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Exploring the neural basis of reaction time variability in ADHD: The importance of examining data at the trial level

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Abstract

Patients with ADHD evidence elevated reaction time variability (RTV) due to periodic long reaction times (RTs). Even though reaction time variability (RTV) reflects intraindividual differences in RT across time, prior research exploring the neural basis of RTV in ADHD has primarily examined associations between neural activation and summary RTV outcomes (e.g., standard deviation of reaction time, tau). Here, we explore group differences in the neural basis of RTV by examining association between trial-level RTs and fMRI BOLD activation obtained during a Stop Signal Task in a large (n = 5719) sample of 9- to 10-year-old children participating in the Adolescent Brain Cognitive Development (ABCD) study. Children with ADHD demonstrated greater RTV than those without ADHD. ADHD-related group differences were not observed between fMRI BOLD activation and summary RTV outcomes. At the trial level, longer RTs were associated with increased BOLD activation in salience/ventral

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

attention and executive control networks and decreased BOLD activation in the default mode network, consistent with time-on-task effects (i.e., stimulus processing time) in which long RTs require maintaining task-positive activation and DMN suppression for more time than short RTs. Moreover, children with ADHD showed weaker associations between long RTs and BOLD activation in these regions than children without ADHD supporting models that point to dysregulated competition between the DMN and executive network as mechanism of cognitive impairment in ADHD.

Keywords

Intraindividual variability; Reaction time variability; Trial-by-trial

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder that causes impairment in multiple settings (American Psychological Association, 2013). While individuals with ADHD, by definition, manifest some combination of inattention, hyperactivity, and/or impulsivity, these symptoms and their severity are often expressed quite variably within individuals. It has been said that “individuals with ADHD are consistently inconsistent” (Kofler et al., 2013) and intraindividual variability may be a core and stable feature of the disorder (Kofler et al., 2013; Salum et al., 2019). One behavioral index of intraindividual variability is reaction time variability (RTV) which refers to inconsistencies in an individual’s speed of responding during computerized tasks. RTV has been suggested to reflect central nervous system integrity and is associated with cognitive functions such as top down attentional control (MacDonald et al., 2009). RTV is thus considered a marker for impaired attention (van der Molen, 1996).

Indeed, RTV is frequently elevated in patients with ADHD (Epstein et al., 2011b; Kofler et al., 2013; Tamm et al., 2012). A review of meta-analyses exploring the neurocognitive profile of ADHD found that RTV was the neuropsychological outcome that best discriminated ADHD patients versus controls (Pievsky and McGrath, 2018). Moreover, increased RTV in ADHD youths has been demonstrated using a wide range of computerized tasks including simple reaction time (RT), continuous performance, stop signal, and n-back tasks (Epstein et al., 2011b). Higher RTV is associated with inattention symptom ratings (Ali et al., 2019; Cai et al., 2021; Epstein et al., 2003; Kofler et al., 2013), ratings of attentional impulsiveness (Swick et al., 2013), objectively coded behavioral inattention (Antonini et al., 2013), and multiple negative sequelae including impaired social processing (Tamm et al., 2019), impaired reading decoding (Tamm et al., 2014), academic underachievement (Sjowall et al., 2017), and poorer overall functioning (van Lieshout et al., 2017). Additionally, RTV is highly heritable (Kuntsi et al., 2014).

In studies examining RTV in ADHD patient populations, a variety of summary RTV indicators have been utilized including the standard deviation of the reaction time (SDRT) as a measurement of spread or variability within participant’s RTs. Others use coefficient of variation (CV) providing a measure of RTV controlling for RT speed. Another approach

to defining RTV is the ex-Gaussian approach. Ex-Gaussian indicators divide an individual's task RT distributions into 1) mean for the normal component of the RT distribution (mu); 2) variability for the normal component of the RT distribution (sigma); and 3) variability for the exponential component of the RT distribution (tau). Research using ex-Gaussian parameters has shown that ADHD-related RTV is the largely the result of an elevation of tau (Bella-Fernandez et al., 2024; Hervey et al., 2006; Leth-Steensen et al., 2000; Vaurio et al., 2009). Thus, RTV in individuals with ADHD appears to be defined by periodic long RTs that occur throughout the RT stream (Castellanos et al., 2005; Epstein et al., 2023; Huang-Pollock et al., 2012; Johnson et al., 2007).

The neurobiological mechanisms leading to increased RTV in ADHD are not well understood and numerous hypotheses have been suggested to account for the neural basis of elevated RTV in ADHD (Kofler et al., 2013; Pievsky and McGrath, 2018). One prominent causal model is the default mode interference hypothesis of attentional deficits in ADHD (Kelly et al., 2008; Mowinckel et al., 2017; Salum et al., 2019; Sonuga-Barke and Castellanos, 2007). In this model, inattentiveness in ADHD may be due to insufficient down-regulation of the default mode network (DMN) during cognitive and goal-oriented processes, which is reflected behaviorally as increased RTV. The DMN's indirect contribution to impaired cognition, including higher RTV, is thought to arise from aberrant interactions with other task-relevant networks. For example, there may be disruptions in the rapid changes in relative activation in the DMN and dorsal attention network (DAN) that are facilitated by the salience network (SN) (Goulden et al., 2014; Menon, 2011, 2023; Menon and Uddin, 2010; Sridharan et al., 2008). The frontoparietal network is also involved and helps maintain specific states until a switch is needed (Menon, 2011, 2023; Seeley et al., 2007; Spreng et al., 2010, 2013). Thus, while much of the RTV literature in ADHD has emphasized increased DMN activation and decreased DAN activation as possible drivers of RTV, multiple networks and their interactions are likely relevant (Norman et al., 2023).

Extant magnetic resonance imaging (MRI) and functional MRI (fMRI) studies examining ADHD-related associations between RTV and neural indices, often with relatively small sample sizes, report contradictory findings. One study reported increased RTV and excess DMN activity in individuals with ADHD during a simple forced-choice task, however, the direct association between RTV and DMN was not directly assessed (Metin et al., 2015). In other studies, *higher* RTV has been associated with increased prefrontal cortex activation and *less* suppression of the DMN parietal brain regions in youth with ADHD (Fassbender et al., 2009; Suskauer et al., 2008). Further, although the DMN has received much attention, not all studies report its involvement in RTV in ADHD (Nilchian, 2019; Pruim et al., 2019; Sidlauskaite et al., 2016; van Belle et al., 2015). Increased RTV in ADHD has also been associated with decreased basal ganglia and thalamus activity (Rubia et al., 2007) and increased pre-supplementary motor and decreased prefrontal activity (Suskauer et al., 2008).

Notably, most neuroimaging studies investigating the association between RTV and functional activation in ADHD have examined associations between summary indices of RTV (as opposed to trial-level data) and brain activation. However, such global associations do not inform us regarding trial-level neuronal activity, particularly on the periodic long RT trials that seem to contribute most to elevated RTV metrics. Another approach to researching

RTV-related neurobiological deficits in individuals with ADHD is to examine trial-level associations between RTs and brain activation. When trial-level activation has been studied in neurotypical adults, *longer* RTs on attention-demanding tasks have been associated with *greater* DAN activity and *lower* DMN activity (Barber et al., 2017; Esterman et al., 2013, 2014; Esterman and Rothlein, 2019; Grinband et al., 2011; Weissman and Carp, 2013; Weissman et al., 2006; Yarkoni et al., 2009). Thus, trial-level analysis with neurotypical samples reports an opposite pattern of RTV-associated DMN activation (i.e., longer RTs associated with greater DMN suppression) than would be expected based on theory.

Since elevated RTV in patients with ADHD appears to be the result of periodic long RTs as evidenced by extreme positive skew, rather than just increased variability around the mean, examining ADHD-related associations between trial-level RTs and brain activation may more accurately characterize the neurobiological basis of ADHD. To date, few studies have investigated trial-level associations in ADHD. One study, which included a small sample of youth with ADHD ($n = 25$), as compared with healthy controls ($n = 27$) and those with disruptive mood dysregulation disorder ($n = 31$), reported that individuals with ADHD showed "blunting of peak activation" particularly in frontoparietal attention regions in trials with long RTs compared to healthy controls, and this blunting was associated with increased RTV (Pagliaccio et al., 2017). A second study included 26 children (aged 9–12 years) with ADHD and 35 typically developing (TD) children and explored proactive and reactive control during a stop signal task. Relevant to this study, results showed that the ADHD group had a weaker association between trial-wise RT and an inhibitory control pattern index, particularly in the salience and frontoparietal networks than the TD group (Gao et al., 2025); although this study did not specifically examine RTV. Thus, initial evidence suggests that exploring trial-level RTs may be a fruitful approach in ADHD.

The current study utilized trial-level stop signal task (SST) RT data from the Adolescent Brain Cognitive Development (ABCD) study to explore whether there are ADHD-related differences in associations between trial-level RTs and BOLD activation. The ABCD sample provides an unprecedented opportunity to examine RTV patterns in a large sample of children (aged 9–10 years). To facilitate comparison with the extant literature, we examined ADHD-related differences in the association of brain activation with summary indices of RTV (i.e., SDRT, CV, tau) in addition to exploring the association of neuronal activation with the trial-level RTs. Based on prior studies examining BOLD associations with individual RTs, we predicted that trials with longer RTs would be associated with less DMN suppression and greater DAN activation.

2. Materials and methods

2.1. Study design and participants

The ABCD Study recruited youth aged 9–10 years across 21 geographically diverse US sites. Informed consent/assent was obtained, and all procedures were approved by a central Institutional Review Board, ensuring research was completed in accordance with the Helsinki Declaration. The present study accessed publicly available ABCD data through the National Data Archive, releases 3.0 (10.15154/1520591) and 4.0 (10.15154/1523041). In release 3.0, baseline trial-level SST data for 10,179 participants was available. Children were

excluded if they performed the task in an invalid manner [i.e., accuracy on the SST was <66 % on non-Stop trials (n = 1199) or their mean stop probability was <25 % or >75 % (n = 260, 196 of which also had accuracy <66 % on non-Stop trials) (Crosbie et al., 2013; Lipszyc and Schachar, 2010)]. An additional 4 children were excluded if the drift diffusion model failed to converge (n = 4). Additionally, children were excluded if their imaging data did not pass quality control standards (n = 1146) determined by the ABCD Data Analysis, Informatics, and Resource Center (Casey et al., 2018) in release 4.0. We further excluded children taking ADHD medication on the day of the scan (n = 400) since ADHD medications improve RTV (Epstein et al., 2011a). Lastly, we excluded children who did *not* meet diagnostic criteria for ADHD but *did* have a history of taking ADHD medications at any point in their lives (n = 1647). Hence, the sample size for the current study was 5719 children (mean age = 9.95, SD = 0.64; 51.1 % female; 81.7 % White, 18.7 % Hispanic, 13.7 % African American, 8.2 % Asian, 3.1 % American Indian, 0.2 % Native Alaskan/Hawaiian, 0.6 % Pacific Islander). Of the 5719 children, 422 (7.3 %) were diagnosed with ADHD (Cordova et al., 2022) and 5297 did not meet diagnostic criteria for ADHD. See Procedures for more detail regarding determination of ADHD group status and Table 1 for descriptive characteristics by group.

2.2. Measures

The Stop Signal Task (SST) is a computerized measure of response inhibition with two 180 trial runs with a brief (median = 43s) break between runs (Casey et al., 2018). On every trial, the participant views a horizontal arrow pointing either right or left. The arrow stimulus remains on the screen for 1000ms, followed by a fixation cross that is jittered for a presentation time of 700–2000ms. Participants indicate the direction of the arrow via a two-button response panel. Thirty (16.6 %) trials in each run were Stop trials on which the horizontal arrow is followed by a 300ms presentation of an upward arrow (i.e., the stop signal). Participants are instructed to inhibit their response when they see the stop signal. The stop signal delay (SSD) between the presentation of the horizontal target arrow and the upward arrow begins at 50ms and varies according to the participant's performance. Successful inhibition results in an SSD increase of 50ms, and unsuccessful inhibition results in an SSD decrease of 50msec, so the rate of inhibition is approximately 50 %. This SSD resets to 50 msec at the start of the second run. RTs <150ms were excluded in the computational models. The SST RT trial data from correct Go-trials were utilized to compute mean RT (MRT), SDRT and CV. SDRT was derived by computing the SD of each individual's RTs. CV was computed by dividing SDRT by the MRT. The ex-Gaussian indicators, mu (mean of normal distribution), sigma (standard deviation of normal distribution), and tau (exponential distribution reflecting tail or positive skew of the RT distribution), were computed using *retimes* (Massidda, 2013; Van Zandt, 2000). Simulation studies suggest that these ex-Gaussian parameters could be estimated accurately using ABCD SST data (Epstein et al., 2023).

2.3. Procedures

2.3.1. Determination of ADHD group status: Following procedures established by Cordova and colleagues, a child was considered to meet ADHD diagnostic criteria if they 1) met ADHD current on the computerized version of the Kiddie Schedule for Affective

Disorders and Schizophrenia for School-Age Children (K-SADS-Comp; Kaufman et al., 2013) by caregiver report, 2) did not meet diagnostic criteria for bipolar disorder or unspecified schizophrenia spectrum or psychosis on the K-SADS-Comp, and 3) had an estimated IQ > 70 (i.e., score >3 on the Wechsler Intelligence Scale for Children, Fourth Edition Matrix Reasoning subtest Wechsler, 2003); i.e., Tier 2 phenotype (Cordova et al., 2022). The ADHD group had an average Attention Problems T-Score of 63.5 (SD = 8.1) and an average DSM-Oriented Attention Deficit/Hyperactivity Problems T-Score of 61.8 (SD = 7.2) on the caregiver-completed Child Behavior Checklist (Achenbach and Rescorla, 2001).

The non-ADHD group did not meet any of the criteria utilized to determine ADHD status. Additionally, in order to confirm the non-ADHD group did not have any subthreshold attentional challenges, children were required to have a T-score ≤55 on the parent-rated Child Behavior Checklist and teacher-rated Brief Problem Monitor Attention Problems subscales. The non-ADHD group had an average Attention Problems T-Score of 51.1 (SD = 1.8) and an average DSM-Oriented Attention Deficit/Hyperactivity Problems T-Score of 50.7 (SD = 1.6) on the caregiver-completed Child Behavior Checklist.

2.3.2. Trial-level z-score computation: The steps used to convert RTs to z-scores included: 1. Trials without RTs (i.e., correct and incorrect stop trials and go-trial omissions) were linearly interpolated using adjacent neighboring go-trial RTs. Specifically, for any sequence of one or more consecutive stop and/or go-omission trials, pseudo-RTs were generated for these trials by linear interpolation using the RTs of the two nearest go-trials.; 2. RTs were converted to z-scores using the within-subject mean and SD of RTs for each SST run; 3. Each RT time course was then subjected to Gaussian smoothing using a 7.2s full width, half maximum (FWHM). The full stream of RTs (even those interpolated) were included in the case that there may be an effect related to stopping (Coxon et al., 2012). We selected the z-score method over other available ways to define trial-level RTV (e.g., variance time course; Esterman et al., 2013) because it has been utilized to specifically explore attention deficits (Weissman et al., 2006), and because it is the only trial level approach that we are aware of that has been used in youth with ADHD (Pagliaccio et al., 2017).

2.3.3. Imaging data processing: Baseline SST fMRI and minimally processed T1 imaging data from the ABCD study, release 4.0, were used for analyses. In total, 166 imaging features were used in the analyses: 148 corresponding to the Destrieux atlas parcellation scheme spanning the neocortex (Destrieux et al., 2010) and 18 spanning deep brain structures and the cerebellum from the “aseg” atlas (Fischl et al., 2002). Additional processing was done in accordance with the ABCD pre-analysis processing steps (Hagler et al., 2019), i.e., removal of initial frames and normalization of voxel time series. Details of the acquisition have been previously published by the ABCD group (Casey et al., 2018). Briefly, 3D T1 scans in the axial plane were attained on Siemens, Prisma, Phillips, and GE 3T scanners with scanning parameters harmonized to facilitate comparison across the 21 sites. The 3D T1-weighted magnetization-prepared rapid acquisition gradient echo scan was obtained for cortical and subcortical segmentation of the brain with the following scan parameters: 176 slices, resolution = 1.0 × 1.0 × 1.0, TR = 2500 msec, TE = 2.88 ms, flip

angle = 8°, and FOV = 256 × 256 mm. High spatial and temporal resolution simultaneous multi-slice (SMS)/multiband EPI task-based fMRI scans, with fast integrated distortion correction, were acquired to examine functional activity during the SST with the following scanning parameters: 60 slices, resolution = 2.4 × 2.4 × 2.4, TR = 800 msec, TE = 30 msec, flip angle = 52°, FOV = 216 × 216 mm, and multiband acceleration = 6.

2.4. Analyses

2.4.1. Behavioral comparisons: Descriptive statistics for demographic characteristics and SST summary indices were computed for the ADHD and non-ADHD groups. Independent samples t-tests or chi-square statistics were used to compare groups on demographic characteristics. ANOVAs were computed comparing the ADHD group to the non-ADHD group for the SST performance metrics controlling for age and sex. Age and sex were included as covariates, given that both influence RTV (Dykiert et al., 2012; Epstein et al., 2023). Effect sizes were also computed.

2.4.2. Imaging analyses

2.4.2.1. Associations between summary RTV metrics and brain activation. First, we examined overall associations between each summary RTV metric and brain activation using the whole sample in a mass univariate approach. The model included age and the RTV metric as continuous independent variables and sex as a categorical independent variable. The model was fit to each image feature (n = 166) as the dependent variable separately; image features were the mean beta weights for the “correct go versus fixation” contrast as computed by the ABCD group and contained in ABCD 4.0 release tabulated imaging data (Hagler et al., 2019). To account for multiple comparisons, we employed the Benjamini-Hochberg step-up procedure (Benjamini and Hochberg, 1995) to control the false discovery rate (FDR) at α = .05.

Second, we examined whether patterns of RTV associations differed between the ADHD and non-ADHD groups using a multivariate approach. Using the full sample, a principal components analysis (PCA) was performed on the image features to yield multivariate components or “patterns” of activation. Components that explained ≥2 % of the variance were retained for group-level analysis. We tested for ADHD-related group differences in RTV associations with each of the components using a general linear model framework. The PCA score for each individual indicated how much of the BOLD signal variance was explained by the component for that individual. The models included ADHD group, age, sex, and the RTV metric as independent variables, as well as an ADHD group-by-RTV metric interaction term. The model was fit to the PCA scores for each of the activation patterns (n = 9) as the dependent variable separately; FDR correction was controlled in the same manner as above.

2.4.2.2. Associations between trial level RTs and brain activation. In this analysis, we examined associations between trial-level RT information (i.e., z-score) and trial-level brain activation information (i.e., BOLD signal). T1 images were skull stripped using FSL’s *bet* (Smith, 2002) and then normalized to 1 mm isotropic MNI space (Grabner et al., 2006) using linear registration in FSL’s *flirt* (Jenkinson et al., 2002; Jenkinson and Smith,

2001). The structural brain images were segmented into white matter (WM), grey matter (GM), and cerebrospinal fluid (CSF) regions using FSL's *fast* (Zhang et al., 2001) and subcortical regions using FSL's *first* (Patenaude et al., 2011). Voxelwise BOLD-z-score association maps were generated for each subject using a two-step regression procedure wherein signal variance associated with nuisance regressors (6 motion parameters, their first derivatives and squares, and the mean signal within the WM, CSF and whole brain were first removed via ordinary least squares regression. Next, BOLD-z-score associations were estimated by performing an amplitude-modulated linear regression fit of these residuals to the z-score timeseries convolved with a canonical hemodynamic-response function. BOLD-z-score effects from multiple runs of the SST task were averaged at the subject level using a fixed effects analysis in FSL's *flameo* (Woolrich et al., 2001). Finally, voxelwise maps for each subject were intersected with atlas definitions of the 166 ROIs.

We then characterized the group-level effect of BOLD-z-score associations using a mass univariate approach. The model included age and sex as independent variables and was fit to each image feature ($n = 166$) separately with FDR controlled as described above.

We additionally examined whether there were group differences in these within-subject BOLD-z-score associations using a multivariate approach. As in the previous analysis, a PCA was used to produce multivariate patterns of BOLD-z-score associations, and components that explained ≥2 % of the variance were retained for analysis. The resulting components ($n = 10$) were separately tested for ADHD-related group differences using a general linear model with ADHD group, age, and sex as independent variables and the PCA score as the dependent variable. FDR correction was utilized as described above.

3. Results

3.1. Demographic and behavioral comparisons

As shown in Table 1, the groups differed significantly on age, sex, and race, with the ADHD group being younger, including a higher percentage of males, and having a different distribution of race/ethnicity than the non-ADHD group; however, these effects were small. After controlling for age and sex, the non-ADHD group had higher Go trial accuracy and faster and less variable RTs compared to the ADHD group. These effects were moderate for MRT, SDRT, and tau, and small for Go trial accuracy, CV, mu, and sigma (see Table 2).

3.2. Imaging analyses

3.2.1. Associations between summary RTV metrics and brain activation:

Using all participants, SDRT, CV, and tau were each significantly associated with BOLD activation in 53, 64, and 54 brain regions, respectively (see Supplemental Materials, Table S1). Twenty-one regions of interest exhibited significant associations with all three of these metrics (see bolded regions in Supplemental Materials, Table S1). Fig. 1 maps the Cohen's *d* effect sizes of the significant associations between SDRT and BOLD activation across all participants (see Supplemental Materials, Fig. S1 for CV and Fig. S2 for tau, the latter which is almost identical to Fig. 2). SDRT, CV, and tau exhibited uniformly positive associations with BOLD activation. For all three metrics, effects tended to be stronger in right lateralized

regions and predominantly spanned regions of the frontoparietal network, DMN, and dorsal and ventral attention networks.

Next, multivariate analyses were conducted to examine whether these associations were different across ADHD and non-ADHD groups. For this multivariate analysis, the 5719-by-166 matrix of correct-go vs. fixation activation was reduced to 9 components (explaining a total of 66 % of the total variance in the data). The ADHD x RTV summary score interactions were not significant for any PCA component after FDR correction.

3.2.2. Associations between trial level RTV and brain activation: Results from the mass univariate analysis for within-subjects BOLD-z-score associations revealed 154 out of 166 regions of interest were significant. Fig. 2 maps the Cohen's *d* effect sizes; also see Supplemental Materials, Table S1. Positive associations predominantly spanned the somatomotor network as well as dorsal and ventral attention networks, whereas negative associations predominantly spanned the DMN and, to a much lesser extent, the frontoparietal network. Effects were most strongly positive (Cohen's $d > 0.5$) in bilateral parietal lobules, bilateral marginal sulci, bilateral inferior supramarginal gyri, right postcentral sulcus, right middle posterior cingulate cortex, right planum temporale, and right posterior lateral sulcus. Effect sizes were most strongly negative (Cohen's $d < -0.5$) in bilateral middle temporal gyri and bilateral angular gyri.

For the multivariate analysis, the 5719-by-166 matrix of BOLD-Z-score associations was reduced to 10 components (explaining 63 % of the total variance). The first component, which explained 17 % of the variance, had a significant ADHD main effect after FDR correction ($T(5717) = -2.911$, *p-FDR* = 0.036), with ADHD participants having *lower* component scores compared to controls. The weights of the first component (i.e., the multivariate pattern of BOLD-z-score associations corresponding to the component) are shown in Fig. 3. Positive weights tended to be strongest in right-lateralized regions and spanned the frontoparietal network, dorsal and ventral attention networks, and, to a lesser degree, the somatomotor network, meaning that BOLD activation was positively associated with RTs in these regions. Negative weights tended to be left-lateralized and overlapped very strongly with DMN regions, meaning that BOLD activation was negatively associated with RTs in these regions (or, put another way, longer RTs were associated with greater suppression in these regions). The ADHD main effect was not significant in any of the other nine components after correcting for multiple comparisons.

4. Discussion

The current study utilized SST RT data in a large sample of children from the ABCD study to explore ADHD-related differences in associations between RT performance and BOLD fMRI activation. Consistent with the literature (Bella-Fernandez et al., 2024; Kofler et al., 2013), group differences in RTV were observed, with the ADHD group showing greater RTV (moderate effect size for SDRT and tau, small effect size for CV) than the non-ADHD group. When examining associations between brain activation and summary indices of RTV (i.e., SDRT, CV, tau) in the full sample, we found that greater RTV was associated with greater activation in regions predominantly spanning regions of the frontoparietal network,

DMN, and dorsal and ventral attention networks; these associations were somewhat stronger in the right hemisphere. Notably, we observed a non-significant association in the DMN. When investigating ADHD versus non-ADHD group differences in associations between brain activation and summary indices of RTV (i.e., SDRT, CV, tau), no significant group differences were observed. In contrast, and consistent with our hypotheses, when exploring the association of neuronal activation with the individual trial-level RTs, trials with longer RTs were associated with greater task-positive activation and greater DMN suppression. Importantly, these associations were weaker in children with ADHD compared to those without an ADHD diagnosis, suggesting inefficient suppression of the DMN and thus supporting the default mode interference model for children with ADHD (Kelly et al., 2008; Mowinckel et al., 2017; Salum et al., 2019; Sonuga-Barke and Castellanos, 2007).

4.1. Associations between summary RTV metrics and brain activation

4.1.1. Full sample – summary metrics: Elevated RTV was associated with increased activation in primarily right-lateralized regions of the frontoparietal network, DMN, and dorsal and ventral attention networks for all participants. These findings are consistent with the fMRI literature demonstrating a role for these regions in RTV in samples with children (Bellgrove et al., 2004; Simmonds et al., 2007). It has been argued that activation in the prefrontal regions associated with higher RTV reflects the critical role of these regions in representing contextual information about stimuli and instructions in preparation of a motor response, such that those with greater variability need to recruit these regions to guide basic response selection and inhibition (Simmonds et al., 2007). In other words, there may be a greater requirement for top-down executive control in those with higher RTV (Bellgrove et al., 2004).

4.1.2. ADHD effects – summary metrics: Despite higher RTV at the behavioral level, we did not find any evidence of brain activation group differences between the ADHD and non-ADHD groups. Considering prior studies finding ADHD group differences in associations between RTV summary indices and brain activation, it was somewhat surprising that no ADHD group differences in activation were detected when utilizing summary metrics of RTV after correction for multiple comparisons. We argue that associations between summary measures of RTV and brain activation are also limited in that, depending on the summary indicator, they may a) reflect variability from both short and long RT trials; b) be highly correlated with RT speed; and c) may reflect a “third variable confound” driven by psychopathology’s associations with both RTV and altered neural response rather than direct relationships between neural response and individual RTs. Additionally, prior samples which have been relatively small may have capitalized on sample-specific variance (David et al., 2013; Turner et al., 2018). Moreover, these summary RTV indicators reflect whole-task RTV, whereas the construct we are attempting to measure, moment-to-moment fluctuations in RT, is episodic. Thus, examining trial-level associations between RTs and brain activation may more accurately reflect the types of behavior we are trying to neurally characterize. Using trial-level z-scores, high z-scores represent long RTs, whereas low z-scores represent short RTs. Differentiating trial-level activation during long versus short RT trials may be important for identifying specific activation patterns associated with potentially distinct cognitive processes of attentional impairments versus impulsive responding.

4.2. Associations between trial level RTV and brain activation

4.2.1. Full sample – trial-level: In the general population, long RTs are associated with increased activation in task-positive regions (Grinband et al., 2011; Weissman and Carp, 2013; Weissman et al., 2006; Yarkoni et al., 2009) and greater suppression of the DMN (Barber et al., 2017). As expected, we also observed this pattern of findings when examining all participants in this work. Specifically, during the SST, longer RTs were associated with higher activation in the dorsal attention and salience networks, while longer RTs were also associated with suppression of the DMN. This is consistent with previous studies, which have demonstrated that positive associations between RTs and BOLD activity are due to "time on task" or stimulus processing time effects, i.e., longer durations of neural activity during long RT trials and not stronger amplitudes of neural activity in response to these trials (Grinband et al., 2011; Yarkoni et al., 2009). Consider Fig. 3, which shows the weights of the first component of BOLD-z-score associations among all participants – the positive weights of this component load heavily on right lateralized frontal-parietal and cingulo-opercular network areas while the negative weights load heavily on DMN regions. This encapsulates the competition between the DMN and task-positive networks. On any given trial, an individual must activate task positive regions and suppress DMN, consistent with theory about which networks support task performance. As RTs increase, task-positive regions are engaged longer while the DMN is suppressed longer, leading to higher and lower observed BOLD activity in those networks, respectively. This stimulus processing time effect results in the counterintuitive finding that longer RTs (worse performance) are associated with *greater* rather than less DMN suppression.

This explanation is also consistent with the mathematical modeling literature which shows that long RTs in forced-choice paradigms (as used here) can be explained by individual differences in speed and efficiency of information processing. A large literature demonstrates that slower, less efficient information processing (requiring more time spent on stimulus processing) largely explains skew in RT distributions on many types of simple forced-choice tasks (Ratcliff and McKoon, 2008) and is the primary driver to ADHD-related cognitive differences (Huang-Pollock et al., 2017; Karalunas et al., 2012). Between-subjects analyses characterize how average levels of two features are related, whereas within-person analyses capture how those features vary within an individual, and often there is no reason to assume that these relationships should be the same (Berry and Willoughby, 2017). Here, results indicate that individuals who, on average, have greater RTV also have greater average levels of DMN activation, but that on any single trial, longer RTs are associated with less DMN activation relative to a person's own average DMN activation. Results highlight the importance of directly testing within-person associations as we do here.

4.2.2. ADHD effects – trial-level: Interestingly, our results show that these associations are *weaker* in ADHD children compared to those without ADHD, such that in ADHD, RTs and BOLD activation are less tightly coupled in task-positive networks as well as in the DMN. This is consistent with reports that competition between the DMN and executive network is dysregulated in ADHD (Castellanos et al., 2008; Sun et al., 2012) and with a recent mega-analysis summarizing resting state fMRI studies showing support for the DMN involvement in ADHD (Norman et al., 2023). For typically developing children, the stimulus

processing time effect described leads to consistent patterns of task-positive activation and DMN suppression that are related to performance on that trial. This dynamic is weaker in ADHD children. Thus, the trial-level findings are at least partially consistent with the default mode interference model for children with ADHD (Kelly et al., 2008; Mowinckel et al., 2017; Salum et al., 2019; Sonuga-Barke and Castellanos, 2007). Further, the weakened associations in the executive network observed for the ADHD group are consistent with previous work reporting blunted activation in frontoparietal attention regions associated with increased RTV (Pagliaccio et al., 2017), and disrupted neural coding associated with inhibitory control deficits in salience and frontoparietal attention regions (Gao et al., 2025).

4.3. Limitations

These findings must be interpreted in the context of study limitations. First, the assumptions of the z-score model may not be accurate for all participants. Specifically, the z-score model converts RTs into z-scores in relation to one's own RT distribution, which assumes that, relative to one's own RT distribution, all participants are equally variable in their RTs. As a result, participants with low RTV and high RTV will have RT trials z-scored as long (e.g., z-score = 2 or 2 SDs above the mean) even though the raw RTs of those participants with low RTV may not be abnormally long relative to the distribution of RTs recorded across all participants. This assumption may attenuate the ability to find neurobiological associations between z-score weightings and BOLD response.

Second, because the ABCD study used the SST, which has 30 (16.6 %) stop trials with no RT, we utilized interpolation to account for trials where an RT was not recorded (e.g., stop trials, omission errors). While interpolation is commonly used in neuroimaging analyses, including response inhibition tasks (Chidharom et al., 2021; Esterman et al., 2013, 2014, 2015; Kondo et al., 2022), the nature of the SST requires interpolation for a significant number of trials. Relatedly, it has been shown that in SST tasks, participants may slow their RTs in anticipation of a possible stop signal (i.e., RTs may increase as a function of stop signal probability via proactive control processes (Vink et al., 2015; Zandbelt and Vink, 2010). We focus on attentional explanations for findings in the current manuscript rather than proactive control of motor response because: 1) effects of proactive control are generally small and are minimized further in tasks using tracking procedures and low proportion of stop trials as done in the current task (Verbruggen and Logan, 2009); 2) recent neural evidence finds distinct neural correlates for stop response accuracy and RTV, suggesting unique rather than largely overlapping mechanisms (Lee and Kang, 2020); and 3) recent work suggests that longer stop signal reaction time in ADHD is actually driven by attentional deficits rather than differences in proactive control (Verbruggen and Logan, 2009; Weigard et al., 2019). At the same time, we cannot rule out the contribution of proactive control mechanisms; see for example Gao et al. (2025) who report disrupted neural coding in both proactive and reactive control conditions for children with ADHD. It is also possible that interpolation may overestimate stop trial RTs due to post-error slowing (Li et al., 2008). This concern is partially mitigated by the smoothing of the RT series employed following interpolation, the low prevalence of stop trials (i.e., 1 in 6), and that effect sizes of the BOLD-z-score associations using all trials (i.e., with stop-trial RTs interpolated) vs. the Cohen's d effect size of the BOLD-z-score associations using only go trials were highly

correlated (see Supplemental Materials, Fig. S3). Nonetheless, future studies using other tasks and directly comparing results with and without interpolated data will be important.

In addition, in the PCA model the first principal component explained only 17 % of the variance in RTs. On one hand, this is a modest amount of variance to explain. On the other hand, explanation of similar amounts of variance is common in neuroimaging studies that seek to understand brain-behavior relationships and is perhaps expected given the complexity of influences on cognitive performance. It is reassuring that even small effects can be meaningful in the context of psychological theory and clinical application (Funder and Ozer, 2019).

Additionally, while we ensured that the non-ADHD group did not meet diagnostic criteria for ADHD, it is possible that they may have met diagnostic criteria for other conditions, which may have reduced our ability to detect group differences in brain activation associated with RTV (especially at the summary level). Prior work in the ABCD ADHD sample has also found attenuated effect sizes for cognitive measures relative to those well-established in the literature (Cordova et al., 2022), possibly due to idiosyncrasies of inclusion criteria or sampling. Overall, the ADHD sample here may be more "cognitively healthy" than other ADHD, which could limit generalizability. However, our within-person analyses were still able to identify differential effects in the ADHD and non-ADHD groups.

5. Conclusion

In summary, these findings may point to a unique neurobiological basis of elevated RTs associated with poorer attention in youth with ADHD. The results are consistent with the suggestion that a developmental maturational imbalance between various networks, including the ventral attention network underlying sustained attention, salience network, and DMN, contributes to the behavioral variability exhibited by children with ADHD (Leisman and Melillo, 2022). Examining trial-level activation and RTV may be a more powerful approach for investigating neural mechanisms related to RTV in ADHD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data used in the preparation of this article were obtained from the Adolescent Brain Cognitive Development℠ (ABCD) Study (https://abcdstudy.org), held in the NIMH Data Archive (NDA). This is a multisite, longitudinal study designed to recruit more than 10,000 children age 9–10 and follow them over 10 years into early adulthood. The ABCD Study® is supported by the National Institutes of Health (NIH) and additional federal partners under award numbers U01DA041048, U01DA050989, U01DA051016, U01DA041022, U01DA051018, U01DA051037, U01DA050987, U01DA041174, U01DA041106, U01DA041117, U01DA041028, U01DA041134, U01DA050988, U01DA051039, U01DA041156, U01DA041025, U01DA041120, U01DA051038, U01DA041148, U01DA041093, U01DA041089, U24DA041123, U24DA041147. A full list of supporters is available at https://abcdstudy.org/federal-partners.html. A listing of participating sites and study investigators can be found at https://abcdstudy.org/consortium_members/. ABCD consortium investigators designed and implemented the study and/or provided data but did not participate in the analysis or writing of this report. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD consortium investigators. The ABCD data repository grows and changes over time. The ABCD data used in this report came from ABCD Curated Annual Release 3.0 (10.15154/1520591; stop signal task data) and 4.0 (10.15154/1523041; imaging data). The ex-Gaussian reaction

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Data availability

Data is available in the National Data Archive.

Data and code availability statement

All data is available through the NIMH Data Archive. The ABCD study provides access to data downloads for qualified affiliates through NIH and the Data Analysis and Analytics Portal (DEAP) https://deap.nimhda.org/. The ABCD data used in this report came from ABCD Curated Annual Releases 3.0 (10.15154/1520591; stop signal task data) and 4.0 (10.15154/1523041; imaging data). The ex-Gaussian reaction time variability summary data is available from the NIMH Data Archive (10.15154/1521162, study ID 1133). The ADHD Tier 2 grouping data is available in the NIMH Data Archive (10.15154/1528394, study ID, 1894), with additional information on methodology reported in Cordova et al. (2022).

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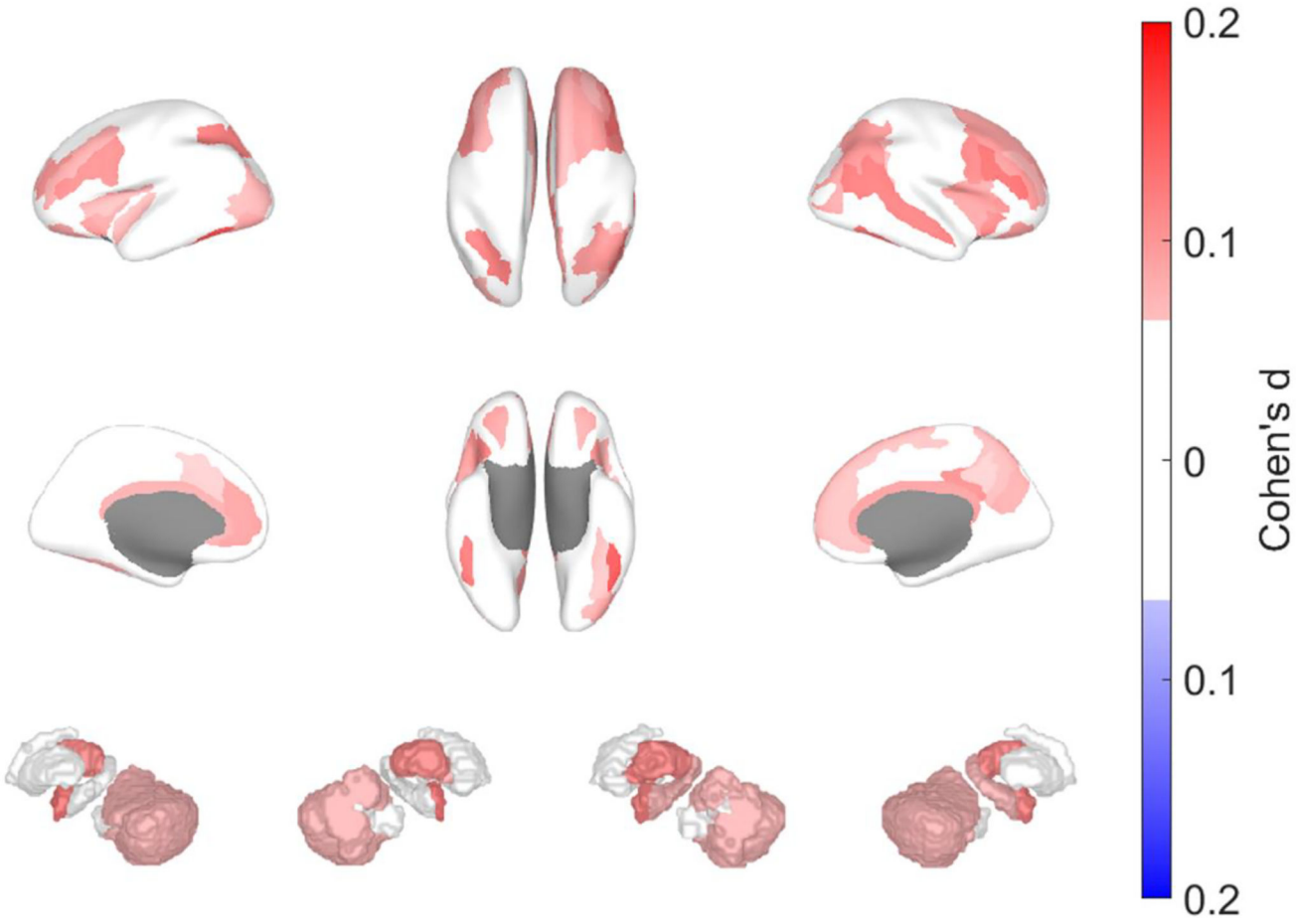

Fig. 1.

Associations, expressed as Cohen's *d* effect sizes, between the reaction time variability metric standard deviation of reaction time (SDRT) and BOLD activation for the contrast correct-go vs. fixation across all participants.

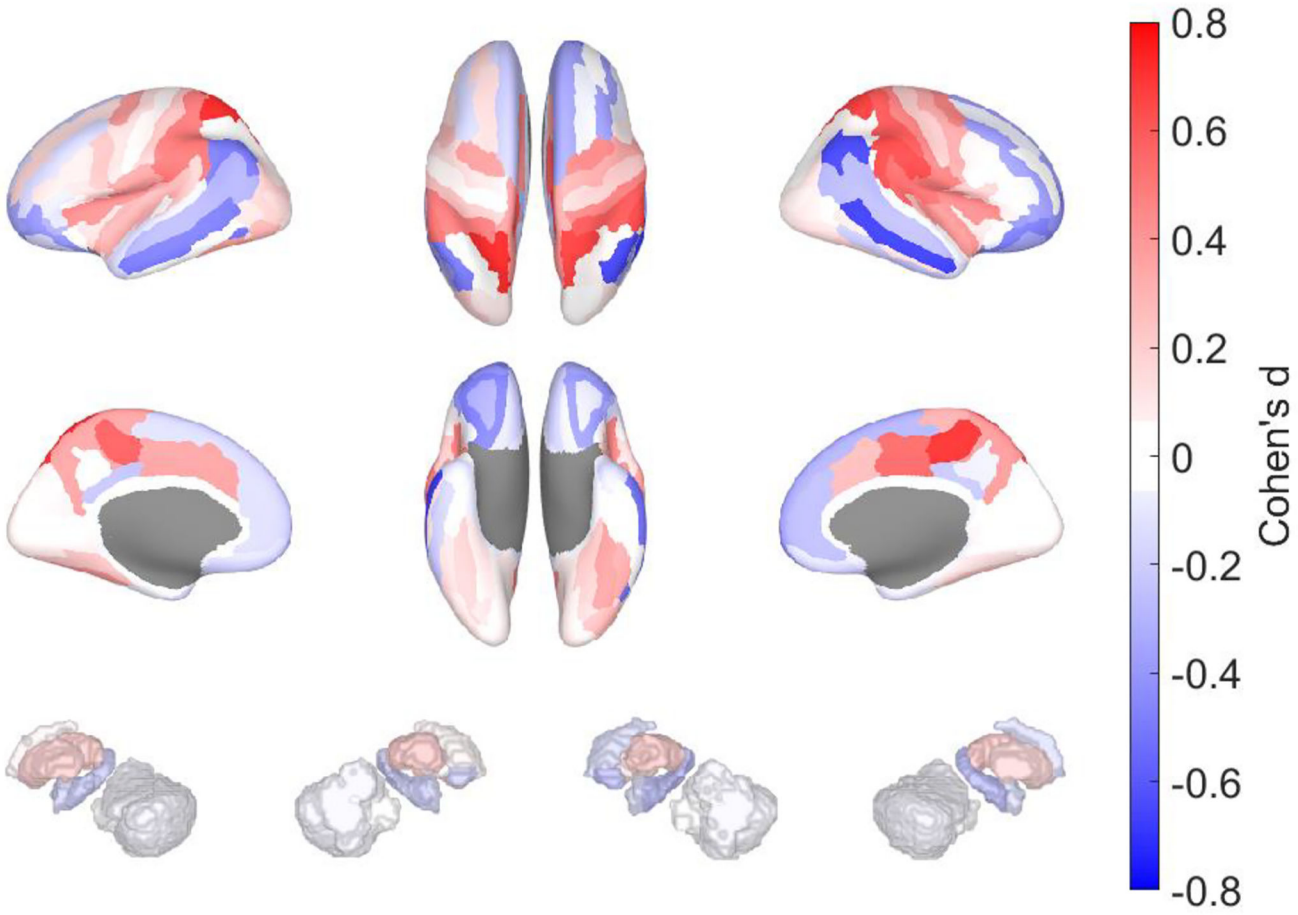

Fig. 2.
Cohen's *d* effect sizes of the within subjects BOLD-z-score association for the full sample.

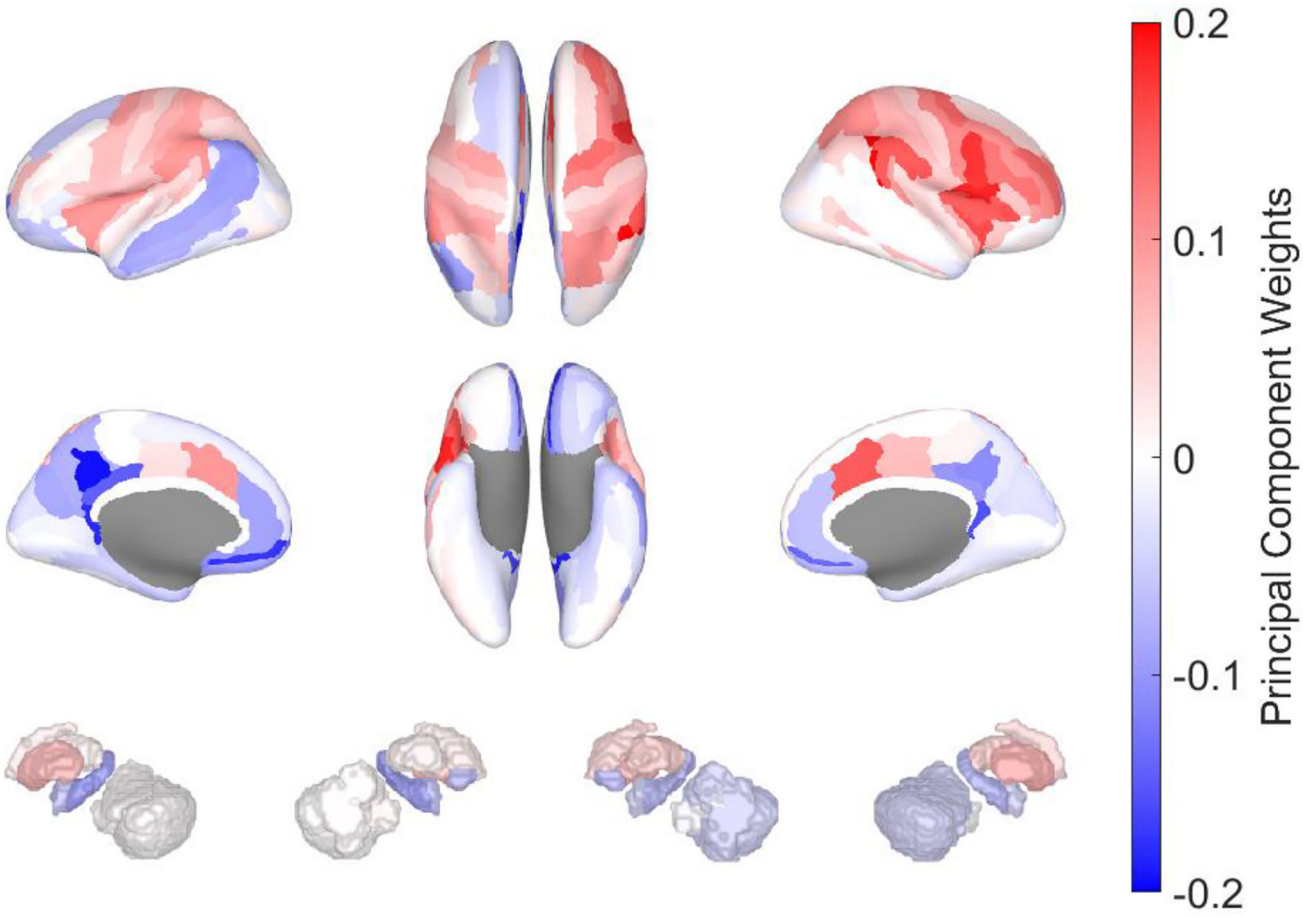

Fig. 3.

Weights of the first component in the BOLD-z-score PCA. Note: A region with a greater magnitude weight contributes more strongly to the pattern of BOLD-z-score associations that explains 17 % of the observed variance. Positive and negative weights indicate relatively higher and lower activation with increasing RTs, respectively. This pattern of BOLD-z-score associations encapsulates the competition between the DMN and task-positive networks, where longer RTs result in task-positive regions being engaged longer and the DMN being suppressed longer. ADHD participants had significantly lower component scores, indicating that this pattern of BOLD-z-score associations was *weaker* in this group compared to controls, suggesting the competition between the DMN and executive network is dysregulated in ADHD.

Table 1

Sample characteristics.

	Full Sample (n = 5719)	ADHD (n = 422)	Non-ADHD (n = 5297)	Group Differences		Effect size
	M (SD)	M (SD)	M (SD)	t	p	
Age	9.95 (0.63)	9.88 (0.64)	9.95 (0.63)	$t(5717) = -2.12$	0.034	$d = 0.11$
	N (%)	*N* (%)	*N* (%)	χ^2	*p*	
Sex				$\chi^2(1) = 31.7$	<0.0001	Φ = 0.07
Female	2922 (51.1 %)	160 (37.9 %)	2762 (52.1 %)			
Male	2797 (48.9 %)	262 (62.1 %)	2535 (47.9 %)			
Race[a]				$\chi^2(6) = 14.1$	0.028	Φ = 0.05
White	4050 (70.8 %)	288 (68.2 %)	3762 (71.0 %)			
Black	540 (9.4 %)	55 (13.0 %)	485 (9.2 %)			
Asian	134 (2.3 %)	4 (0.9 %)	130 (2.5 %)			
American Indian/ Alaska Native	25 (0.4 %)	3 (0.7 %)	22 (0.4 %)			
Pacific Islander	8 (0.1 %)	0 (0 %)	8 (0.2 %)			
Multiracial	609 (10.6 %)	53 (12.6 %)	556 (10.5 %)			
Other (not specified)	285 (5.0 %)	17 (4.0 %)	268 (5.1 %)			
Hispanic/Latinx	1071 (18.7 %)	63 (14.9 %)	1008 (19.0 %)	$\chi^2(1) = 3.8$	0.052	Φ = 0.03

Note. ADHD = attention-deficit/hyperactivity disorder.

[a]Race is unknown for 68 participants.

Table 2

Stop signal task metrics.

	Full Sample *n* = 5719		ADHD *n* = 422		Non-ADHD *n* = 5297		Group differences	
	Mean	**SD**	**Mean**	***SD***	**Mean**	***SD***	**F**	**ηp^2**
Go accuracy (%)	88.8	7.3	86.2	7.8	89.0	7.2	$F(3,5715) = 56.1^{**}$	0.03
Mean RT (ms)	553.4	88.6	570.5	95.1	552.0	87.9	$F(3,5715) = 181.4^{**}$	0.09
SDRT (ms)	174.5	36.4	184.0	37.1	173.7	36.2	$F(3,5715) = 167.5^{**}$	0.08
CV (ms)	31.7	5.4	32.5	5.4	31.6	5.4	$F(3,5715) = 12.07^{**}$	0.01
Mu (ms)	394.2	80.3	403.4	85.0	393.5	79.9	$F(3,5715) = 79.5^{**}$	0.04
Sigma (ms)	73.4	27.4	78.5	29.1	73.0	27.2	$F(3,5715) = 84.7^{**}$	0.04
Tau (ms)	159.2	42.1	167.1	43.0	158.6	41.9	$F(3,5715) = 115.5^{**}$	0.06

Note. RT = reaction time, SDRT = standard deviation of RT, CV = coefficient of variation, ηp^2 = partial eta squared; ηp^2 = *0.01* indicates a small effect, ηp^2 = 0.06 indicates a medium effect, ηp^2 = 0.14 indicates a large effect.

$^{**}p < .001$.