Frontoparietal Connectivity During Cognitive Control in Autism Spectrum Disorder

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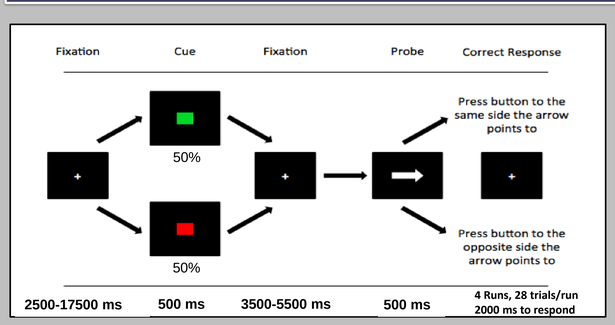
Introduction

Many individuals with Autism Spectrum Disorder (ASD) exhibit executive control (EC) deficits that persist into adolescence and young adulthood. However, it is unclear if this is due to deficits in proactive control (engaged *before* a demanding task) or reactive control (engaged *during* the task). In other studies from our lab, proactive control has been found to be both intact and impaired. Since poorer EC functioning in ASD is linked to worse life outcomes, determining the exact nature of deficits is crucial for treatment strategies.

The current study uses fMRI data from the first wave of a five year cohort-sequential study of adolescents and young adults with ASD to examine the neural correlates of EC. Sustained activity of the frontoparietal task control network (FPTC) and salience network (SN) is important for proactive control, whereas transient activity in these networks in addition to the cingulo-opercular task control network (COTC) and the ACC node of the SN appears critical for reactive control. Thus, comparing the functional connectivity in those with ASD compared to typically developing controls (TYP) should help elucidate differences and impairments in control strategies.

Preparing to Overcome Prepotency (rPOP) Task



RT = Response Time
ACC = Accuracy
Inverse Efficiency Score (IES) =
RT/ Accuracy
Higher IES = lower efficiency

MRI Data Acquisition: 3 Tesla Siemens Trio, 32 channel head coil; BOLD & MPRAGE
fMRI Data Preprocessing: 'Performed in FSL (v5.0.9). Included, BBR coregistration, normalization using FLIRT and FNIRT, motion correction using MCFLIRT, slice-timing correction, brain extraction, spatial smoothing (FWHM = 6mm), grand mean intensity normailzation, and highpass temporal filtering (sigma = 45.0ms)
Data QA: Runs removed if: ***< 70% task accuracy *> .9 mm displacement or 3 degrees rotation *> 20% outlier volumes** (volumes with framwise displacement > 0.9mm)
fMRI Data Analysis: General linear model approach implemented in FSL. Cue and probe phase of red and green trials modeled separately. Error trials modeled separately as nuisance variable and included. Standard motion parameters and displacement regressors included.
Functional Connectivity: gPPI ROI -ROI connectivity analyses performed in CONN functional connectivity toolbox (http://www.nitrc.org /projects/conn) to look at differences in connectivity between groups (ASD, TYP) for Red Trials > Green Trials at the cue and at the probe. ROIs from four networks (FPTC, SN, COTC, DMN) were selected from the Power et al. (2011) atlas . Results displayed survived FDR correction, q < .01.

Participants

	ASD (n = 64)	TYP (n = 77)
Males *(%)*	53 *(82.8%)*	61 *(79.2%)*
Females *(%)*	11 *(17.2%)*	16 *(20.8%)*
Age *(SD)*	18.1 *(2.8)*	17.7 *(3.1)*
Full Scale IQ *(SD)* *	103.7 *(12.9)*	110.1 *(11.2)*
Verbal IQ *(SD)* *	98.1 *(14.0)*	105.9 *(12.4)*
Non-Verbal IQ *(SD)*	109.1 *(15.0)*	111.7 *(12.5)*
ADOS-2 CSS *(SD)*	7.7 *(1.7)*	-

Eligibility
- WASI-2
  FSIQ ≥ 70

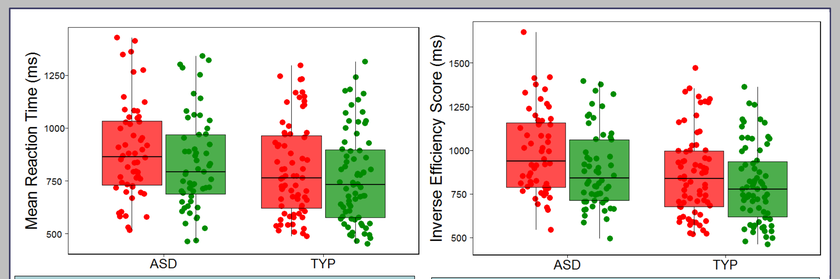
ASD
- ADOS-2
- DSM 5 Criteria Checklist for ASD

TYP
- No DSM 5 Diagnoses
- No psychotropic medication
- SCQ

***FSIQ and VIQ greater for TYP group compared to ASD group**

Results

Behavioral Results: ASD Impaired

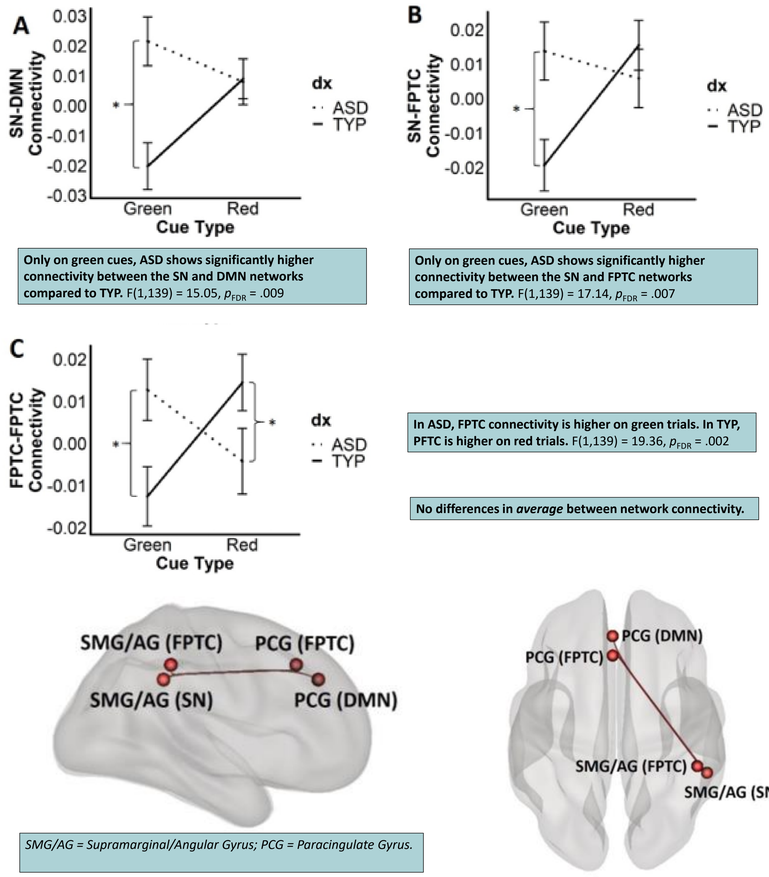


Main Effect Color: RT Red > RT Green F = 119.9, $p < .001$
Interaction: ASD Red > TYP Red & ASD Green = TYP Green F = 7.9, $p = .005$

Main Effect Color: IES Red > IES Green F = 71.3 $p < .001$
Main Effect Dx: ASD IES > IES Green F = 3.9 $p = .048$
Interaction: ASD Red > TYP Red & ASD Green = TYP Green F = 4.3, $p = .039$

Functional Connectivity

At the Cue: Interactions



Only on green cues, ASD shows significantly higher connectivity between the SN and DMN networks compared to TYP. F(1,139) = 15.05, $p_{FDR} = .009$

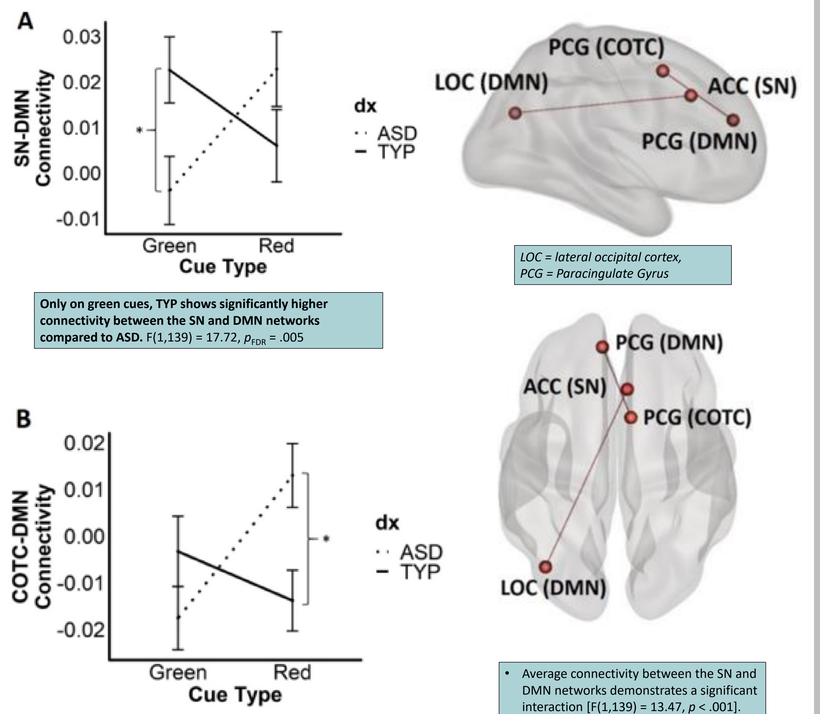
Only on green cues, ASD shows significantly higher connectivity between the SN and FPTC networks compared to TYP. F(1,139) = 17.14, $p_{FDR} = .007$

In ASD, FPTC connectivity is higher on green trials. In TYP, PFTC is higher on red trials. F(1,139) = 19.36, $p_{FDR} = .002$

No differences in *average* between network connectivity.

SMG/AG = Supramarginal/Angular Gyrus; PCG = Paracingulate Gyrus.

At the Probe: Interactions



Only on green cues, TYP shows significantly higher connectivity between the SN and DMN networks compared to ASD. F(1,139) = 17.72, $p_{FDR} = .005$

LOC = lateral occipital cortex, PCG = Paracingulate Gyrus

Only on red cues, ASD shows significantly higher connectivity between the COTC and DMN networks compared to TYP. F(1,139) = 16.56, $p_{FDR} = .009$

- Average connectivity between the SN and DMN networks demonstrates a significant interaction [F(1,139) = 13.47, $p < .001$].
- Driven by significantly higher connectivity on red trials in ASD, with no difference in TYP.
- Marginally significantly higher connectivity on red trials in ASD relative to TYP

Discussion

Conclusion

- ASD exhibit deficits in EC as evidenced by a lower efficiency on red trials.
- At the cue, both groups activate the FPTC and SN networks
  - ASD: higher connectivity on green trials
  - TYP: higher connectivity on red trials
- Suggests ASD engage proactive control on green trials (over-responsivity) while TYP engage more proactively on red trials
- At the probe, more activation of SN and DMN networks in ASD
  - ASD: higher connectivity on red trials
  - TYP: lower connectivity on red trials
- ASD may be activating reactive control on red trials at the probe, since less proactive control was activated at the cue
- While ASD do not appear impaired in PFTC connectivity, they engage it differently from TYP – possibly in a less efficient way
- This inefficiency may lead to the behavioral deficits shown on the task
- Longitudinal analyses will be possible after completion of the second wave of the study.

This work was supported by the National Institute of Health:
1 R01 MH106518-01A1 *(PI: Solomon)*

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