Links between atypical local and long-distance connectivity in autism

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INTRODUCTION

- Autism spectrum disorder (ASD) is a prevalent neurodevelopmental disorder characterized by impaired social communication and interaction, and by repetitive behaviors and restricted interests.
- Extensive evidence indicates atypical long-distance connectivity in ASD [reviewed in 1-2]. A few recent studies have also found atypical local connectivity [3-6].
- According to one often cited speculation [7], local overconnectivity may be accompanied by long-distance underconnectivity in ASD [8-9].
- However, there is little direct empirical evidence relevant to the question of how abnormal local connectivity relates to long-distance connectivity. More specifically, it remains unclear whether variable density of local connectivity in ASD (local over- and underconnectivity) may be associated with relatively isolated or overly integrative distributed processing.

OBJECTIVE

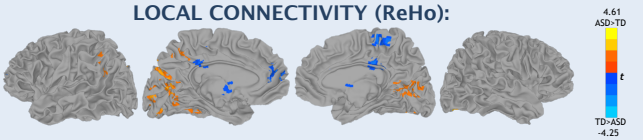
To examine the relationship between local connectivity and long-distance connectivity in children with ASD and typically developing (TD) peers.

DISCUSSION

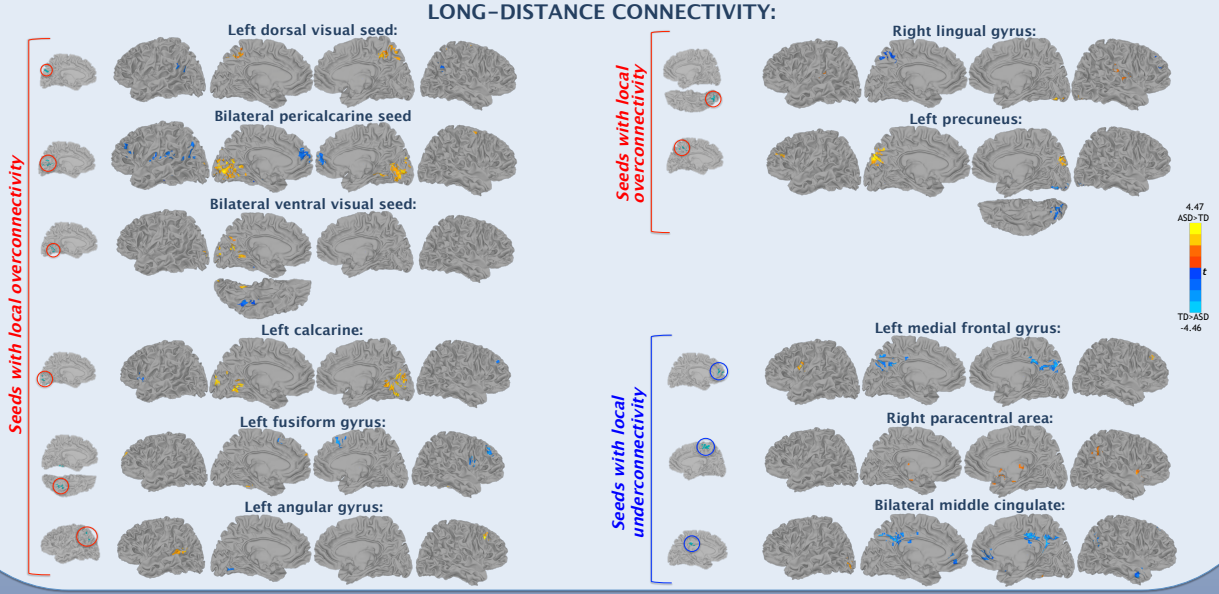
- Local overconnectivity in posterior regions was mostly associated with underconnectivity in distal regions, suggesting a link between local over- and long-distance underconnectivity specifically for visual regions and reduced cooperation with frontal lobe in ASD.
  - Underconnectivity between mV/V1 seeds and mPFC may relate to impaired social cognition and atypical function of the default mode network in ASD.
- Locally overconnected superior visual regions were also underconnected with left pSTS and STG, possibly implying reduced cooperation between dorsal stream and some biological motion and receptive language regions.
- Locally overconnected inferior visual areas were additionally overconnected with adjacent visual cortices, but *underconnected* with fusiform gyrus in ASD.
  - Regions within ventral visual stream were overconnected, with the sole exception of FFG, which was atypically disconnected from the rest of the ventral stream (as well as from right superior and inferior frontal cortex). However, FFG itself was characterized by atypically increased local connectivity in ASD.
- Similarly, locally overconnected right lingual gyrus and and left precuneus were underconnected with each other.
- Overall, regions of atypical local connectivity (increased or reduced) predominantly showed reduced interlobar long-distance connectivity.

RESULTS

LOCAL CONNECTIVITY (ReHo):



LONG-DISTANCE CONNECTIVITY:



METHODS

PARTICIPANTS

- 39 typically developing (TD) and 39 participants with ASD
- Matched on age, nonverbal IQ, and average head motion (RMSD)

Group	N	Sex	Handedness	Age M(SD) Range	Nonverbal IQ M(SD) Range	RMSD M(SD) Range
ASD	39	6 female	7 left	14.1 (2.5) 9.2-17.9	107.1 (13.6) 80-136	.065 (.034) .018-.148
TD	39	7 female	5 left	14.0 (2.2) 9.6-17.8	107 (13.7) 62-129	.065 (.038) .017-.168
				p = .821	p = .990	p = .980

DATA ACQUISITION

A 6:10 minutes resting-state scan was acquired on a GE 3T MR750 scanner (TR: 2000ms; TE: 30ms; 3.4mm isotropic voxels).

DATA PREPROCESSING

- Motion, slice-time, and field-map correction
- Co-registration of functional to anatomical images
- Standardization to MNI space
- Spatial smoothing to 6mm FWHM
- Bandpass filtering (.008 < f < .08 Hz)
- Removal of nuisance regressors (6 rigid-body motion, signal from white matter, ventricular matter, and derivatives)
- Analysis conducted with global signal regression (GSR)
- Time points with motion >.5mm (and following 2 time points) were censored
- Participants with ≥150 time points remaining were selected

1. DATA ANALYSIS: Local Connectivity (ReHo)

- **Regional homogeneity (ReHo)** uses Kendall's coefficient of concordance (KCC) to assess homogeneity of a given center voxel and its neighboring voxels.
- Within a given cluster of voxels, KCC is equal to the parameter W (ranging from 0 to 1)

$$W = \frac{\sum (R_i)^2 - n(\bar{R})^2}{\frac{1}{12}K^2(n^3 - n)}$$

- Individual voxel-wise ReHo maps were obtained and were standardized to KCC-ReHo z-values.
- Group differences examined with a two-sample t-test
- Monte-Carlo simulation applied to correct for multiple comparisons

2. DATA ANALYSIS: Long-Distance Connectivity

- **Significant clusters from between-group t-test (comparing ReHo KCC) were used to create seeds for whole brain (long-distance) fcMRI analyses.**
- A large significant ReHo overconnectivity cluster in posterior regions was split into 3 equal parts (dorsal, middle (pericalcarine), and ventral), based on z-coordinates, and whole brain analyses were run separately for each seed.
- Mean time series were extracted from each seed and were correlated with voxel time courses across the brain in each participant .
- Fisher's r-to-z' transformation was conducted to transform these correlation coefficients to normally distributed values for subsequent t-tests.
- Statistical maps were cluster-corrected at p < .05.

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