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Archival Report

Reconfiguration of Functional Brain Network Organization and Dynamics With Changing Cognitive Demands in Children With Attention-Deficit/Hyperactivity Disorder

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ABSTRACT

BACKGROUND: The pathophysiology of attention-deficit/hyperactivity disorder (ADHD) is characterized by atypical brain network organization and dynamics. Although functional brain networks adaptively reconfigure across cognitive contexts, previous studies have largely focused on network dysfunction during the resting state. In this preliminary study, we examined how functional brain network organization and dynamics flexibly reconfigure across rest and 2 cognitive control tasks with different cognitive demands in 30 children with ADHD and 36 typically developing children (ages 8–12 years).

METHODS: We leveraged graph theoretical analyses to interrogate the segregation (modularity, within-module degree) and integration (global efficiency, node dissociation index) of frontoparietal, cingulo-opercular/salience, default mode, somatomotor, and visual networks. We also conducted edge time series analyses to quantify connectivity dynamics within and between these networks.

RESULTS: Across resting and task-based states, children with ADHD demonstrated significantly lower whole-graph modularity and a greater node dissociation index between default mode and visual networks. Furthermore, a significant task-by-diagnosis interaction was observed for frontoparietal network within-module degree, which decreased from rest to task in children with ADHD but increased in typically developing children. Finally, children with ADHD displayed significantly more dynamic connectivity within and across cingulo-opercular/salience, default mode, and somatomotor networks, especially during task performance. Exploratory analyses revealed associations between network dynamics, cognitive performance, and ADHD symptoms.

CONCLUSIONS: By integrating static and dynamic network analyses across changing cognitive demands, this study provides novel insight into how context-specific, context-general, and timescale-dependent network connectivity is altered in children with ADHD. Our findings highlight the involvement and clinical relevance of both association and sensory/motor systems in ADHD.

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Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by developmentally inappropriate inattention, impulsivity, and hyperactivity (1). These symptoms are commonly accompanied by deficits in cognitive control, the ability to flexibly regulate behavior to pursue goals (2,3). The pathophysiology of ADHD is increasingly understood in terms of dysfunctional interactions across large-scale brain networks (4,5). Nonetheless, existing research has primarily focused on the resting state despite evidence that brain networks adaptively reconfigure to support context-specific cognition (6–8). Moreover, this literature has largely examined functional brain network organization assumed to be stable across time, even though network dynamics are also altered in ADHD (9–11). Accordingly, in this study, we examined how functional brain network organization and dynamics reconfigure between rest and cognitive control tasks in children with ADHD compared with typically developing (TD) children.

Previous studies characterizing aberrant resting-state functional connectivity (FC) in ADHD have implicated networks underlying cognitive control (frontoparietal, cingulo-opercular/salience), internally oriented cognition (default mode), and sensorimotor processes (visual, somatomotor) (12–16). While most studies have focused on FC strength (17–19), recent work has leveraged computational techniques from network neuroscience, such as graph theory, to interrogate the broader organization of the brain in ADHD (5). Two topological properties critical for emergent cognition and often

altered in neuropsychiatric disorders involve network segregation (the degree to which the brain organizes into distinct networks) and network integration (how these networks interact) (7,20,21). Graph theoretical studies of ADHD have exclusively focused on rest and have reported both increased (22,23) and decreased (24) segregation. Conversely, ADHD has been linked to lower whole-brain integration (22–24) but greater integration between default mode and task-relevant networks (18,25). However, whether these global and network-specific alterations vary across tasks remains unknown. Because tasks constrain neural variability and magnify individual differences in cognition (26), examining network organization across contexts can offer novel insight into topological alterations in ADHD.

Despite trait-like similarities across rest and tasks (27–29), brain organization dynamically reconfigures between rest and tasks to meet the constrained cognitive demands of specific task contexts (6,8). In adults and TD children, network integration increases during working memory, decision making, and visual perception tasks but decreases during motor execution and response inhibition tasks (30–32). Integrated states efficiently coordinate distinct processes involved in complex cognition, while segregated states promote functional specialization by preventing task-irrelevant processes from interfering with task-relevant cognition (6,33). Nevertheless, how brain organization reconfigures across contexts in children with ADHD has not been examined.

The abovementioned studies evaluated stable brain organization across time (static FC). However, FC dynamically fluctuates from moment to moment to regulate cognition (6,34). Network dynamics may be particularly relevant for ADHD given the high intraindividual variability in behavior and attention characteristic of this disorder (35,36). ADHD has been associated with less dynamic FC within the default mode network (11). Findings regarding dynamic interactions between default mode and task-relevant networks have been inconsistent, with both more (9,10,37) and less (38,39) dynamic FC found in ADHD, partly due to differences in the networks examined and the techniques used to estimate dynamic FC. Nonetheless, investigations of network dynamics in ADHD have also exclusively focused on rest.

Executing, or transitioning into, cognitively demanding activities is often challenging for individuals with ADHD (40,41). Accordingly, evaluating task-evoked network organization and dynamics seems necessary for characterizing the pathophysiology of ADHD. In this preliminary study, we investigated how functional brain network organization and dynamics reconfigure between rest and 2 cognitive control tasks in children with ADHD versus TD children; a simpler task probed response inhibition, while a more complex task added a working memory component to increase cognitive load. We focused on frontoparietal, cingulo-opercular/salience, default mode, somatomotor, and visual networks engaged during these tasks and implicated in ADHD (12–16). We implemented graph theory to characterize the integration/segregation of these networks. To examine network dynamics, we leveraged the recent edge time series approach that quantifies how brain activity cofluctuates over time (42–44). Given greater resting-state integration between default mode and task-relevant networks (18,25) but inconsistent alterations in dynamic FC (9,11,37–39) in ADHD, we hypothesized that compared with TD children, children with ADHD would exhibit greater integration, reduced segregation, and distinct dynamic FC overall. Because children with ADHD show deficits in sustaining and adapting to task contexts (45,46), we also hypothesized reduced changes in network topology and dynamics across contexts in ADHD.

METHODS AND MATERIALS

Participants

Participants included 54 children with ADHD and 56 TD children (8–12 years) who completed functional magnetic resonance imaging (MRI) scanning. To minimize motion artifacts, we excluded children with insufficient scanning time points (n_{ADHD} = 23, n_{TD} = 20; see the Supplement). We excluded 1 additional participant with ADHD due to limited brain coverage (see Functional Connectivity). Therefore, this study included 30 children with ADHD ($mean_{age}$ = 9.91 years, 14 female) and 36 TD children ($mean_{age}$ = 10.14 years, 19 female). The ADHD and TD groups did not differ on age, sex, race, socioeconomic status, or IQ (Table 1). Included and excluded participants did not differ on age, sex, race, or ADHD symptom severity (false discovery rate–corrected ps [p_{FDRs}] $>$ .120). For detailed inclusion/exclusion criteria, see the Supplement. This study was approved by the Johns Hopkins University School of Medicine Institutional Review Board. Parents provided consent, and children provided assent.

Go/No-Go Tasks

Participants completed 2 in-scanner go/no-go (GNG) tasks with spaceships as stimuli (see the Supplement). Participants responded to go stimuli and withheld responses to no-go stimuli. Whereas the "simple" version (GNGs) had straightforward stimulus-response mappings (green = go, red = no-go), the more complex, repeat version (GNGr) added a one-back working memory component to response decisions (different color = go, repeated color = no-go). We calculated the coefficient of variation (standard deviation/mean) in response time (CVRT) to estimate intraindividual response time variability (47,48), as increased response time variability may be an endophenotype of ADHD and is commonly operationalized using CVRT (49,50).

ADHD Symptoms

Symptom severity was assessed using the Hyperactive/Impulsive and Inattentive subscale T scores from the Conners' Parent Rating Scales-Revised or Conners-3 (51,52).

MRI Data Acquisition and Processing

MRI scans were collected on a 3T Philips Achieva whole-body MR machine at the Kennedy Krieger Institute F.M. Kirby Research Center for Functional Brain Imaging (see the Supplement). Participants completed a resting-state scan (eyes open, white fixation cross, gray background) lasting 5.3 minutes (128 volumes, n = 6), 6.5 minutes (156 volumes, n = 40), or 9 minutes (216 volumes, n = 1) and 2 scans for each GNG task, each lasting 3.8 minutes (91 volumes, n = 3) or 4.1 minutes (98 volumes, n = 63).

fMRI data were preprocessed using fMRIPrep (53), including echoplanar imaging to T1-weighted coregistration, susceptibility artifact correction, spatial normalization, and motion

Table 1. Demographic, Clinical, and Neuroimaging Characteristics by Diagnostic Group

Characteristic	ADHD, *n* = 30	TD, *n* = 36	Corrected *p* Value
Age, Years	9.91 (1.21)	10.14 (0.92)	.512
Sex, Female/Male	14/16	19/17	.621
Race			.512
African American	2 (6.7%)	3 (8.3%)	
Asian	0 (0.0%)	1 (2.8%)	
Biracial	3 (10.0%)	5 (13.9%)	
White	25 (82.3%)	27 (75.0%)	
Ethnicity			N/A
Hispanic/Latino	2 (6.7%)	1 (2.8%)	
Not Hispanic/Latino	28 (93.3%)	35 (97.2%)	
Parent Socioeconomic Status	51.15 (10.17)	55.85 (7.48)	.210
General Ability Index	116.50 (14.07)	119.22 (10.84)	.512
ADHD Presentation			
Combined	20 (66.7%)	0 (0.0%)	
Hyperactive/impulsive	1 (3.3%)	0 (0.0%)	
Inattentive	9 (30.0%)	0 (0.0%)	
ODD Diagnosis	11	0	N/A
ADHD Inattention T Score	72.63 (9.62)	45.23 (4.76)	<.001[a]
ADHD Hyperactivity/Impulsivity T Score	64.67 (12.06)	47.68 (4.64)	<.001[a]
Currently Taking Stimulant Medication	24 (80.0%)	0 (0.0%)	N/A
FD During Resting-State Scan, mm	0.15 (0.08)	0.15 (0.06)	.850
FD During GNGs Task Scan, mm	0.23 (0.16)	0.14 (0.07)	.010[a]
FD During GNGr Task Scan, mm	0.21 (0.11)	0.16 (0.09)	.068
Time Points During Resting-State Scan	139.72 (22.66)	135.34 (24.47)	.536
Time Points During GNGs Task Scan	149.83 (39.81)	176.17 (24.49)	.008[a]
Time Points During GNGr Task Scan	158.63 (30.93)	171.17 (24.61)	.117

All results are presented as mean (SD) or *n* (%). Socioeconomic status data are from (91). General Ability Index from the Wechsler Intelligence Scale for Children (WISC)-IV (92) is provided as an estimate of IQ. T scores were obtained from Conners' Parent Rating Scales–Revised (n = 10) (51) or Conners-3 (n = 56) (52). Diagnoses were confirmed using the Diagnostic Interview for Children and Adolescents IV (93). *p* Values were obtained from 2-sample *t* tests (or, in the case of sex and race, 2-sample χ^2 tests), false discovery rate (FDR)–corrected. Race was coded as White (sample majority) vs. non-White (sample minority) in the χ^2 test to provide sufficient cell sizes for a reliable inferential analysis. Given small cell sizes, ethnicity was not statistically compared between children with ADHD and TD children.

ADHD, attention-deficit/hyperactivity disorder; FD, framewise displacement (prior to motion correction); GNGr, repeat go/no-go task; GNGs, simple GNG task; ODD, oppositional defiant disorder; TD, typically developing.

[a]$p < .05$.

parameter estimation. We implemented several postprocessing steps following established guidelines (54,55) using a customized processing pipeline (56), including nuisance regression, bandpass filtering, and motion censoring (see the Supplement).

Children with ADHD showed significantly higher mean framewise displacement before motion correction than TD children during the GNGs task (Table 1). Head motion has been shown to be associated with and has similar genetic loadings with ADHD (57). Thus, as was done previously in this dataset (9,25), our main analyses did not match groups on mean framewise displacement so as to not obscure meaningful ADHD-related variance. However, we implemented stringent motion correction and confirmed the direction of our findings in supplemental analyses controlling for mean framewise displacement (Tables S7–S12).

Functional Connectivity

We parcellated the brain into 300 regions of interest (ROIs) (3.5-mm radius) using a common functional atlas (58) with additional subcortical coverage (59). We focused on fronto-parietal, cingulo-opercular/salience, default mode, dorsal somatomotor, and visual networks (Figure 1). We excluded 10 ROIs that were outside the field of view for some participants, yielding 211 ROIs. One participant was excluded because of dropout in 12 additional ROIs.

Subsequent steps were conducted in R. Blood oxygen level–dependent (BOLD) time series were extracted from each ROI separately for each run. We detrended and standardized time series for the 2 runs of each GNG task to control for signal intensity differences across runs. We then concatenated the runs of each task to maximize the amount of data. For static FC, we calculated FC separately for each context by correlating the time series between each ROI pair and Fisher *r*-to-*z* transforming each context-level correlation matrix. For dynamic FC, we used the BOLD time series for each context.

Graph Construction

The Fisher *z*-transformed FC matrices were thresholded to remove weak correlations that might be spurious due to noise.

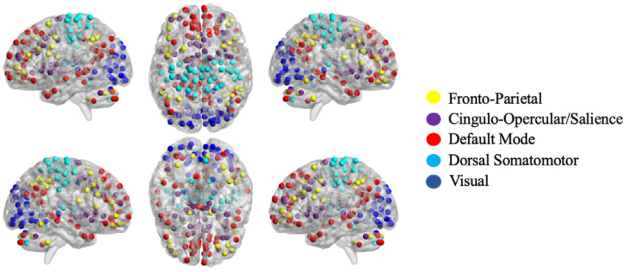

Figure 1. Regions of interest (ROIs) from the frontoparietal network (34 ROIs), cingulo-opercular/salience network (40 ROIs), default mode network (61 ROIs), dorsal somatomotor network (39 ROIs), and visual network (37 ROIs). ROIs taken from an established functional parcellation (59). [Figure generated using BrainNetViewer (90).]

Similar to prior work (30,60), to identify findings that are consistent across thresholds, we calculated graph metrics at each threshold (z = 0.20, 0.25, 0.30, 0.35) and averaged across thresholds for analysis (see the Supplement).

Graph Metrics

We calculated weighted, undirected graph metrics using the *igraph* and *braingraph* packages (61,62). Across the 5-network system, we assessed network integration (global efficiency) and network segregation (modularity). Global efficiency measures how efficiently information flows across the brain based on the mean of the inverse path lengths between all node pairs (63). Modularity evaluates the degree to which the brain segregates into distinct networks with strong within-network connectivity and was calculated using the parcellation-defined network affiliations (64).

Next, we measured network integration (node dissociation index [NDI]) and network segregation (within-module degree [WD]) for each ROI and averaged within each network to examine network-level topology. NDI assesses between-network connectivity by summing each node's connection weights with nodes in every other network divided by the total weighted connections (65). WD measures within-network connectivity (66). We computed unstandardized WD by summing each node's connection weights with all other nodes in the same network (66). We also calculated an average NDI across subgraphs comprising each pair of networks to quantify integration between each network pair.

Dynamic FC

We quantified dynamic FC using edge time series (42–44). This technique has several strengths over other approaches (e.g., sliding windows), including higher temporal resolution, using the native BOLD data without additional processing or selecting model-based parameters (e.g., window length/overlap), and not requiring contiguous time series to enable scrubbing.

We converted regional time series into edge time series by multiplying the z-scored BOLD signal value for each ROI pair at each time point, reflecting the synchronous cofluctuation of activity between pairs of brain regions. The root sum square (RSS) was calculated as the square root of the sum of the squared values across all edge cofluctuations within a time point. High RSS indicates strong activity cofluctuation at a given time point. We calculated the mean RSS for edges within and between networks, generating 15 RSS time series (5 within-network, 10 between-network). The standard deviation of each RSS time series (sdRSS) was computed to quantify the variability in activity cofluctuation across time within each network and between each pair of networks. Higher values indicate more dynamic FC.

Statistical Analyses

We conducted mixed-effects models predicting each metric of task performance (CVRT), network organization (graph theory), and network dynamics (sdRSS) from diagnosis (between-subjects), rest-to-GNGs reconfiguration (within-subjects), and GNGs-to-GNGr reconfiguration (within-subjects). Interactions between each task comparison and diagnosis were also examined. For each metric, we determined whether the final model included only 3 main effects or also included the 2 interactions from relative model fit [lower Akaike information criterion (67,68)]. This method detects interactions while balancing statistical power with model parsimony and fit. Because our interest was in diagnostic group differences, we only report main and interactive effects of diagnosis in the main text (see Tables S1–S3 for main effects of task).

We corrected for multiple comparisons using the FDR. For static FC, we corrected main effects for 2 comparisons on the whole-graph level (modularity, global efficiency) and 5 comparisons for each network-level metric (NDI, WD), corresponding to the 5 networks examined. Because only 1 interaction model was selected, FDR adjustments were not made. For network pairs, we corrected effects for 4 comparisons for each network (1 per pair with that network). For dynamic FC, we corrected main effects for 5 comparisons for within-network analyses and 10 comparisons for between-network analyses. Finally, we corrected interaction effects for 2 comparisons for within-network analyses and 5 comparisons for between-network analyses.

In exploratory brain-behavior analyses, regression models predicted each phenotype from each brain metric that differed between children with ADHD and TD children, separately per task and diagnostic group. Brain-symptom analyses were only conducted for the ADHD group. Because these analyses were exploratory, we did not correct for multiple comparisons.

Analyses controlled for sex and mean-centered age. Graph analyses also controlled for mean-centered mean FC to account for systematic variation in FC strength across diagnostic groups, ensuring that differences reflect topology rather than simply FC strength (69,70). Mixed-effects models also controlled for interindividual variation (subject-level intercept).

RESULTS

Go/No-Go Task Performance

CVRT significantly increased from the GNGs task to the GNGr task (main effect of task, $\beta = 0.07$, $p < .001$) and was significantly higher in children with ADHD than in TD children (main effect of diagnosis, $\beta = -0.07$, $p = .048$). CVRT did not increase across tasks differently between diagnostic groups (task-by-diagnosis interaction, $\beta = -0.02$, $p = .683$).

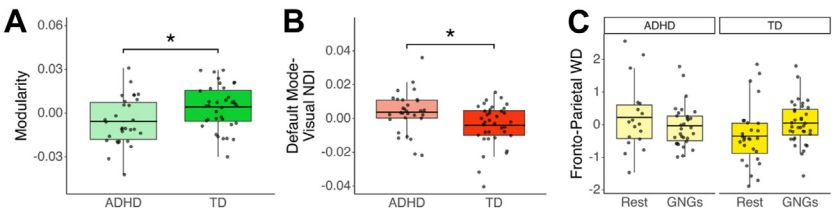

Figure 2. Static functional brain network organization in children with attention-deficit/hyperactivity disorder (ADHD) (n = 30) and typically developing (TD) children (n = 36). **(A)** Compared with TD children, children with ADHD showed significantly lower modularity across the 5-network system. **(B)** Network pair analyses revealed a significantly greater node dissociation index (NDI) between default mode and visual networks in children with ADHD compared with TD children. **(C)** From rest to the simple go/no-go task (GNGs), the within-module degree (WD) of the frontoparietal network decreased in children with ADHD but increased in TD children. Plots for main effects **(A, B)** depict unstandardized residuals extracted from mixed-effects models predicting each graph metric from task context (rest vs. GNGs, GNGs vs. repeat GNG task) while covarying for mean-centered age, mean-centered average functional connectivity, sex, and random subject-level intercept and averaging within each diagnostic group across the 3 task contexts. Plot for the interactive effect **(C)** depicts unstandardized residuals extracted from mixed-effects models predicting the graph metric from mean-centered age, mean-centered average functional connectivity, sex, and random subject-level intercept. Boxplot midlines represent the mean. *$p_{FDR} < .05$. FDR, false discovery rate.

Static FC

Functional Brain Network Organization. First, we examined differences in functional brain network organization between children with ADHD and TD children regardless of context (main effect of diagnosis). Compared with TD children, children with ADHD showed significantly lower modularity ($\beta = 0.42$, $p_{FDR} = .041$) (Figure 2A), but no other whole-graph or network-level differences were observed (Tables S1–S3). Because neural alterations in ADHD may be localized to specific network pairs (5,9,10,17,18,25), we conducted exploratory NDI analyses for each network pair. We found that children with ADHD exhibited significantly greater NDI specifically between default mode and visual networks ($\beta = -0.53$, $p_{FDR} = .032$) (Figure 2B and Table S4).

Task-Evoked Reconfiguration of Functional Brain Network Organization. Next, we determined whether children with ADHD and TD children displayed distinct topological reconfiguration across contexts. We found a significant task-by-diagnosis interaction for frontoparietal network WD from rest to the GNGs task ($\beta = -0.51$, $p = .038$) (Figure 2C and Tables S1–S3). Specifically, frontoparietal WD increased in TD children but decreased in children with ADHD. We further interrogated this effect with 2 post hoc analyses. To address our hypotheses about diagnosis-specific reconfiguration, we repeated the analyses separately for each diagnostic group, focusing on the main effect of task. To assess task-specific diagnostic group differences in topology, we conducted similar models to the main analyses separately for rest and the GNGs task (without random intercept), focusing on the main effect of diagnosis. We found nonsignificant rest-to-GNGs reconfiguration in both diagnostic groups and no group differences within either task (all p values $> .158$).

Dynamic FC

Functional Brain Network Dynamics. Next, we examined diagnostic group differences in dynamic FC regardless of context (main effect of diagnosis). Compared with TD children, children with ADHD showed significantly greater sdRSS within cingulo-opercular/salience ($\beta = -0.44$, $p_{FDR} = .026$), default mode ($\beta = -0.60$, $p_{FDR} = .028$), and dorsal somatomotor ($\beta = -0.84$, $p_{FDR} = .003$) networks (Figure 3A). Regarding between-network dynamics, children with ADHD showed significantly greater sdRSS between the default mode network and most other networks (cingulo-opercular/salience: $\beta = -0.44$, $p_{FDR} = .021$; dorsal somatomotor: $\beta = -0.89$, $p_{FDR} = .002$; visual: $\beta = -0.58$, $p_{FDR} = .031$), between the dorsal somatomotor network and each of the other networks (frontoparietal: $\beta = -0.75$, $p_{FDR} = .007$; cingulo-opercular/salience: $\beta = -0.84$, $p_{FDR} = .003$; visual: $\beta = -0.65$, $p_{FDR} = .021$), and between the cingulo-opercular/salience network and most other networks (frontoparietal: $\beta = -0.42$, $p_{FDR} = .025$) (Figure 3A). No other group differences were observed (Tables S5 and S6).

Task-Evoked Changes in Functional Brain Network Dynamics. We additionally assessed whether network dynamics changed differently across contexts in children with ADHD and TD children. We found a significant interaction from rest to the GNGs task within the default mode network ($\beta = 0.77$, $p_{FDR} = .037$), within the dorsal somatomotor network ($\beta = 0.74$, $p_{FDR} = .037$), and between these 2 networks ($\beta = 0.98$, $p_{FDR} = .031$) (Figure 3B–D and Tables S5 and S6). Specifically, sdRSS within and between these networks increased in children with ADHD but remained stable in TD children. Next, we conducted follow-up analyses similar to our static FC analyses. From rest to the GNGs task, sdRSS in children with ADHD increased marginally within the default mode network ($\beta = -0.49$, $p = .061$), significantly within the dorsal somatomotor network ($\beta = -0.59$, $p = .015$), and significantly between these 2 networks ($\beta = -0.80$, $p = .003$). There were no significant rest-to-GNGs changes for TD children (all p values $> .288$). Furthermore, compared with TD children, children with ADHD showed significantly greater sdRSS during the GNGs task within the default mode network ($\beta = -0.59$, $p = .016$), within the dorsal somatomotor network ($\beta = -0.78$, $p = .001$), and between these 2 networks ($\beta = -0.85$, $p < .001$). There were no group differences during rest (all p values $> .684$).

Brain-Behavior Associations

Finally, we explored how brain organization was related to CVRT and ADHD symptoms. Static brain organization was not significantly associated with behavior. Dynamic brain organization was associated with behavior only during the GNGr task (Figure 4). In TD children, higher sdRSS within the cingulo-opercular/salience network ($\beta = 0.46$, $p = .011$) and between the frontoparietal and cingulo-opercular/salience networks ($\beta = 0.49$, $p = .005$) was associated with higher CVRT. In children with ADHD, higher sdRSS between the default mode

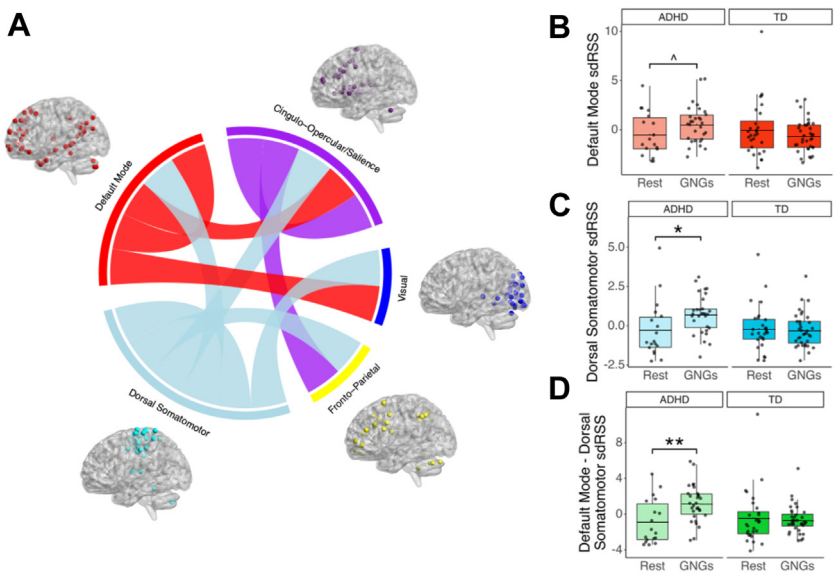

Figure 3. Functional brain network dynamics in children with attention-deficit/hyperactivity disorder (ADHD) (n = 30) and typically developing (TD) children (n = 36). **(A)** Dynamic functional connectivity (FC), estimated as standard deviation of root sum square (sdRSS), within and between frontoparietal, cingulo-opercular/salience, default mode, dorsal somatomotor, and visual networks across the 3 task contexts. Arcs depict connections with significantly greater sdRSS in children with ADHD than in TD children. There were no instances in which TD children had greater sdRSS within or between networks. Arc colors were selected based on the color of the network with the most significant group differences in sdRSS (default mode for default mode network pairs, dorsal somatomotor for dorsal somatomotor network pairs, cingulo-opercular/salience for cingulo-opercular/salience network pairs). **(B–D)** From rest to the simple go/no-go (GNGs) task, sdRSS increased in children with ADHD but remained the same in TD children **(B)** within the default mode network, **(C)** within the dorsal somatomotor network, and **(D)** between the default mode and dorsal somatomotor networks. Plots for interactive effects **(B–D)** depict unstandardized residuals extracted from mixed-effects models predicting each sdRSS metric from mean-centered age, sex, and random subject-level intercept. Boxplot midlines represent the mean. $^{\wedge}p < .10$, $^{*}p < .05$, $^{**}p < .01$.

and visual networks was associated with higher CVRT ($\beta = 0.42$, $p = .033$). Lastly, in children with ADHD, higher dorsal somatomotor sdRSS was associated with lower inattention ($\beta = -0.37$, $p = .036$), whereas higher dorsal somatomotor-visual sdRSS was associated with higher hyperactivity/impulsivity ($\beta = 0.47$, $p = .022$). No other associations reached statistical significance (all p values $> .050$).

DISCUSSION

In the current study, we examined the reconfiguration of functional brain network organization and dynamics between rest and cognitive control tasks in children with ADHD and TD children. Regardless of context, children with ADHD demonstrated reduced modularity (segregation) across the brain, increased NDI (integration) between default mode and visual networks, and greater sdRSS (dynamic FC) within and across most networks. We also observed diagnosis-specific reconfiguration from rest to the GNGs task. Frontoparietal WD (segregation) decreased in children with ADHD but increased in TD children. Conversely, sdRSS within and between the default mode and dorsal somatomotor networks increased in children with ADHD, but not in TD children. These preliminary findings reveal context-specific and context-general

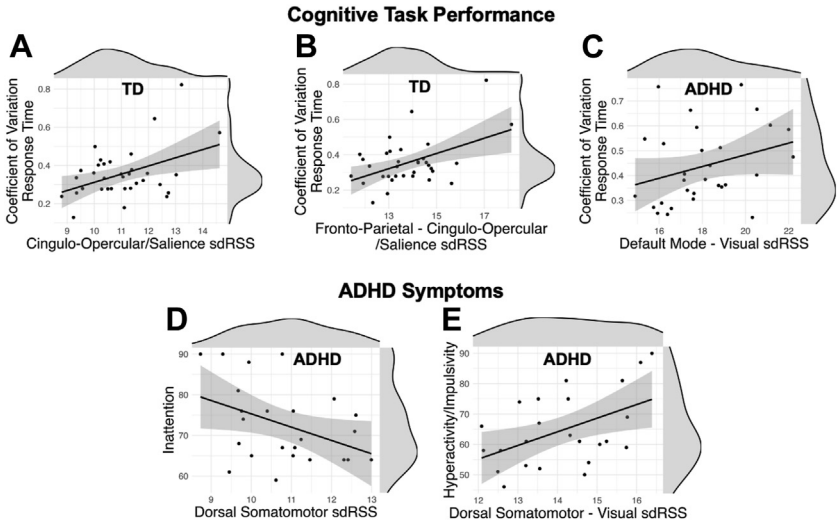

Figure 4. Exploratory associations between functional brain network dynamics and behavior. Brain-behavior and brain-symptom associations were statistically significant for dynamic but not static brain organization, and only when probed during the more complex, repeat go/no-go task (GNGr). In typically developing (TD) children, a higher standard deviation of root sum square (sdRSS) was associated with a higher coefficient of variation of response time (CVRT) **(A)** within the cingulo-opercular/salience network and **(B)** between the cingulo-opercular/salience and frontoparietal networks. **(C)** In children with attention-deficit/hyperactivity disorder (ADHD), higher sdRSS between the default mode and visual networks was associated with higher CVRT. **(D)** In children with ADHD, higher sdRSS within the dorsal somatomotor network was associated with lower inattention. **(E)** In children with ADHD, higher sdRSS between the dorsal somatomotor and visual networks was associated with higher hyperactivity/impulsivity. Shaded areas around regression lines represent confidence intervals around predicted values. Shaded areas around the axes represent variable distributions.

alterations in the topology and dynamics of large-scale brain networks in children with ADHD.

Functional Brain Network Organization

Across the 5-network system, children with ADHD demonstrated reduced modularity, regardless of context. This finding extends prior work by indicating lower network segregation in ADHD not only during rest (24) but also during cognitive control tasks. A segregated topology promotes functional specialization by upregulating communication within networks and downregulating communication between networks (6,33,71). These findings suggest that for children with ADHD, the brain may assume less specialized topological configurations and be more vulnerable to interference from task-irrelevant processes.

While the topology of individual networks did not differ across groups, exploratory network pair analyses revealed that in children with ADHD, the default mode network had higher NDI with the visual network rather than with cognitive control networks as expected. These findings could reflect different strategies across diagnostic groups. Children with ADHD may rely more on visual strategies during cognitive control to compensate for the higher demands of regulatory behavior (72,73). Accordingly, the default mode network may intrude on distinct task-relevant networks based on the strategies deployed by each group (i.e., frontoparietal/cingulo-opercular networks in TD children, visual network in children with ADHD). Indeed, default mode and sensory networks exhibit anticorrelated activity during audiovisual tasks in adults (74). While these networks may be less specialized in ADHD, these findings highlight the relevance of not only higher-order association networks but also lower-order sensory networks in ADHD.

Regarding task-evoked reconfiguration, frontoparietal WD increased from rest to the GNGs task in TD children, consistent with findings indicating higher frontoparietal within-network FC with increasing cognitive demands in adults (75–77). The opposite was observed in ADHD. Therefore, the magnitude of task-evoked reconfiguration was not reduced in children with ADHD as we hypothesized, but the pattern was still unique across groups. One possibility is that children with ADHD exhibit not only behavioral but also neural difficulties in adapting to shifting cognitive contexts (45,46). This interpretation is consistent with transcranial magnetic stimulation work reporting weaker rest-to-task increases in cortical excitability in children with ADHD (78). Alternatively, our results could reflect that children with ADHD apply altered, compensatory neural strategies for cognitive control (72,73). Interestingly, we did not find diagnostic group differences in GNGs-to-GNGr reconfiguration, suggesting greater challenges with transitioning into rather than across tasks in children with ADHD. Larger-scale studies examining brain and behavior across multiple tasks and sequences should further evaluate this hypothesis and its clinical implications.

Functional Brain Network Dynamics

Because network dynamics may be critical for ADHD (9,11,37–39), we assessed dynamic FC using edge time series (42–44), which has not been previously applied to ADHD. We observed higher sdRSS within and between most networks in children with ADHD, especially during cognitive tasks. These findings are consistent with some resting-state studies reporting more dynamic FC within the default mode network and between the default mode and cognitive control networks (10,11), but conflict with others indicating less dynamic FC within the default mode network and between the default mode and somatomotor networks (11). Combined with our static analyses, these observations could suggest that reduced network segregation/specialization may be related to more variable network interactions in ADHD. Prior studies of ADHD examined dynamic FC during rest using methods that require nontrivial decisions (e.g., sliding window duration) and that cannot censor high-motion time points. This study adds important new findings by demonstrating more dynamic FC in children with ADHD, especially during cognitive tasks, while bypassing these limitations.

Contrary to our predictions, we observed increased, rather than decreased, task-evoked changes in dynamic FC in children with ADHD. Specifically, sdRSS within and between default mode and dorsal somatomotor networks increased from rest to the GNGs task in children with ADHD but remained stable in TD children. Stable task-based FC across contexts may support sustained engagement of task-relevant and sustained disengagement of task-irrelevant cognition (6,79). Compared with adults, TD children exhibit more dynamic FC during a cognitive task, which relates to poorer performance (80). Therefore, our findings may reflect ADHD-related difficulties in sustaining task-relevant FC patterns during cognitive control, which may underlie inattention and response variability associated with ADHD (9,35,36).

Brain-Behavior Associations

Exploratory analyses revealed that dynamic but not static FC was associated with behavior. Higher sdRSS was related to higher intraindividual RT variability (CVRT) in a network- and diagnosis-dependent manner, consistent with evidence that stable task-based FC may be adaptive (80,81) and that dynamic FC captures aspects of behavior that are insensitive to static FC (10,82,83). Furthermore, we found that network dynamics could reflect either vulnerability (greater somatomotor-visual sdRSS was associated with elevated hyperactivity/impulsivity) or adaptation (greater somatomotor sdRSS was associated with reduced inattention), consistent with compensation and neurodiversity models of ADHD (72). Network dynamics were related to behavior only during the GNGr task, consistent with evidence that brain-behavior associations are strengthened with higher cognitive load (26,84). These preliminary findings suggest that brain-behavior links depend on diagnosis, timescale, cognitive context, and symptom dimension.

Limitations

Given our relatively modest sample size, larger-scale investigations could examine whether our findings differ across ADHD presentations and could replicate our brain-behavior associations to disentangle neurobiological mechanisms of impairment versus compensation. Furthermore, our participants were ages 8 to 12 years, predominantly White/non-

Hispanic, and remained relatively still during scanning. They also had limited co-occurring disorders, thereby providing an initial investigation that future work with more representative samples should build upon. Moreover, we did not match groups on head motion in our main analyses, although rigorous motion correction and supplemental analyses reinforce the robustness of our findings. Lastly, each region can belong to distinct networks across individuals (85,86). Here, we used established parcellations to define homogeneous networks across groups and individuals to facilitate consistency with prior work. However, future work should characterize whether neural alterations reflect differences in topology/dynamics, topography/arealization, or both.

Conclusions

The current study revealed that altered patterns of functional brain network organization and dynamics may represent a neurobiological signature of childhood ADHD across rest and cognitive control tasks. While our static analyses implicated default mode and visual networks in ADHD, our dynamic analyses additionally implicated cognitive control and dorsal somatomotor networks. Given a growing literature demonstrating visuomotor problems in ADHD (87,88), our findings reinforce the potential utility of biologically informed multimodal interventions targeting not only higher-order cognition but also basic sensorimotor processing (89). Overall, this preliminary study provides novel insight into the neurobiological mechanisms underlying childhood ADHD and associated impairments in cognitive control.

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CM was responsible for conceptualization, methodology, software, validation, formal analysis, data curation, writing the original draft of the manuscript, and visualization. MEM was responsible for conceptualization, methodology, and reviewing and editing the manuscript. ADC was responsible for methodology and reviewing and editing the manuscript. NDF was responsible for reviewing and editing the manuscript. KSR was responsible for investigation, resources, data curation, reviewing and editing the manuscript, and funding acquisition. SAC was responsible for reviewing and editing the manuscript. JJP was responsible for reviewing and editing the manuscript. OS was responsible for reviewing and editing the manuscript. SHM was responsible for investigation, resources, reviewing and editing the manuscript, project administration, and funding acquisition. JRC was responsible for conceptualization, methodology, software, data curation, reviewing and editing the manuscript, supervision, and project administration.

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