Impaired Maturational Changes of Network Organization in ASD: An ICA Study Using Resting State fMRI

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INTRODUCTION

Background:

- Converging evidence indicates that brain abnormalities in ASD involve atypical network connectivity, yet the particular connectivity patterns and the extent to which they deviate from those seen in typical development are currently debated.
- While there is evidence supporting both greater and weaker brain network connectivity in individuals with ASD, as compared to their typically developing (TD) peers, the developmental framework emphasizing age-associated changes in connectivity is often overlooked, or altogether ignored.
- Recent findings suggest that, while typical development is associated with increasingly segregated and increasingly integrated brain networks[1], this pattern appears to be disrupted in ASD.

Objective:

- To examine developmental trajectories of network connectivity in a sample of children and adolescents with ASD, as compared to TD controls, using a data-driven, model-free approach to quantify large-scale patterns of functional connectivity.

METHODS

Participants:

- Children and adolescents with ASD and TD controls ages 7-17 years (see *Participant Characteristic Table* for demographic and diagnostic data) underwent diagnostic and cognitive testing and imaging scans in the context of an ongoing neuroimaging project.

MRI Data Acquisition:

- GE 3T MR750 scanner with an 8-channel head coil:
  - T1 weighted SPGR anatomical sequence: 1mm^3 resolution.
  - 6:10min resting state (eyes open) EPI sequence: 185 whole-brain volumes, TR = 2000ms; TE = 30ms; 3.4mm^3 isotropic resolution.

MRI Data Processing and ICA Analyses:

- *Preprocessing*: slice-time-, motion-, and field-map-correction; co-registration to T1 and normalization (to MNI) with FNIRT; spatial smoothing to a FWHM of 10mm; .008<*f*<.08Hz bandpass filter; 16 nuisance regressors: 6 motion parameters, signal from WM and ventricles, and their respective derivatives (no censoring).
- *Independent Component Analysis (ICA)* was applied to rs-fMRI data from publicly available ABIDE dataset.[2]
  - A low-motion subset of 40 age-matched TD participants from ABIDE was selected, in order to estimate a typical template of network distribution and composition at this age range.
  - The dual regression approach implemented in FSL MELODIC was applied to estimate individual (participant-specific) spatial maps corresponding to the ICA-identified functional networks (or independent components) derived from the ABIDE data.
- *Relationship with age and behavioral scores:* Z scores associated with each network were then correlated with age within each group, and with diagnostic measures within the ASD group.

RESULTS

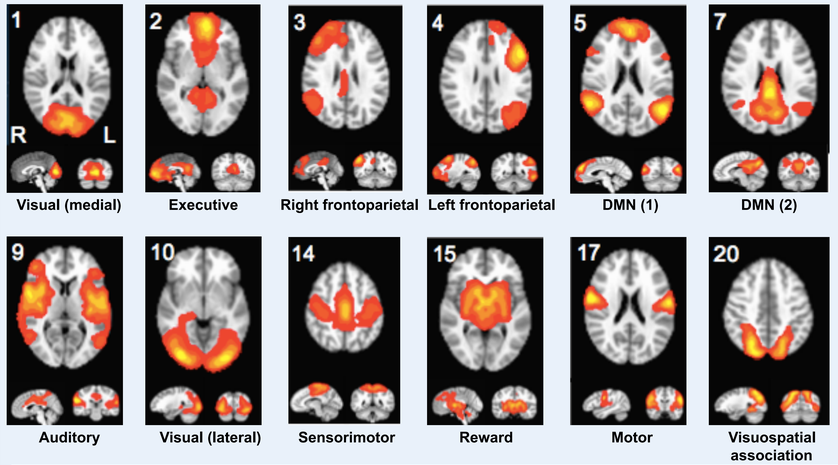

Figure 1. Twelve functional networks (or independent components, representing networks of brain regions with temporally correlated fMRI BOLD signals) out of 20-component ICA (8 noise components not shown). Three most informative orthogonal slices for each component are displayed. ICA spatial maps were converted to z-statistic images (thresholded at z > 3) and are displayed in standard MNI brain space. These components are largely comparable with published *adult* templates by Smith and colleagues[3,4].

***Participant Characteristics*:**

	ASD† (n = 37)	TD§ (n = 39)	ABIDE TD (n = 40)
Gender (M/F)	32/5	31/8	33/7
Handedness (R/L)	33/4	32/7	39/1
	M ± SD (range)	*M* ± SD (range)	*M* ± SD (range)
Age (years)	13.7 ± 2.6 (7.6-17.8)	12.8 ± 2.6 (8.0-16.8)	13.4 ± 2.6 (8.0-17.7)
Verbal IQ*	103 ± 20.6 (55-147)	106.9 ± 12.1 (73-133)	110.8 ± 12.7 (80-141)
Non-verbal IQ*	104 ± 18.7 (52-140)	107.7 ± 12.1 (83-137)	108 ± 16.1 (67-137)
Full-scale IQ*	104.3 ± 19.2 (56-141)	108.3 ± 11.9 (79-132)	110.6 ± 14.5 (81-142)
ADOS			
Social Interaction	8.7 ± 3 (4-14)	n/a	n/a
Communication	4.1 ± 2.3 (0-10)	n/a	n/a
Repetitive Behavior	2.3 ± 1.5 (0-6)	n/a	n/a
ADI-R			
Social Interaction	18.8 ± 6.4 (6-28)	n/a	n/a
Communication	15.5 ± 6.5 (2-27)	n/a	n/a
Repetitive Behavior	6.6 ± 2.2 (3-11)	n/a	n/a

Notes: *Wechsler Abbreviated Scale of Intelligence (WASI)

† Diagnoses confirmed by Autism Diagnostic Observation Schedule (ADOS[6]), Autism Diagnostic Interview-Revised (ADI-R[6]), and clinical judgment according to DSM-IV criteria.[7]

§ TD participants had no family history of ASD, no personal history of neurologic or psychiatric conditions. The three groups were matched on motion (RMSD; M_{ASD} = 0.085; M_{TD} = 0.078; M_{ABIDE} = 0.061; all *p*s > .20).

RESULTS (Cont.)

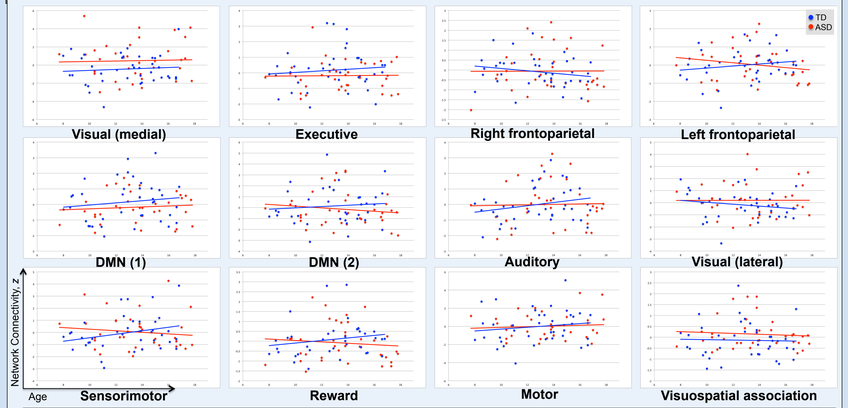

Figure 2. Scatterplots of partial correlations between age and network integration, across 12 ICA-identified functional networks (after partialling out effect of in-scanner motion on connectivity values).

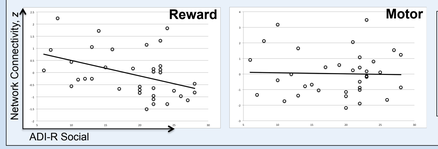

Figure 3. Scatterplots demonstrating differential relationship between network integration and social symptoms for two networks (after partialling out effect of both in-scanner motion *and* age on connectivity values).

SUMMARY and CONCLUSIONS

- Comparison of developmental trajectories of 12 prominent functional networks revealed atypical relationship between the degree of network integration and age in the ASD group, for some – but not for other – networks.
  - Namely, some networks (e.g., visual, motor) appeared to have matured by the age of 7, in both TD and ASD, showing no relationship with age (between ages 7 and 17).
  - Other networks (i.e., left frontoparietal, sensorimotor, reward) had opposite maturational trajectories in the two groups: continually increasing connectivity in TD vs. decreasing connectivity in ASD.
- Additionally, some networks were more implicated in the ASD symptomatology than others (see Fig.3):
  - Eg, lesser network integration of the Reward network was related to greater ASD symptoms.
- These data underscore the importance of considering developmental trends and trajectories when characterizing brain network abnormalities in ASD.

References:

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