

Supplementary Material

Altered social cognition and connectivity of default mode networks in the co-occurrence of autistic spectrum disorder and attention deficit hyperactivity disorder

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Supplemental Materials

Sample selection: Diagnosis of ASDAs reported in the ABIDE website, http://fcon_1000.projects.nitrc.org/indi/abide II /, the diagnosis of ASD was supported by as the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R) in 5/7 Sites, often combined with clinical judgment based on expertise and DSM-IV-TR diagnostic criteria. The Social Responsiveness Scale (SRS), Child Behavior Checklist (CBCL) and Social Communication Questionnaire (SCQ) were also administered to an informant known to the participant in 1/7 Sites. Details of image acquisition for each site can be found on the ABIDE website http://fcon_1000.projects.nitrc.org/indi/abide II /.

Additional analyses on the significant connectivity findings with site

We further analyzed the associations between the significant connectivity in each site with our finding in the all sample. For the results of the intra-iFC, regardless of the statistical significance, the tendency of results within each site except for the UCD_1 site in which included 12 ASD (including 3 ASD_coADHD and 9 ASD_nonADHD) is consistent with our existing results, controlling for age and sex. For the results of the inter-iFC, except for the sites of EMC_1(including 7 ASD_coADHD and 8 ASD_nonADHD) and IP_1 (including 5 ASD_coADHD and 3 ASD_nonADHD), the tendency of results within each of other 5 sites is consistent with our existing results. In summary, our results are relatively stable. Besides, we tested the differences across the sites by using ANOVA in each group, controlling for age and sex. We found that the significant connectivity had no significant differences across the sites in the ASD_coADHD group (intra-iFC: $F=1.927$, $P=0.088$; inter-iFC: $F=1.945$ $P=0.085$), but in the ASD_nonADHD and TD group, the differences were significant ($P_s<0.05$).

Additional analyses on the significant connectivity findings with age

Data from various studies suggest that a crucial distinctive feature underlying ASD–ADHD subtypes may be the differential developmental patterns, we divided the sample into three groups (childhood group: age<12, n=256; adolescence group: 12≤age<18, n=55; adulthood group: age≥18, n=29) according to age (5.1-35.6). Due to the small sample size of the adulthood group (8.55% of all sample, only 5 ASD_coADHD included), we focused our analysis on the adolescence and childhood groups. First, we tested the associations between the significant connectivity in adolescence group with our finding in the all sample, the tendency of results within adolescence group was consistent with our existing results. However, we had not detected the associations between the significant connectivity and autistic traits measured by ADI-R social scale, of which the reason we think was the sample size. Next, we tried to describe the development patterns of the significant connectivity in three groups, but because of the mismatch of sample size among the three groups (1: childhood group; 2: adolescence group; 3: adulthood group), the results may need more evidence to support in the future. The development patterns (from childhood to adolescence) of the ASD_coADHD group (red lines) was different from the ASD_nonADHD (blue lines) and TD groups (black lines) for the intra-iFC within the R.PCC (Supplementary Figure 3A), but not for the intra-iFC within the L.PCC (Supplementary Figure 3B) and the inter-iFC (Supplementary Figure 3C). These results might partly explain the crucial distinctive feature underlying ASD–ADHD subtypes. For the results of the intra-iFC (Supplementary Figure 3A and B), we can find that the significant connectivity of the adolescence group can be more easily to distinguish the ASD_coADHD and ASD_nonADHD groups compared to the childhood group. This may add the evidence for the view that adolescence which may after childhood be a second crucial time window mentioned in the review.

Supplementary Figures

Supplementary Figure 1. Data were selected from the ABIDE II database(http://fcon_1000.projects.nitrc.org/indi/abide/abide_II). Specifically, we selected the participants for this analysis from the sites that featured all the basic inclusion criteria, described in the top two steps of the flowchart: NYU_1, NYU_2, KKI_1, UCD_1, IP_1, KUL_3, EMC_1. Additional

information about the final sample are reported in Table 1 in the main text, and in supplementary Table 1.

Supplementary Figure 2. 23 rs-fMRI networks extracted by the independent component analysis.

Supplementary Figure 3. The development patterns of the significant connectivity in three groups.

A: The development patterns of the intra-iFC of the right posterior cingulate cortex (PCC). **B:** The development patterns of the intra-iFC of the left posterior cingulate cortex (PCC). **C:** The development patterns of the inter-iFC between DMN and Somatomotor network.

Supplementary Tables

Supplementary Table 2

Participants demographics

	All sample	
	Mean(SD)[Range]	
	Autism Group(N=162)	TD Group(N=177)
Age, year	11.0(4.9)[5.1-26.6]	11.0(4.0)[5.9-35.6]
Performance IQ	105.5(16.2)[61-149]	106.1(11.2)[71-125]

Gender	male(N=135) female(N=27)	male(N=133) female(N=44)
ADI_R_social	18.1(6.3)[0-29]	N/A
(N_{ASD} =113; N_{TD}=0)		
SRS	74.4(14.0)[42-113]	43.6(5.4)[34-65]
(N_{ASD} =113; N_{TD}=140)		

Abbreviations: SD= standard deviation; ADI-R= Autism Diagnostic Interview-Revised; SRS: social responsiveness scale;

Participants from the following sites from ABIDE II were included in the final sample of 339 participants: NYU_1, NYU_2,

KKI_1, UCD_1, IP_1, KUL_3, EMC_1.

Supplementary Table 2

The scan parameters and diagnostics of ASD in 7 sites

Site	NYU_1	NYU_2	KKI_1	UCD_1	IP_1	KUL_3	EMC_1
Diagnostics and Phenotypic Assessments	ADOS	ADOS	ADOS-G	ADOS-G	ADOS	DSM-IV-TR	SRS CBCL
	ADI-R	ADI-R	and/or ADI-R	SCQ	ADI-R		SCQ
Site location	New York, USA	New York, USA	Baltimore, Maryland, USA	Davis, USA	Paris, France	Leuven, Flanders, Belgium	Rotterdam, Netherlands
Eyes status	open	open	open	open	closed	open	closed
Number of Measurements (n)	180	180	156	151	85	162	160
The scan parameters	TR (ms)	2000	2000	2500	2000	2700	2500
	TE (ms)	30	15	30	24	45	30
	Number of Slices (n)	34	33	47	36	32	45

Slice thickness (mm)	3	3	3	4	4	2.7	4
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Abbreviations: NYU_1: NYU Langone Medical Center: Sample 1; NYU_2: NYU Langone Medical Center: Sample 2; KKI: Kennedy Krieger Institute; UCD: University of California Davis; IP: Institut Pasteur and Robert Debré Hospital; KUL: Katholieke Universiteit Leuven; EMC: Erasmus University Medical Center Rotterdam; ADOS: Autism Diagnostic Observation Schedule ; ADI-R= Autism Diagnostic Interview-Revised; SRS: social responsiveness scale; CBCL: Child Behavior Checklist; SCQ: Social Communication Questionnaire; TR: Repetition Time; TE: Echo Time.

Supplementary Table 3

Altered Intra-network Functional Connectivity in Patients with ASD as Compared to TD

Inter-iFC	ASD (SD)	TD (SD)	t	<i>p</i> uncorrected	<i>q</i> FDR corrected
IC 2-IC 8	0.098(0.242)	0.172(0.243)	-2.776	0.006	0.047*
IC 2-IC 13	0.032(0.239)	0.123(0.239)	-3.511	<0.001	0.011*
IC 3-IC 13	0.055(0.264)	0.137(0.284)	-2.745	0.006	0.048*
IC 4- IC 7	0.484(0.303)	0.582(0.300)	-2.999	0.003	0.032*
IC 4- IC 13	0.030(0.245)	0.144(0.289)	-3.896	<0.001	0.004*
IC 7- IC 17	0.366(0.257)	0.228(0.272)	4.769	<0.001	<0.001*
IC 9- IC 11	0.480(0.354)	0.369(0.312)	3.050	0.002	0.032*
IC 9- IC 13	0.051(0.265)	0.138(0.274)	-2.981	0.003	0.032*
IC 9- IC 18	0.296(0.364)	0.152(0.319)	3.882	<0.001	0.004*
IC 11- IC 13	0.031(0.268)	0.132(0.291)	-3.311	0.001	0.018*
IC 11- IC 18	0.462(0.336)	0.360(0.330)	2.813	0.005	0.045*
IC 17- IC 18	0.029(0.294)	-0.081(0.252)	3.713	<0.001	0.006*
IC 17- IC 22	0.046(0.275)	-0.045(0.254)	3.160	0.002	0.026*
IC 17- IC 23	0.328(0.239)	0.247(0.270)	2.941	0.003	0.033*

Abbreviations: Inter-iFC: functional connectivity between networks; IC= independent component; SD= standard deviation; ASD = Autism Spectrum Disorder; TD= Typical development.

*Significant at $q < .05$ after FDR correction.