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Components of Executive Control in Autism Spectrum Disorders: An fMRI examination of dual-mechanism accounts

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Abstract

Background.—It remains unclear whether executive control (EC) deficits in autism spectrum disorders (ASD) represent a failure in proactive EC (engaged and maintained *before* a cognitively demanding event), or reactive EC (engaged transiently as the event occurs). We addressed this question by administering a paradigm investigating components of EC in a sample of autistic and typically developing (TD) individuals during functional magnetic resonance imaging (fMRI).

Methods.—141 participants (N_{ASD}=64, N_{TD}=77) completed a rapid Preparing to Overcome Prepotency task during fMRI that required participants to respond to an arrow probe based on the color of an initially presented cue. We examined functional recruitment and connectivity in the fronto-parietal task control, cingulo-opercular task control, salience and default mode networks during cue and probe phases of the task.

Results.—Autistic participants showed evidence of behavioral EC impairment. Analyses of functional recruitment and connectivity revealed that autistic participants showed significantly greater activity during the cue in networks associated with proactive control processes but on less cognitively demanding trials. On the more cognitively demanding trials, cue activity was similar across groups. During the probe, connectivity between regions associated with reactive control processes was uniquely enhanced on more-demanding (relative to less demanding) trials in ASD, but not in TD.

Conclusions.—The current data suggest that rather than arising from a specific failure to engage proactive or reactive forms of EC, the deficits in EC commonly observed in ASD may be due

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to reduced proactive EC and a consequent over-reliance on reactive EC on more cognitively demanding tasks.

Keywords

executive control; cognitive control; executive functions; functional recruitment; functional connectivity; autism spectrum disorder

INTRODUCTION

Individuals with autism spectrum disorders (ASD) often display deficits in executive control (EC), the set of cognitive processes that interact to facilitate flexible, goal-oriented behaviors (1–7). EC is thought to rely on three core components: cognitive flexibility, updating and maintenance, and inhibition (8–9). In addition, EC is thought to operate as a dual-mechanism (10): *proactive* control involves the maintenance of task context to bias attention and action preparation, whereas in *reactive* control, task and context information is retrieved at a late-stage upon action execution. Behavioral research has demonstrated that individuals with ASD can be impaired in some, or all, of the core components of EC (6, 11-17; for opposing views see 18-20), and that impairments are related to negative functional outcomes (21–24). However, whether impairments represent a failure in proactive, reactive, or both facets of EC remains unclear, with data from our lab and others providing evidence that proactive EC is both impaired (25–26) and spared (27–29).

Resting-state (30–31) and task-based (32) functional connectivity (FC) analyses in typically developing (TD) individuals provide evidence of a task-positive neural network (TPN: 33) that can be dissociated into three sub-networks: a fronto-parietal task control network (FPTC) anchored in the bilateral dorsolateral prefrontal cortex (dlPFC) and posterior parietal cortex (PPC), that guides flexible higher-order EC (34–35) and maintains task context (10); a cingulo-opercular task control (COTC) network anchored in the anterior and ventral anterior cingulate cortex [ACC, a region that detects conflict and facilitates rapid behavior change (26, 36–39)], lateral anterior PFC and dorsal anterior insula cortices (IC) which maintain control and tonic alertness (31, 40); and a salience network (SN) anchored in the dorsal ACC and ventral IC that detects and integrates interoceptive, autonomic and emotional information (41–42)[1]. In addition to these task-positive networks, a ‘default-mode’ (DMN) network anchored in the posterior cingulate cortex (PCC), medial PFC, and superior PPC, typically exhibits task-induced *deactivation* (43).

Proactive EC is thought to rely on context maintenance driven by early sustained activity within the dlPFC, a core region of the FPTC network (10, 44), whereas reactive control transiently engages the dlPFC, the ventrolateral PFC (a critical part of the COTC network) and the ACC (a node of both the SN and COTC networks) (26). The IC in the SN may function to upregulate FPTC and COTC activity and down-regulate DMN activity in response to cues signaling the need for enhanced control (45–46). Although distinctions between network contributions to dual-mechanisms of EC have yet to be fully elucidated,

[1]The SN and COTC networks display such a degree of overlap that both are often classified as SN, however evidence shows that resting-state functional connectivity strongly differs between these two networks (30–31).

we can summarize that FPTC and SN activity appears common to both forms of EC, however reactive EC additionally engages the COTC and supplementary SN regions.

Task-based neuroimaging studies in ASD generally support the existence of aberrant functional recruitment of these networks in EC paradigms. In tasks requiring context maintenance, autistic adolescents exhibit decreased FPTC activity during an initial cue (7), but increased FC between the vlPFC and ACC during a subsequent probe (26), suggesting an over-reliance on *reactive* control (see also 47 in children). On tasks requiring inhibition, autistic adolescents (7, 15) and adults (48–52)- exhibit reduced PFC, ACC, IC, and PPC activity. Analyses of *resting-state* FC have also provided support for aberrant inter-network FC between the SN, FPTC, COTC, and DMN in adolescents (53), through the lifespan (54) and in adults-(55). Research has also observed evidence for both *hypo*- and *hyper*-activity of SN regions in autistic adolescents and adults ASD (56–61), alongside dysfunctional FC with the other networks in adolescents (53, 56), leading some to suggest that the root of EC difficulties in ASD may be inefficient switching between the networks mediated by the SN (62). Furthermore, relative to TD, the SN, DMN, and FPTC exhibit delayed and less efficient (i.e., under-connected) development in preadolescents and adolescents with ASD (26, 55, 63–64). It is important to note, however, that this research differs with respect to sample size and age, making concrete conclusions difficult.

The current work sought to advance and clarify the behavioral and neural mechanisms of EC in ASD by administering a rapid event-related version of the Preparing to Overcome Prepotency task (65) in a large sample of adolescent autistic and TD individuals while they underwent functional magnetic resonance imaging (fMRI). We chose to focus on adolescents because this is a time of significant normative cognitive maturation and a time when those with ASD may fall further behind, making it an important period to study. Consistent with most prior research, we hypothesized that autistic participants would exhibit behavioral deficits on trials requiring enhanced EC, although there was a possibility that no deficits would be apparent (27–29). Analyzing neural recruitment and FC during the cue and probe phases of the task allowed us to address whether early and sustained activity in the dlPFC, vlPFC, ACC, and IC nodes of the FPTC and SN networks indicative of proactive control is impaired or intact in ASD, and subsequently whether autistic participants exhibit an overreliance on probe-related reactive control mediated by the vlPFC and ACC regions of the COTC and SN.

METHODS AND MATERIALS

Participants

Participants included 141 individuals (N_{ASD} =64, mean age = 17.69 years; SD = 2.79; N_{TD} = 77, mean age = 17.25 years; SD = 3.09) enrolled in the Cognitive Control in Autism (CoCoA) study, at the University of California, Davis MIND Institute (Table 1). All participants were recruited from the greater Sacramento area through advertisements, advocacy groups, and the MIND Institute's subject tracking system and research volunteer registry. Subjects with ASD were assessed with a Diagnostic and Statistical Manual (DSM) - 5 Criteria Checklist, the Autism Diagnostic Observation Schedule 2 (ADOS-2; 66), the Social Communication Questionnaire (SCQ, 67), and were not taking any psychotropic

medications other than psychostimulants (washed out 48 hours before taking part in the study). Subjects with TD were screened for ASD symptoms on the SCQ and a DSM checklist. Participants had a Wechsler Abbreviated Scale of Intelligence (WASI)-II FSIQ (68) of at least 70, were screened for MRI contraindications, 91.5% were right handed as assessed by the Edinburgh handedness inventory (69), and all received financial remuneration (see also supplement section 1). Thirty-one additional participants were recruited but excluded due to excess motion (6 TD, 6 ASD), low accuracy (5 TD, 12 ASD), or being behavioral outliers (1 TD, 1 ASD). The protocol was approved by the University of California Davis Institutional Review Board.

Measures

Rapid Preparing to Overcome Prepotency (rPOP) Task.—The rPOP task is a version of the POP task (e.g.,6–7, 65) adapted for rapid event-related fMRI (Fig. 1). It measures participants' ability to maintain context and subsequently overcome prepotent response tendencies. At the beginning of each trial, participants were presented with a colored cue for 500ms: a green cue instructed them to respond to a subsequent arrow probe by pressing the button matching the arrow's direction, whereas a red cue instructed them to respond to the probe by pushing the button opposite to the arrow's direction. Proportions of green and red cue trials were even, and the cue was followed by a jittered (3500–5500ms) fixation cross during which the task context should be maintained proactively to facilitate subsequent responding. The probe was presented for 500ms and consisted of a white arrow pointing left or right, with probe direction randomly and evenly distributed within red and green cues. Participants had 2000ms to respond (late responses were registered as non-responses). A fixation cross followed probe presentation for a jittered inter-trial interval (ITI) between 2500–22500ms. The experiment was split into 4 5-minute runs of 28 trials each (total of 112 trials).

Behavioral analysis

Scores on accuracy and latency of response to probe were submitted to 2 (cue type: red vs. green) x 2 (diagnosis: ASD vs. TD) ANOVAs. As red trials are presumed to require increased EC, deficits in EC would be revealed through poorer performance on these trials in comparison to green trials.

fMRI analysis

Protocol.—MRI data were acquired on a 3T Siemens Tim Trio system with a 32-channel phased-array head coil. An MPRAGE sequence was used to acquire T1-weighted structural images (TR=2530ms, TE=3.5ms, slice thickness=1 mm, FOV=256 mm, voxel size=1 mm iso, PAT mode=GRAPPA, PE=2). Functional T2*-weighted images sensitive to BOLD contrast were acquired during the four individual task runs using an EPI sequence (TR=2000, TE=24, FOV=224, Voxel Size=3.5 mm iso, flip angle=90°, EPI factor=64).

Preprocessing (see also supplement section 2).—Functional analysis was carried out in FSL (v5.0.9, 70) using a standard FEAT pipeline including non-brain removal, functional-to-structural registration, motion correction [framewise displacement (32) between successive acquisition volumes - volumes with displacements greater than 0.9mm

were included as confounds in the model, while any participants with greater than 20% of volumes showing such large displacements were removed from further analysis, n = 9][2], distortion correction, spatial smoothing (FWHM = 6 mm), high-pass temporal filtering, and group-level normalization to the MNI 2mm template. A subject-level GLM included four regressors of interest modelling: i) green cues, ii) red cues, iii) probes following green cues, iv) probes following red cues. A single nuisance regressor comprising incorrect and non-response trials and the first trial of each run was also included. All events were modelled with their duration. Six participant-specific motion parameters and a set of confound regressors identifying functional volumes with greater than 0.9 mm framewise displacement (a separate regressor was used for each high-displacement TR) were also included in the model.

Whole-brain functional recruitment.—Before our primary ROI recruitment and connectivity analyses, we examined differences in activity between green and red trials at the cue and probe between and within groups. Given the exploratory nature of this approach we limit reporting within this manuscript to key findings. See supplement sections 2 and 4 for details of this analysis.

Region-of-interest (ROI) recruitment analysis.—Functional recruitment analyses were restricted to a set of independently derived 6mm radius spherical ROIs (31) that encompassed 115 nodes of the four critical networks: FPTC (25 nodes), COTC (14 nodes), SN (18 nodes), and DMN (58 nodes). For node coordinates please see the supplement. Mean percentage blood-oxygenation level dependent (BOLD) signal change was extracted from each ROI at the subject-level for green and red cues and probes separately using FSLs Featquery and averaged across ROI's of the same network. These network-averaged values were submitted to 2 (cue type: red vs. green) x 2 (diagnosis: ASD vs. TD) ANOVAs and corresponding *p*-values were corrected using the Holm-Bonferroni method (71).

Functional connectivity.—Functional connectivity analyses were performed in the CONN Toolbox (v18.a; 72). FSL-preprocessed functional and structural data was passed into CONN following two additional steps, 1) tissue-segmentation using FSL's FAST to separate CSF, WM and GM, and 2) removal of noise-signals from WM and CSF using PCA. Our analysis examined potential interactions in connectivity between diagnosis and cue type between all 115 ROI's using bivariate correlation, ROI-to-ROI, generalized psychophysical interaction (gPPI) models. This approach was chosen as it optimized our ability to analyze connectivity between specific regions of the brain that are thought to underpin EC. This analysis was carried out for both the cue and probe phases of the task separately and was FDR-corrected using nonparametric permutation testing (α=0.05, 10,000 permutations) at the seed-level ($q < .01$).

[2]Following exclusions and confound removal there remained significantly greater framewise displacement in ASD than TD ($t(139) = 4.14$, $p < .001$).

RESULTS

Prior to analysis, behavioral data was required to pass rigorous exclusion criteria, which included minimum accuracy and valid trials checks (see supplement section 3).

Behavioral

There was a significant effect of cue type on accuracy [$F(1, 139) = 18.71$, $p < .001$], with higher accuracy on green (M = 94.36, SD = 5.01) versus red (M = 92.05, SD = 7.41) trials (Fig. 2). There was also a significant effect of diagnosis [$F(1, 139) = 6.55$, $p = .012$], with TD (M = 94.38, SD = 5.45) participants more accurate than ASD (M = 92.02, SD = 5.45). However, there was no interaction between the two factors [$F(1, 139) = 0.69$, $p = .406$].

There was a significant effect of cue type on participants' mean reaction time (RT) [$F(1, 139) = 119.86$, $p < .001$], with lower RT on green (M = 798.00, SD = 222.28) as opposed to red (M = 841.99, SD = 220.67) trials (Fig. 2). There was no significant effect of diagnosis on participants' RT [$F(1, 139) = 2.09$, $p = .150$], but there was a significant interaction between the two factors [$F(1, 139) = 7.99$, $p = .005$]. Pairwise comparisons revealed that green trials had faster mean response latency than red trials for both the ASD [$t(63) = 8.52$, $p < .001$] and TD [$t(76) = 6.59$, $p < .001$] groups. However, while RTs to green trials were equivalent between ASD and TD [$t(139) = 1.13$, $p = .261$], ASD participants were marginally slower to respond to red trials than were TD [$t(139) = 1.75$, $p = .082$][3].

Whole-brain recruitment

At the cue, there was an interaction between cue type and diagnosis in a single region, the right VI of the Cerebellum (216 voxels; peak voxel: x = 18, y = −56, z = −22; max z-value = 4.21, Fig. 3) that was significantly more activated in ASD relative to TD on green [$t(139) = 2.42$, $p = .01$], but not red trials [$t(139) = 0.48$, $p = .630$]. Within diagnosis groups, activity in this region was significantly higher on green relative to red trials in ASD [$t(63) = 3.01$, $p = .004$], and marginally significantly higher on red relative to green trials in TD [$t(76) = 1.91$, $p = .060$]. There was no interaction between cue type and diagnosis during the probe phase. We refrain from interpreting this finding as our brain coverage was optimized for regions of the higher cortex and thus coverage of the cerebellum was inconsistent.

ROI recruitment

Cue.—Average functional recruitment in all networks excluding the DMN was found to significantly interact between cue types and groups [COTC: $F(1,26) = 23.33$, $p < .001$; FPTC: $F(1,48) = 81.74$, $p < .001$; SN: $F(1,34) = 32.57$, $p < .001$; Fig. 4]. For all three networks, this interaction was driven by increased recruitment in ASD relative to TD on the easier green trials [COTC: $t(26) = 3.81$, $p < .001$; FPTC: $t(48) = 2.01$, $p = .050$; SN: $t(34) = 2.98$, $p = .005$], and greater recruitment on green relative to the more difficult red trials *within* ASD [COTC: $t(13) = 6.08$, $p < .001$; FPTC: $t(24) = 7.81$, $p < .001$; SN: $t(17) = 2.29$, $p = .035$], while activity on red was greater than green in TD for the FPTC and SN networks [FPTC: $t(24) = 5.30$, $p < .001$; SN: $t(17) = 6.28$, $p < .001$].

[3]Including age as a covariate in both analyses did not meaningfully change the pattern of results observed.

Probe.—Only the DMN displayed a significant interaction [$F(1,114) = 8.63$, $p = .020$; Fig. 5]. DMN activity on red trials was marginally higher in TD relative to ASD [$t(114) = 1.81$, $p = .073$], while within diagnosis group activity was enhanced on green relative to red trials for ASD and TD [ASD: $t(57) = 6.71$, $p < .001$; TD: $t(57) = 3.78$, $p < .001$].

Functional connectivity

Cue.—Three connections showed an interaction between group and cue type. An SN node located in the right supramarginal/angular gyrus displayed a similar pattern of connectivity within a DMN and a FPTC node, both of which are located in the medial paracingulate gyrus [SN-DMN: $F(1,139) = 15.05$, $p_{FDR} = .009$; SN-FPTC: $F(1,139) = 17.14$, $p_{FDR} = .007$; see figure 6A/B]. Both of these connections demonstrated significantly higher connectivity in ASD relative to TD on the easier green trials [SN-DMN: $t(139) = 3.68$, $p < .001$; SN-FPTC: $t(139) = 2.95$, $p = .004$], but no between-group difference on the more difficult red trials [SN-DMN: $t(139) = 0.09$, $p = .924$; SN-FPTC: $t(139) = 0.87$, $p = .391$]. W*ithin* TD, connectivity on red trials was higher than on green trials [SN-DMN: $t(76) = 3.67$, $p < .001$; SN-FPTC: $t(76) = 4.86$, $p < .001$]. Within ASD, SN-DMN connectivity was marginally higher on green trials [$t(63) = 1.84$, $p = .071$], whereas SN-FPTC connectivity did not differ [$t(63) = 1.08$, $p = .284$]. Additionally, a single FPTC-FPTC connection in similar regions was identified as varying significantly between group and cue types [$F(1,139) = 19.36$, $p_{FDR} = .002$, see Fig. 5C]. This connection demonstrated significantly higher connectivity in ASD relative to TD on green trials [$t(139) = 2.49$, $p = .014$], and marginally significantly higher connectivity in TD relative to ASD on red trials [$t(139) = 1.83$, $p = .070$]. Moreover, connectivity on red trials was higher than on green trials within the TD group [$t(76) = 3.92$, $p < .001$], and higher on green trials relative to red trials within the ASD group [$t(63) = 2.37$, $p = .021$].

Probe.—Two connections varied in connectivity significantly between diagnostic group and cue type: an SN-DMN connection between the ACC and lateral occipital cortex [$F(1,139) = 17.72$, $p_{FDR} = .005$; Fig. 7A], and a COTC-DMN connection *within* the paracingulate gyrus [$F(1,139) = 16.56$, $p_{FDR} = .009$; Fig. 7B]. The SN-DMN connection showed significantly higher connectivity in TD relative to ASD on green trials [$t(139) = 2.53$, $p = .013$], but no difference on red trials [$t(139) = 1.46$, $p = .146$]. Within ASD, there was higher connectivity on green as opposed to red trials [$t(63) = 3.31$, $p = .002$], and within TD the reverse was true [$t(76) = 2.53$, $p = .014$]. The COTC-DMN connection showed significantly higher connectivity in ASD relative to TD on red trials [$t(139) = 2.83$, $p = .005$], but no difference on green trials [$t(139) = 1.38$, $p = .170$]. Within ASD, connectivity was significantly higher on red versus green trials [$t(63) = 4.48$, $p < .001$], but no difference in connectivity between trial types was apparent in TD [$t(76) = 1.45$, $p = .151$].

DISCUSSION

This study aimed to clarify conflicting prior reports of executive control (EC) deficits in ASD. We found that autistic individuals demonstrated impaired RT performance on red trials (requiring prepotent response inhibition) compared to green trials (requiring no inhibition), signaling that they were less successful at engaging EC than those with TD. These data are

consistent with most previous research (6, 11–17). However, the current work went further by using fMRI to elucidate how proactive and reactive control mechanisms may contribute to this impairment.

Proactive EC is thought to rely on preparatory engagement of dlPFC nodes of the FPTC (44) and SN (45–46). Across both functional recruitment and connectivity analyses during the cue phase of the task, we observed engagement of these regions in both groups, however the context within which this engagement occurred differed. Network-level functional *recruitment* in both networks (and the COTC) was uniquely enhanced in ASD on green trials relative to red trials *and* relative to green trials in TD. In our analysis of functional connectivity (FC), we observed enhanced SN connectivity with both the FPTC and DMN regardless of trial type (although to a greater extent on green trials) in ASD participants, while this connectivity was uniquely enhanced only on *red* trials in TD participants. Considering previous reports that the SN plays a critical role in signaling the need for increased FPTC, and decreased DMN activity in line with salient external stimuli (42, 46, 62), this observation is potentially consistent with an over-prescription of saliency to green cues in the ASD group (given the localization of SN connectivity to the right supramarginal gyrus, 73). Indeed, our observation that *within*-network connectivity in the FPTC network was enhanced on green relative to red trials for ASD and on red relative to green trials for TD, further suggests that ASD participants engaged EC-related regions to a greater degree on green trials. Importantly, these data do not suggest any specific impairment in the ability to engage proactive EC, as there were no significant differences in recruitment and connectivity between diagnostic groups on red trials (although patterns of activity did differ across groups).

Given a situation in which ASD and TD participants invoke different strategies during cue processing, we might expect to see a dissociation in neural responses between trial types during the probe, with ASD invoking greater reactive EC on non-proactively controlled, more difficult red trials. Our functional recruitment analysis provided moderate support for this - activity in the DMN was reduced on red trials to a significantly greater degree in ASD, consistent with greater task-engagement (43). Moreover, SN-DMN and SN-COTC connectivity was enhanced on red relative to green trials for ASD while the reverse was true for TD. Prior research indicates that coupling between the SN and other networks is most evident when rapid changes in behavior are required (36), especially when such changes are unexpected (74). Coupled with the observation that the SN nodes observed were located in the cingulate cortex – a region typically involved in the detection of conflict (e.g., 37–38) and routinely implicated in reactive EC (26, 39) - these data may signal a more late-stage, reactive form of control on red trials in ASD.

Taken together, the current work suggests that no specific failures of the neural instantiation of either proactive or reactive EC are apparent in ASD. Considering proactive control, our data demonstrated that autistic participants engaged networks similar to TD, but to a greater degree on green trials, suggesting that rather than having impairments in proactive control, ASD participants simply engage it differently than TD. During subsequent processing of the probe, individuals with ASD must therefore engage greater reactive control on red trials, a notion consistent with previous observations of enhanced reactive ACC activation on tasks

requiring cue context maintenance in ASD (7, 26, 47). Given that some researchers believe reliance on *reactive* EC to be less efficient and more susceptible to interference (75–76), and that red trials constitute the more difficult of the trial types, ASD participant's reliance on reactive control for these trials may conceivably underlie the associated behavioral impairment.

However, our results do not clarify *why* ASD participants engage in a different, less efficient, strategy than TD. We tentatively suggest that these data may begin to illuminate the connections between EC and recognized deficiencies in cognitive flexibility in ASD (20). It is possible that ASD participants begin the task with a focus on proactive EC for green trials but fail to learn to switch or increase engagement of proactive EC to red trials even as the experiment continues. Future research would benefit from experimentally manipulating trial types in a systematic manner to determine whether initially encountered trial types affect consequent neural processing. In addition, research has shown that training individuals in proactive control strategies can lead to enhanced task performance (77–79), and more TD-like PFC activation in schizophrenia patients (80). To the best of our knowledge such an approach has yet to be taken in behavioral or neuroimaging paradigms including ASD participants, making this a promising avenue for future research.

Finally, our participants were in middle-late adolescence, a period of great neural and behavioral maturation (81). Previous research in TD has highlighted a relationship between developmental stage and the type of EC most predominantly utilized, with greater reliance on proactive control as age increases (82–86). Combined with the current findings, this tentatively suggests that those with ASD may be delayed in their development of EC as they are with several other cognitive processes (87). However, this assumption must be squared with conflicting observations that later-stage adolescents with ASD rely more on reactive control than their younger counterparts (26). Cross-sectional work as reported here is inherently limited in what it can reveal about development, underscoring the importance of future longitudinal research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DISCLOSURES

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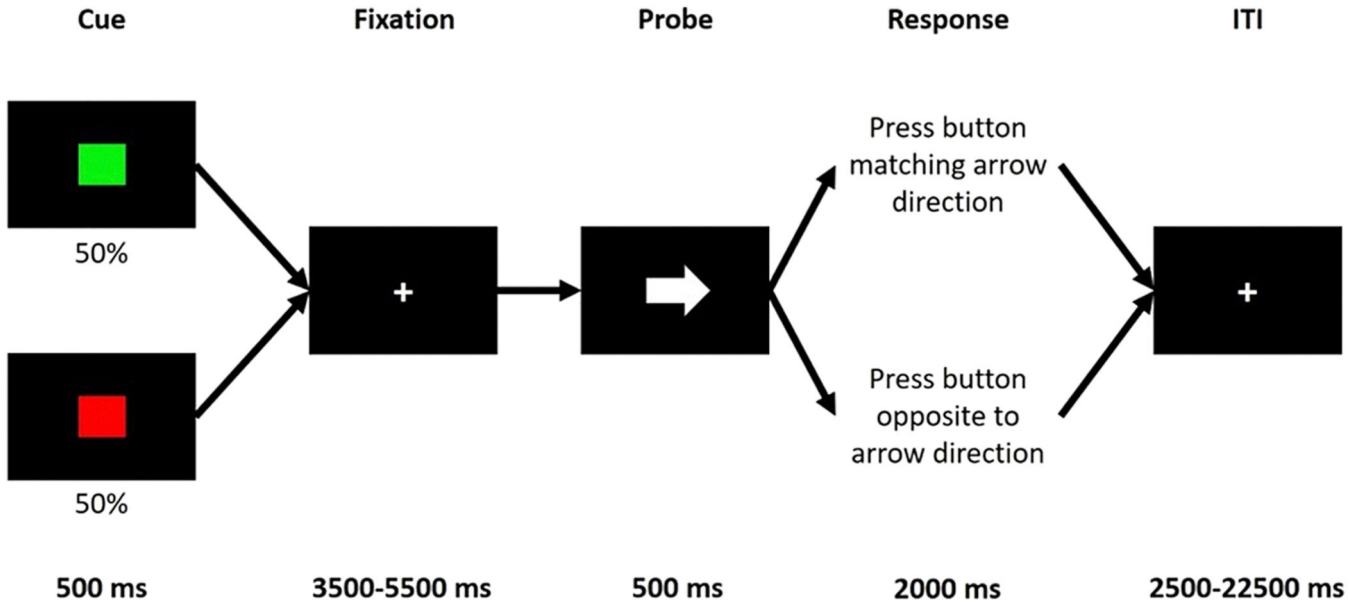

Figure 1.
Rapid Preparing to Overcome Prepotency (rPOP) task schematic. ITI = Inter-trial interval.

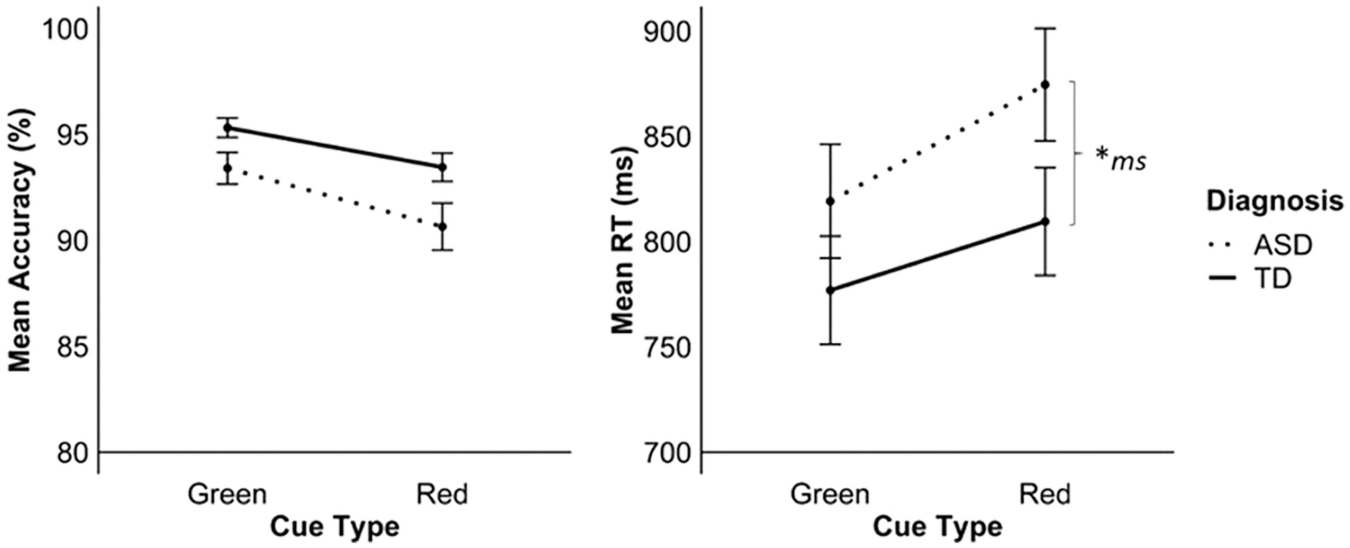

Figure 2.

Mean Accuracy and reaction time (RT) split by diagnosis and cue type. Error bars represent standard error of the mean. * represents the marginally significant (ms) difference in RT driving the interaction observed.

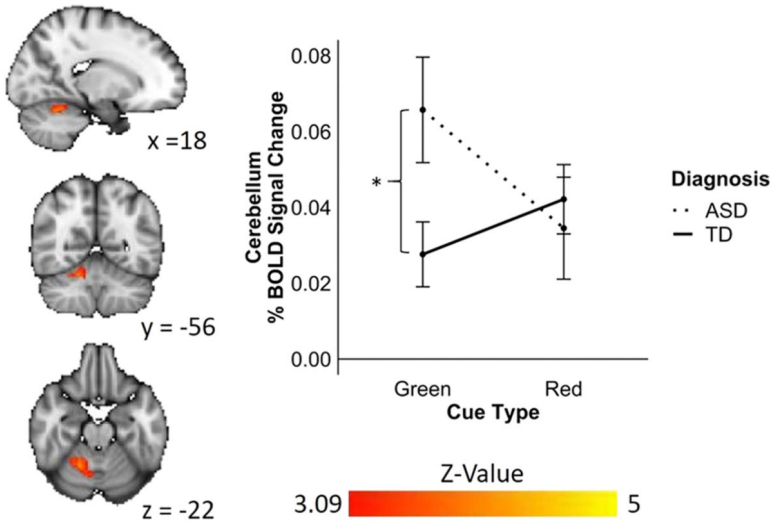

Figure 3.

Whole-brain interaction analyses revealed enhanced activity in the right VI of the Cerebellum in ASD uniquely on green trials at cue. The figure shows group data from 141 participants displayed on sagittal, axial, and coronal slices of the MNI 2mm brain template, alongside mean % BOLD signal change split by diagnosis and cue type (error bars represent standard error of the mean). Brain regions were identified based on a 2(Cue Type: Green vs. Red) x 2 (Diagnosis: ASD vs. TD) ANOVA with cluster-forming thresholds of $Z > 3.09$ and $p < .05$ (FWE-corrected).

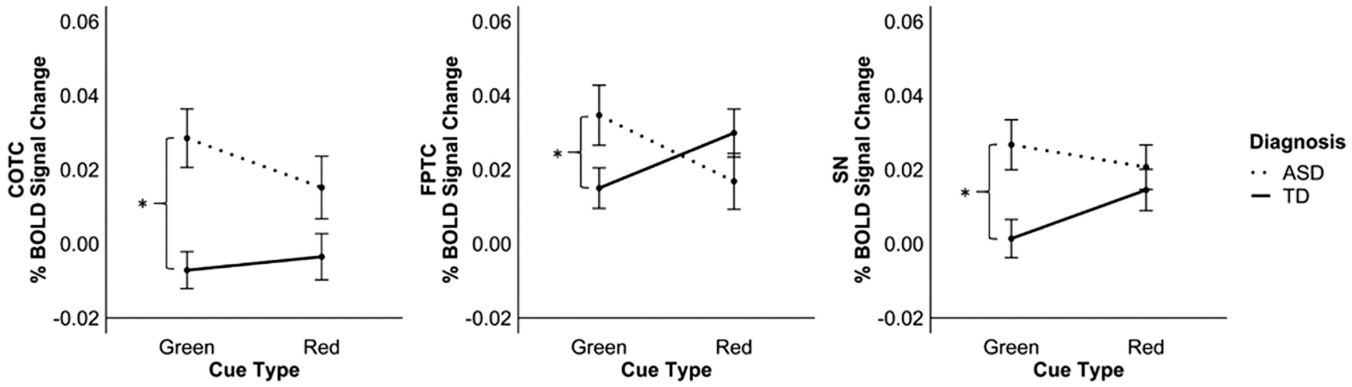

Figure 4.

Average % BOLD signal changes in the cingulo-opercular task control (COTC), fronto-parietal task control (FPTC), and salience SN networks at cue. Error bars represent standard error of the mean. * represent significant pairwise differences driving the observed interactions.

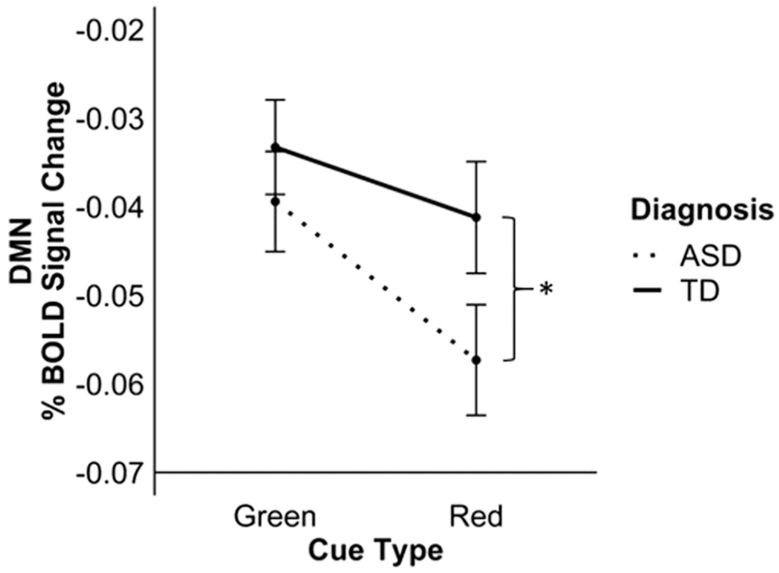

Figure 5.

Average % BOLD signal changes in the default mode network (DMN) at probe. Error bars represent standard error of the mean. * represents significant pairwise difference driving the observed interaction.

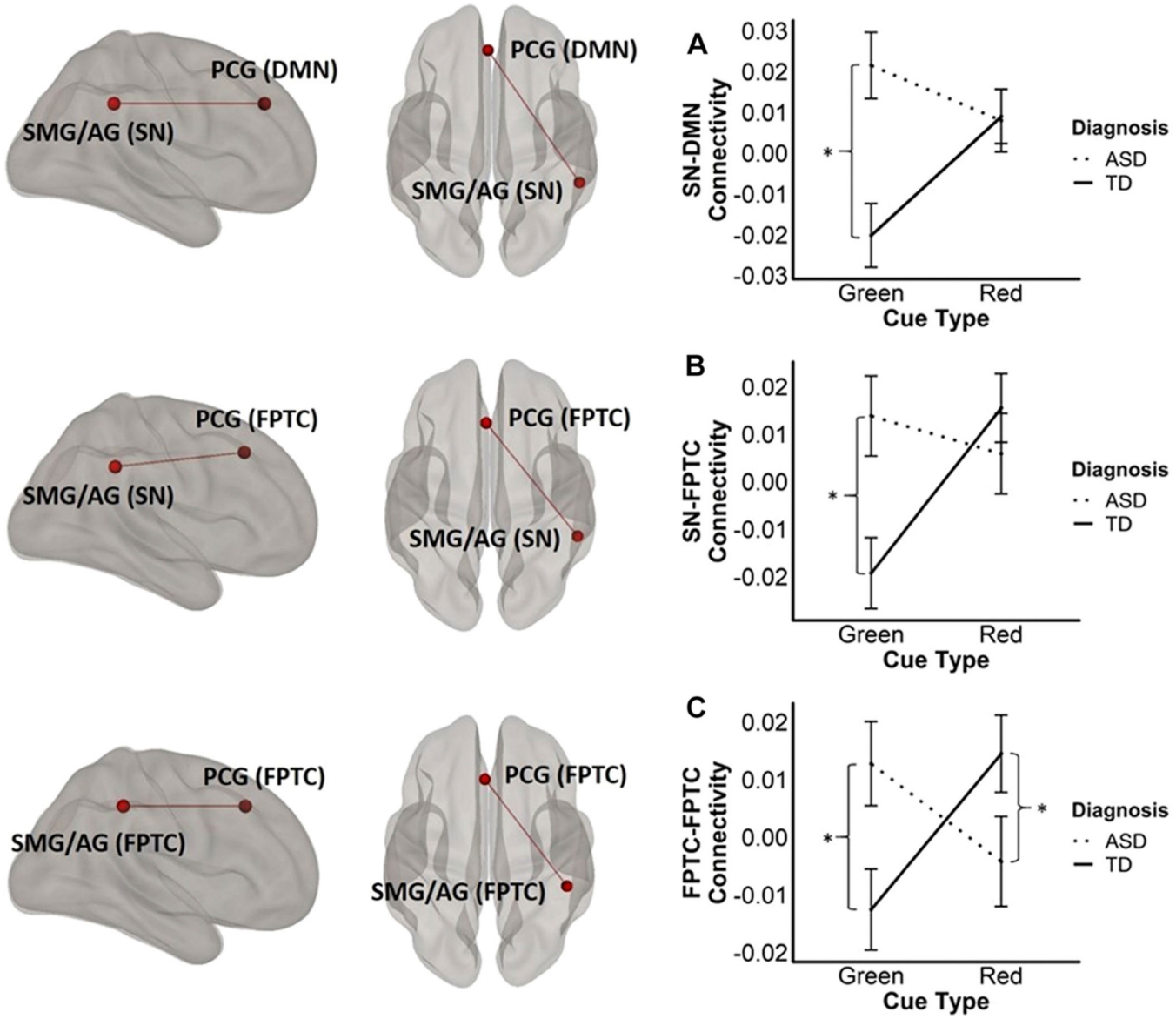

Figure 6.

Average connectivity values relative to baseline for three connections identified in the interaction analysis at cue. Error bars represent standard error of the mean. * represent significant pairwise differences driving the observed interactions. SMG/AG = Supramarginal/Angular Gyrus; PCG = Paracingulate Gyrus; SN = Salience network; DMN – default mode network; FPTC = fronto-parietal task control network.

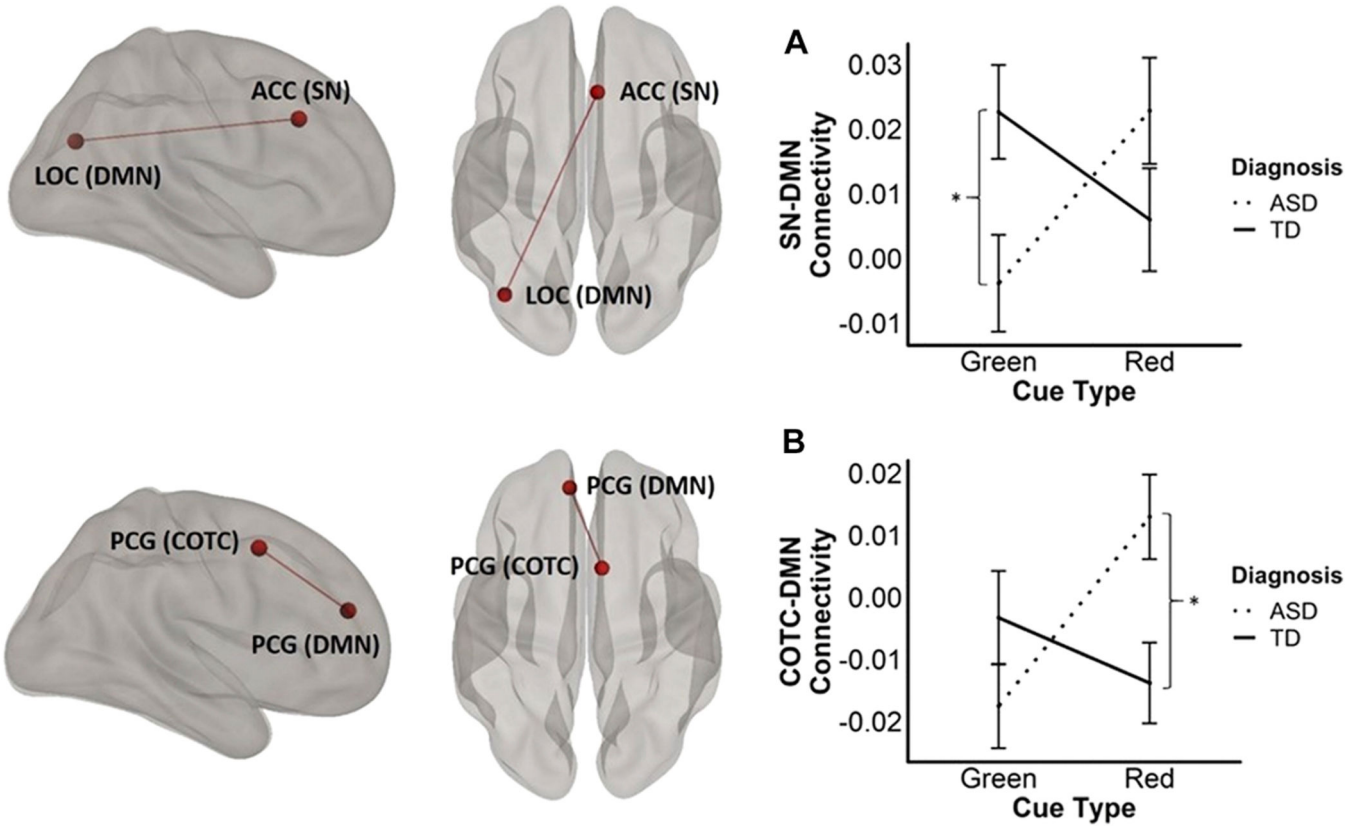

Figure 7.

Average connectivity values relative to baseline for ACC-LOC (A), and right PCG-PCG (B) connections identified in the interaction analysis at probe. Error bars represent standard error of the mean. * represent significant pairwise differences driving the observed interaction. Note: ACC = Anterior Cingulate Cortex; LOC = Lateral Occipital Cortex; PCG = Paracingulate Gyrus; SN = Salience network; DMN – default mode network; COTC = cingulo-opercular task control network.

Table 1.

Participant characteristics.

	TD: N = 77	ASD: N = 64	Comparison
WASI-II FSIQ	110.05 (11.23)	103.72 (12.88)	.002[a]
WASI-II VCI	105.97 (12.37)	98.11 (13.99)	.001[a]
WASI-II PRI	111.74 (12.48)	109.14 (15.02)	.264
Age	17.25 (3.09)	17.69 (2.79)	.381
Sex	16 F; 61 M	11 F; 53 M	.589
ASEBA DSM ADHD	51.47 (2.65)	59.06 (7.59)	<.001
ADOS SA	N/A	7.72 (1.46)	N/A
ADOS RRB	N/A	7.08 (2.39)	N/A
ADOS CSS	N/A	7.72 (1.69)	N/A

[a]Although between groups differences in IQ existed, IQ was not related to any of the dependent variables of interest – thus there was no credible evidence that IQ moderated any of the observed effects and therefore these variables were not included as covariates.

WASI = Wechsler Abbreviated Scale of Intelligence; **FSIQ** = Full-scale Intelligence Quotient; **VCI** = Verbal Comprehension Index; **PRI** = Perceptual Resoning Index; **ASEBA** = Achenbach System of Empirically Based Assessment; **DSM** = Diagnostic & Statistical Manual; **ADHD** = Attention Deficit Hyperactivity Disorder; **ADOS** = Autism Diagnostic Observation Schedule; **SA** = Social Affect; **RRB** = Restricted and Repetitive Behaviors; **CSS** = Calibrated Severity Score