maternal education, or family income, but children in different racial/ethnic groups participated to differing extents. Included children were slightly older, had lower total ratings on CBCL items, and had lower scores on EF tests than did excluded children. These variables were included as covariates of no interest in all analyses. Essentially identical results were found when the published EF component defined in principal components analysis (69) was used as the latent factor of EFs (Tables S1–S6).

The results of the sensitivity analyses using nonparticipation weights (Tables S7–S12) are essentially identical to the results of the primary analyses. Tables S13 to S16 show that there were no significant interactions with sex in the SEMs after adjustments for multiple testing. Results of the SEMs using bootstrapping were essentially identical to the primary analyses (Tables S27–S32). Tables S17 to S26 show that EFs were directly associated, and tractwise FA and MD were indirectly associated, with conduct problems and ADHD in the correlated-factors model. Compared with the bifactor model, the difference was that EFs, FA, and MD were also indirectly associated with internalizing psychopathology. Findings were similar when latent factors of FA and MD in each of the correlated tracts defined in the measurement model of SEMs instead of tractwise analyses (Figures S1 and S2).

DISCUSSION

The present findings are important because they describe brain–behavior associations in a large sample of children at ages that antedate the widespread initiation of psychoactive substance use and other serious forms of psychopathology (70). These analyses replicate and clarify associations between EFs and multiple dimensions of psychopathology through the general factor found in previous studies (12,22,23,25), with the present findings indicating stronger associations between EFs and the specific conduct problems and ADHD dimensions in this age range. This finding is consistent with studies of clinic-referred samples that found deficits in EFs and cognitive abilities to be associated with ADHD and conduct problems (71–76).

When a correlated-factors measurement model of psychopathology was used instead of the bifactor model, EFs were still directly associated and tractwise FA and MD were indirectly associated with conduct problems and ADHD. The difference was that EFs, FA, and MD were also associated with internalizing psychopathology in the correlated-factors model. This is because internalizing psychopathology contains a considerable variance that is shared with conduct problems and ADHD in correlated-factors models, which confounds tests of associations between brain and behavior. This is not an issue in bifactor models, because the shared variance is partitioned to the general factor, making the specific factors orthogonal.

Table 4. Standardized Path Coefficients for Direct Associations of Fractional Anisotropy in Each of 17 Bilateral White Matter Tracts With Each Dimension of General and Specific Psychopathology Defined in the Bifactor Model in the Full Structural Equation Model, Controlling for Correlations Among the Tracts

	General Factor				Specific Internalizing				Specific Conduct Problems				Specific ADHD			
Tract	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]
Fornix	−.009	.02	−.048, .030	.659	.048	.02	.009, .087	.017	−.008	.025	−.057, .041	.747	−.038	.025	−.087, .011	.128
Cingulate Bundle	−.021	.024	−.068, .026	.374	.018	.023	−.027, .063	.441	.016	.028	−.039, .071	.567	−.016	.028	−.071, .039	.575
Parahippocampal Cingulum	−.002	.02	−.041, .037	.901	.012	.02	−.027, .051	.547	.037	.026	−.014, .088	.154	−.012	.024	−.059, .035	.628
Anterior Thalamic Radiation	−.038	.028	−.093, .017	.183	.01	.03	−.049, .069	.730	.014	.035	−.055, .083	.691	−.062	.035	−.131, .007	.076
Uncinate Fasciculus	−.001	.024	−.048, .046	.951	.03	.024	−.017, .077	.202	.048	.029	−.009, .105	.104	−.043	.028	−.098, .012	.133
Inferior Longitudinal Fasciculus	−.015	.026	−.066, .036	.566	.048	.026	−.003, .099	.070	.03	.033	−.035, .095	.355	−.034	.031	−.095, .027	.279
Inferior Fronto-occipital Fasciculus	−.019	.028	−.074, .036	.495	.066	.027	.013, .119	.013	.007	.035	−.062, .076	.843	−.028	.033	−.093, .037	.388
Temporal Superior Longitudinal Fasciculus	−.039	.035	−.108, .030	.262	.087	.035	.018, .156	.012	.054	.042	−.028, .136	.200	−.02	.041	−.100, .060	.619
Parietal Superior Longitudinal Fasciculus	−.007	.04	−.085, .071	.868	.06	.042	−.022, .142	.153	.017	.052	−.085, .119	.746	−.077	.049	−.173, .019	.121
Superior Corticostriate-frontal	−.04	.044	−.126, .046	.360	.081	.046	−.009, .171	.076	.005	.057	−.107, .117	.925	−.086	.053	−.190, .018	.107
Superior Corticostriate-parietal	−.093	.034	−.160, −.026	.007	.008	.036	−.063, .079	.816	−.021	.043	−.105, .063	.627	−.051	.044	−.137, .035	.248
Striatal Inferior Frontal	−.095	.032	−.158, −.032	.003	−.002	.033	−.067, .063	.960	−.003	.04	−.081, .075	.949	−.06	.041	−.140, .020	.138
Inferior Frontal Superior Frontal	−.019	.025	−.068, .030	.456	.014	.026	−.037, .065	.588	.038	.032	−.025, .101	.235	−.019	.031	−.080, .042	.534
Corticospinal/ Pyramidal	−.05	.03	−.109, .009	.090	.008	.031	−.053, .069	.800	−.024	.038	−.098, .050	.527	−.073	.036	−.144, −.002	.045
Forceps Major	−.022	.032	−.085, .041	.495	.062	.031	.001, .123	.046	.075	.037	.002, .148	.042	.023	.036	−.048, .094	.523
Forceps Minor	−.031	.033	−.096, .034	.346	.021	.032	−.042, .084	.514	.044	.042	−.038, .126	.300	−.075	.039	−.151, .001	.056
Corpus Callosum Body	−.08	.051	−.180, .020	.116	.056	.051	−.044, .156	.265	.065	.064	−.060, .190	.311	−.047	.06	−.165, .071	.434

See the C paths in Figure 2.

ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; SE, standard error.

[a]Tabled *p* values are unadjusted. No coefficient for direct associations was significant after correction for 68 tests of direct associations at a 5% false discovery rate.

The EF findings suggest a pattern of widespread associations across white matter tracts, consistent with some previous studies (30). The patterns of associations of FA and MD with both EFs and externalizing psychopathology shown in Figures 4 and 5 are essentially identical. Because increased myelination may be reflected in both higher FA and lower MD, and increased myelination across development allows for more rapid communication among brain regions crucial to executive functioning (77), these findings may implicate widespread variations in myelination in the underlying neurobiology of variations in EFs. These could be the result of genetic or other factors that are not tract specific and occur early in neurodevelopment. Nonetheless, consistent with the results of previous studies (27,31,78), the strongest associations of FA and MD in this study were in the superior longitudinal fasciculus and inferior fronto-occipital fasciculus. Unlike those of other studies, the present findings also implicate early developing corticostriate projections in EFs, perhaps because of the age of the children.

Table 5. Standardized Path Coefficients for Direct Associations of Mean Diffusivity in Each of 17 Bilateral White Matter Tracts With Each Dimension of General and Specific Psychopathology Defined in the Bifactor Model in the Full Structural Equation Model, Controlling for Correlations Among the Tracts

	General Factor				Specific Internalizing				Specific Conduct Problems				Specific ADHD			
Tract	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]
Fornix	.002	.023	−.043, .047	.935	−.008	.026	−.059, .043	.764	.057	.031	−.004, .118	.07	.052	.031	−.009, .113	.093
Cingulate Bundle	−.002	.030	−.061, .057	.951	−.038	.028	−.093, .017	.18	−.019	.035	−.088, .050	.584	.039	.035	−.030, .108	.265
Parahippocampal Cingulum	.01	.023	−.035, .055	.659	−.039	.023	−.084, .006	.09	−.021	.027	−.074, .032	.449	.015	.027	−.038, .068	.57
Anterior Thalamic Radiation	.036	.032	−.027, .099	.256	−.051	.033	−.116, .014	.117	.016	.041	−.064, .096	.689	.034	.042	−.048, .116	.412
Uncinate Fasciculus	.028	.031	−.033, .089	.368	−.025	.032	−.088, .038	.439	−.032	.041	−.112, .048	.437	.089	.039	.013, .165	.023
Inferior Longitudinal Fasciculus	.02	.029	−.037, .077	.485	−.017	.029	−.074, .040	.564	−.040	.037	−.113, .033	.281	.064	.035	−.005, .133	.073
Inferior Fronto-occipital Fasciculus	.023	.045	−.065, .111	.614	−.047	.045	−.135, .041	.292	−.127	.055	−.235, −.019	.021	.046	.056	−.064, .156	.417
Temporal Superior Longitudinal Fasciculus	.041	.052	−.061, .143	.435	−.062	.054	−.168, .044	.259	−.103	.066	−.232, .026	.117	.093	.068	−.040, .226	.169
Parietal Superior Longitudinal Fasciculus	.037	.063	−.086, .160	.555	−.094	.065	−.221, .033	.145	−.109	.078	−.262, .044	.162	.062	.080	−.095, .219	.438
Superior Corticostriate-frontal	.096	.061	−.024, .216	.118	−.098	.062	−.220, .024	.114	−.083	.076	−.232, .066	.278	.066	.076	−.083, .215	.388
Superior Corticostriate-parietal	.057	.055	−.051, .165	.302	−.093	.057	−.205, .019	.106	−.090	.071	−.229, .049	.202	.055	.072	−.086, .196	.444
Striatal Inferior Frontal	.076	.048	−.018, .170	.114	−.058	.049	−.154, .038	.232	−.095	.058	−.209, .019	.106	.006	.062	−.116, .128	.924
Inferior Frontal Superior Frontal	.05	.039	−.026, .126	.191	−.039	.041	−.119, .041	.346	−.059	.051	−.159, .041	.24	.084	.050	−.014, .182	.089
Corticospinal/Pyramidal	.037	.046	−.053, .127	.425	−.059	.048	−.153, .035	.219	−.084	.059	−.200, .032	.155	.076	.058	−.038, .190	.189
Forceps Major	.023	.033	−.042, .088	.489	−.031	.033	−.096, .034	.34	−.053	.042	−.135, .029	.203	.042	.041	−.038, .122	.308
Forceps Minor	.02	.039	−.056, .096	.608	.013	.042	−.069, .095	.746	−.040	.052	−.142, .062	.45	.099	.049	.003, .195	.045
Corpus Callosum Body	.029	.066	−.100, .158	.666	−.066	.068	−.199, .067	.329	−.054	.088	−.226, .118	.535	.118	.084	−.047, .283	.158

See the C paths in Figure 2.

ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; SE, standard error.

[a]Tabled *p* values are unadjusted. No coefficient for direct associations was significant after correction for 68 tests of direct associations at a 5% false discovery rate.

The novel findings of these analyses are the indirect associations between psychopathology and microstructure through EFs. They suggest the hypothesis that some aspects of the etiologic and stochastic factors that cause individual differences in white matter (79) also directly influence EFs and, in turn, contribute to risk for conduct problems and ADHD. This hypothesis can be tested when future waves of data from the ABCD Study are available (80). Such prospective tests could help determine if research focused on the neural circuits involved in EFs will shed important light on the mechanisms of psychopathology. Interesting supportive evidence for this hypothesis already comes from the IMAGEN study, which recently reported a significant association between a polygenic risk score for ADHD and FA in several white matter tracts, including the bilateral superior and inferior longitudinal fasciculi (81).

Effect Sizes

Some of the magnitudes of associations revealed in the present analyses were appreciable, such as the associations of ADHD and conduct problems with EFs, but most were small. Therefore, it is important to consider the value of such effect sizes. They are too small to be useful in clinical prediction at the individual level, but are they large enough to be of scientific importance? To frame this discussion, it is essential to recall that many large studies have identified almost exclusively small but reliable associations between behavior and both genetic variants and measures of brain structure and function (82). Thus, the present effect sizes are well within the range of previous neurobiological findings. Moreover, there are good reasons why small effect sizes for associations between brain and behavior should be expected in large studies. First, large studies tend to use brief and inexpensive measures of psychopathology, which means that psychopathology is measured with modest sensitivity and reliability. Second, although brain and psychopathology change markedly over time, particularly during adolescence (83–85), most large neurobiological studies have used snapshot assessments at a single point in developmental time. One reason that the forthcoming longitudinal waves of ABCD Study data collection and other

Table 6. Standardized Path Coefficients for Indirect Associations of Fractional Anisotropy in Each of 17 Bilateral White Matter Tracts With Each Dimension of General and Specific Psychopathology Defined in the Bifactor Model in the Full Structural Equation Model, Controlling for Correlations Among the Tracts

	General Factor				Specific Internalizing				Specific Conduct Problems				Specific ADHD			
Tract	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]
Fornix	−.002	.001	−.004, .000	.177	−.002	.001	−.004, .000	.141	−.010[b]	.004[b]	−.018, −.002[b]	.007[c]	−.017[b]	.006[b]	−.029, −.005[b]	.005[c]
Cingulate Bundle	−.003	.002	−.007, .001	.153	−.003	.002	−.007, .001	.115	−.016[b]	.004[b]	−.024, −.008[b]	<.001[c]	−.028[b]	.007[b]	−.042, −.014[b]	<.001[c]
Parahippocampal Cingulum	−.002	.001	−.004, .000	.172	−.002	.001	−.004, .000	.143	−.009[b]	.003[b]	−.015, −.003[b]	.010[c]	−.016[b]	.006[b]	−.028, −.004[b]	.007[c]
Anterior Thalamic Radiation	−.004	.002	−.008, .000	.141	−.004	.002	−.008, .000	.11	−.021[b]	.005[b]	−.031, −.011[b]	<.001[c]	−.038[b]	.009[b]	−.056, −.020[b]	<.001[c]
Uncinate Fasciculus	−.003	.002	−.007, .001	.143	−.003	.002	−.007, .001	.108	−.018[b]	.005[b]	−.028, −.008[b]	<.001[c]	−.033[b]	.007[b]	−.047, −.019[b]	<.001[c]
Inferior Longitudinal Fasciculus	−.003	.002	−.007, .001	.148	−.003	.002	−.007, .001	.114	−.018[b]	.005[b]	−.028, −.008[b]	<.001[c]	−.032[b]	.008[b]	−.048, −.016[b]	<.001[c]
Inferior Fronto-occipital Fasciculus	−.003	.002	−.007, .001	.144	−.004	.002	−.008, .000	.107	−.021[b]	.005[b]	−.031, −.011[b]	<.001[c]	−.037[b]	.008[b]	−.053, −.021[b]	<.001[c]
Temporal Superior Longitudinal Fasciculus	−.006	.004	−.014, .002	.136	−.007	.004	−.015, .001	.099	−.036[b]	.007[b]	−.050, −.022[b]	<.001[c]	−.063[b]	.011[b]	−.085, −.041[b]	<.001[c]
Parietal Superior Longitudinal Fasciculus	−.008	.006	−.020, .004	.132	−.01	.006	−.022, .002	.096	−.050[b]	.009[b]	−.068, −.032[b]	<.001[c]	−.09[b]0	.014[b]	−.117, −.063[b]	<.001[c]
Superior Corticostriate Frontal	−.009	.006	−.021, .003	.133	−.01	.006	−.022, .002	.096	−.052[b]	.010[b]	−.072, −.032[b]	<.001[c]	−.093[b]	.015[b]	−.122, −.064[b]	<.001[c]
Superior Corticostriate-parietal	−.003	.002	−.007, .001	.157	−.004	.003	−.010, .002	.122	−.021[b]	.006[b]	−.033, −.009[b]	.001[c]	−.038[b]	.011[b]	−.060, −.016[b]	.001[c]
Striatal Inferior Frontal	−.004	.003	−.010, .002	.147	−.004	.003	−.010, .002	.112	−.023[b]	.006[b]	−.035, −.011[b]	<.001	−.041[b]	.01[b]	−.061, −.021[b]	<.001
Inferior Frontal Superior Frontal	−.003	.002	−.007, .001	.157	−.003	.002	−.007, .001	.12	−.016[b]	.005[b]	−.026, −.006[b]	.001	−.028[b]	.008[b]	−.044, −.012	<.001
Corticospinal/Pyramidal	−.004	.003	−.010, .002	.142	−.005	.003	−.011, .001	.104	−.026[b]	.006[b]	−.038, −.014[b]	<.001	−.046[b]	.009[b]	−.064, −.028[b]	<.001
Forceps Major	−.004	.003	−.010, .002	.14	−.004	.003	−.010, .002	.106	−.023[b]	.006[b]	−.035, −.011[b]	<.001	−.042[b]	.009[b]	−.060, −.024[b]	<.001
Forceps Minor	−.002	.001	−.004, .000	.215	−.002	.002	−.006, .002	.189	−.011	.006	−.023, .001	.046	−.020	.010	−.040, .000	.041
Corpus Callosum Body	−.008	.005	−.018, .002	.137	−.009	.005	−.019, .001	.102	−.047[b]	.01[b]	−.067, −.027[b]	<.001	−.084[b]	.016[b]	−.115, −.053[b]	<.001

See Figure 1.
ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; SE, standard error.
[a]Tabled *p* values are unadjusted.
[b]Coefficients are significant after correction for 68 tests of direct associations at a 5% false discovery rate.
[c]Significant *p* values after correction.

Table 7. Standardized Path Coefficients for Indirect Associations of Mean Diffusivity in Each of 17 Bilateral White Matter Tracts With Each Dimension of General and Specific Psychopathology Defined in the Bifactor Model in the Full Structural Equation Model, Controlling for Correlations Among the Tracts

	General Factor				Specific Internalizing				Specific Conduct Problems				Specific ADHD			
Tract	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]	β	SE	95% CI	*p* Value[a]
Fornix	.002	.001	.000, .004	.217	.002	.002	−.002, .006	.134	.011[b]	.004[b]	.003, .019[b]	.010[c]	.021[b]	.008[b]	.005, .037[b]	.007[c]
Cingulate Bundle	.003	.002	−.001, .007	.185	.004	.003	−.002, .010	.096	.022[b]	.006[b]	[.010, .034[b]	<.001[c]	.039[b]	.009[b]	.021, .057[b]	<.001[c]
Parahippocampal Cingulum	.003	.002	−.001, .007	.179	.003	.002	−.001, .007	.094	.017[b]	.004[b]	.009, .025[b]	<.001[c]	.031[b]	.007[b]	.017, .045[b]	<.001[c]
Corticospinal/Pyramidal	.005	.003	−.001, .011	.174	.006	.004	−.002, .014	.088	.030[b]	.007[b]	.016, .044[b]	<.001[c]	.055[b]	.011[b]	.033, .077[b]	<.001[c]
Uncinate Fasciculus	.003	.002	−.001, .007	.185	.004	.003	−.002, .010	.099	.022[b]	.006[b]	.010, .034[b]	<.001[c]	.039[b]	.01[b]	.019, .059[b]	<.001[c]
Inferior Longitudinal Fasciculus	.002	.002	−.002, .006	.201	.003	.002	−.001, .007	.118	.016[b]	.005[b]	.006, .026[b]	.003[c]	.028[b]	.009[b]	.010, .046[b]	.002[c]
Inferior Fronto-occipital Fasciculus	.005	.004	−.003, .013	.181	.007	.004	−.001, .015	.093	.036[b]	.009[b]	.018, .054[b]	<.001[c]	.065[b]	.015[b]	.036, .094[b]	<.001[c]
Temporal Superior Longitudinal Fasciculus	.006	.005	−.004, .016	.182	.008	.005	−.002, .018	.094	.042[b]	.011[b]	.020, .064[b]	<.001[c]	.075[b]	.017[b]	.042, .108[b]	<.001[c]
Parietal Superior Longitudinal Fasciculus	.009	.006	−.003, .021	.176	.012	.007	−.002, .026	.089	.059[b]	.013[b]	.034, .084[b]	<.001[c]	.106[b]	.021[b]	.065, .147[b]	<.001[c]
Superior Corticostriate-frontal	.009	.007	−.005, .023	.174	.012	.007	−.002, .026	.087	.061[b]	.013[b]	.036, .086[b]	<.001[c]	.110[b]	.02[b]	.071, .149[b]	<.001[c]
Superior Corticostriate-parietal	.008	.006	−.004, .020	.175	.010	.006	−.002, .022	.089	.052[b]	.012[b]	.028, .076[b]	<.001[c]	.094[b]	.019[b]	.057, .131[b]	<.001[c]
Striatal Inferior Frontal	.007	.005	−.003, .017	.173	.010	.006	−.002, .022	.085	.049[b]	.010[b]	.029, .069	<.001[c]	.088[b]	.016[b]	.057, .119[b]	<.001[c]
Inferior Frontal Superior Frontal	.003	.002	−.001, .007	.210	.004	.003	−.002, .010	.130	.020[b]	.007[b]	.006, .034	.007[c]	.035[b]	.012[b]	.011, .059[b]	.005[c]
Anterior Thalamic Radiation	.006	.004	−.002, .014	.178	.008	.005	−.002, .018	.092	.040[b]	.009[b]	.022, .058	<.001[c]	.071[b]	.015[b]	.042, .100[b]	<.001[c]
Forceps Major	.003	.002	−.001, .007	.192	.004	.002	.000, .008	.107	.019[b]	.006[b]	.007, .031[b]	.001[c]	.035[b]	.01[b]	.015, .055[b]	.001[c]
Forceps Minor	.000	.001	−.002, .002	.801	.000	.001	−.002, .002	.800	.002	.007	−.012, .016	.798	.003	.012	−.021, .027	.798
Corpus Callosum Body	.006	.004	−.002, .014	.196	.008	.005	−.002, .018	.111	.039[b]	.012[b]	.015, .063[b]	.002[c]	.070[b]	.021[b]	.029, .111[b]	.001[c]

See Figure 2.
ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; SE, standard error.
[a]Tabled *p* values are unadjusted.
[b]Coefficients are significant after correction for 68 tests of direct associations at a 5% false discovery rate.
[c]Significant *p* values after correction.

studies are so important is that single measures of brain and psychopathology at a single age almost certainly underestimate the magnitudes of brain–behavior associations. Third, the noninvasive measurement of individual differences in brain structure and function in living research participants is a remarkable scientific advance, but one that is still in its infancy. Given the modest reliability and validity of measures on both sides of the equation, it is perhaps surprising that any replicable and interpretable brain–behavior associations have been found. Fourth, the present study measured only individual differences in white matter microstructure when many other aspects of brain structure and function could be related to psychopathology. Just as polygenic risk scores are used to combine very small genetic liabilities, it may well be necessary to find an analogous way to combine many small risks associated with a broad range of variations in brain to enhance prediction.

Finally, one would expect large associations between indices of brain structure and psychopathology only if those associations were not robustly moderated by every aspect of each person's experiences in families, school, neighborhoods, and subcultures. This is not to mention the potential moderation of brain–behavior associations by illness, nutrition, and other factors. When one considers that multiple aspects of brain structure almost certainly are related to risk for psychopathology, and that we do not know if these associations combine additively or interactively, the identification of small but reliable effect sizes is not to be dismissed. It will take time to interpret findings of small effect sizes, but this complexity should not surprise or deter us (86).

Limitations

Because data collection was limited to sites with MRI facilities, the ABCD Study sample is not representative of the United States population. Furthermore, the exclusion of participants without valid MRI data resulted in somewhat better-functioning children being included in the sample. This could misestimate population parameters even when weighting was used.

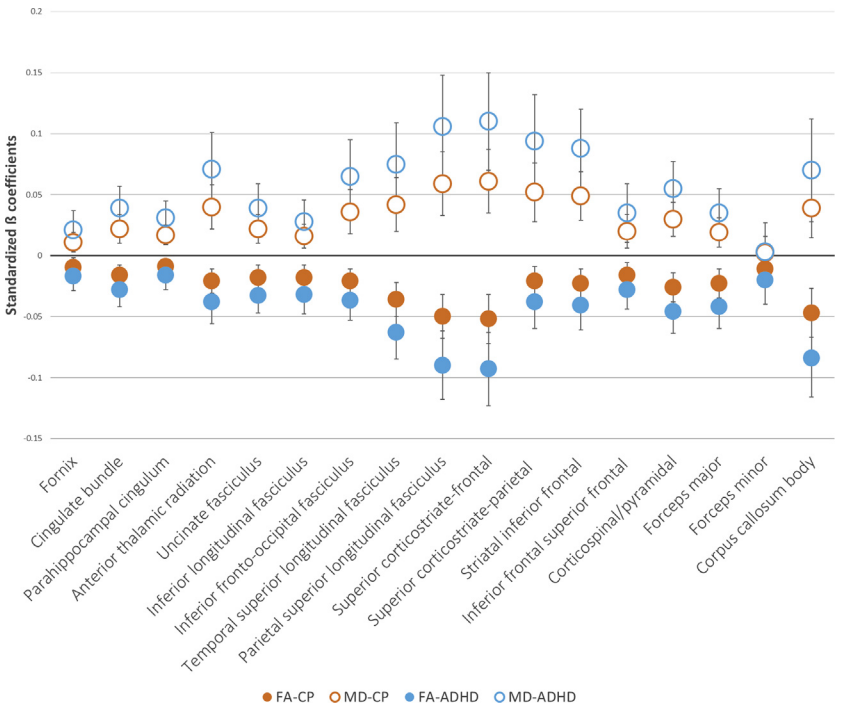

Figure 4. Standardized coefficients for independent indirect associations between latent factors of attention-deficit/hyperactivity disorder (ADHD) and conduct problems (CP) and fractional anisotropy (FA) and mean diffusivity (MD) in 17 bilateral white matter tracts through executive functions (compare with Tables 3 and 6).

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Data used in the preparation of this article were obtained from the ABCD Study (https://abcdstudy.org), held in the National Institute of Mental Health Data Archive. This is a multisite, longitudinal study designed to recruit >10,000 children 9 to 10 years of age and follow them over 10 years into early adulthood. The ABCD Study is supported by the National Institutes of Health and additional federal partners (Grant Nos. U01DA041022, U01DA041028, U01DA041048, U01DA041089, U01DA041106, U01DA041117, U01DA041120, U01DA041134, U01DA041148, U01DA041156, U01DA041174, U24DA041123, U24DA041147, U01DA041093, and U01DA041025). A full list of ABCD Study supporters is available at https://abcdstudy.org/nih-collaborators. A listing of participating sites and a complete listing of the study investigators can be found at https://abcdstudy.org/principal-investigators.html. ABCD Consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in analysis or writing of this report.

This manuscript reflects the views of the authors and may not reflect the opinions or views of the National Institutes of Health or ABCD Consortium investigators.

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The ABCD Study data used in this study can be accessed at https://nda.nih.gov/abcd. The ABCD data repository grows and changes over time. The ABCD data used in this report came from RRID:SCR_015769, doi: 1.15154/1503209. The preprocessing and analysis code are available on GitHub. The data used for all these analyses is available for download from the National Institute of Mental Health Data Archive (nda.nih.gov) under Study 945 (doi: 1.15154/1519200).

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