Social Cognitive and Affective Neuroscience (SCAN)

Supplementary Information

Age-Related Changes in Intrinsic Function of the Superior Temporal Sulcus in Autism Spectrum Disorders

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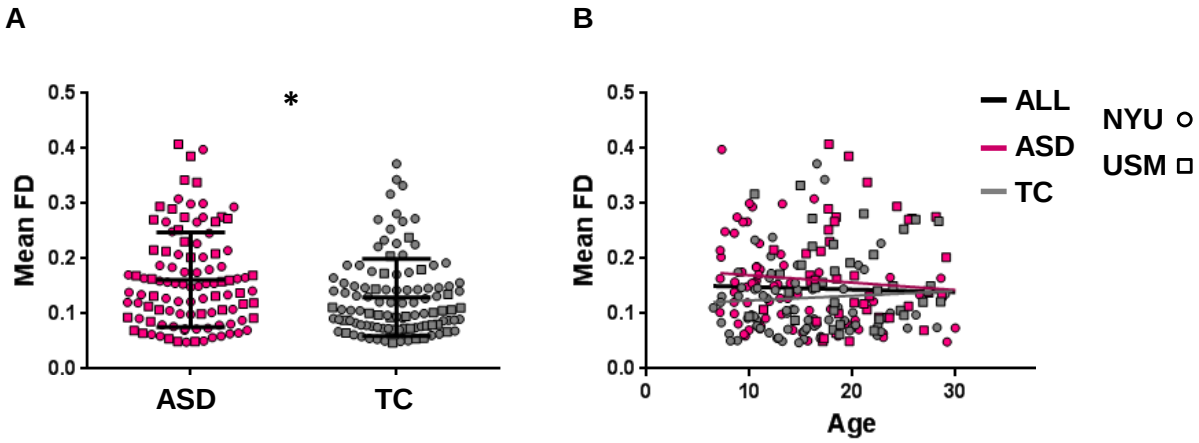
Supplementary Figures and Tables

Supplementary Figure 1. Mean framewise displacement (FD)

Panel A. Across sites, micro-movements were greater within the ASD group (pink) compared to the TC group (grey) [$t_{(213)}$= 2.99; p<.001].

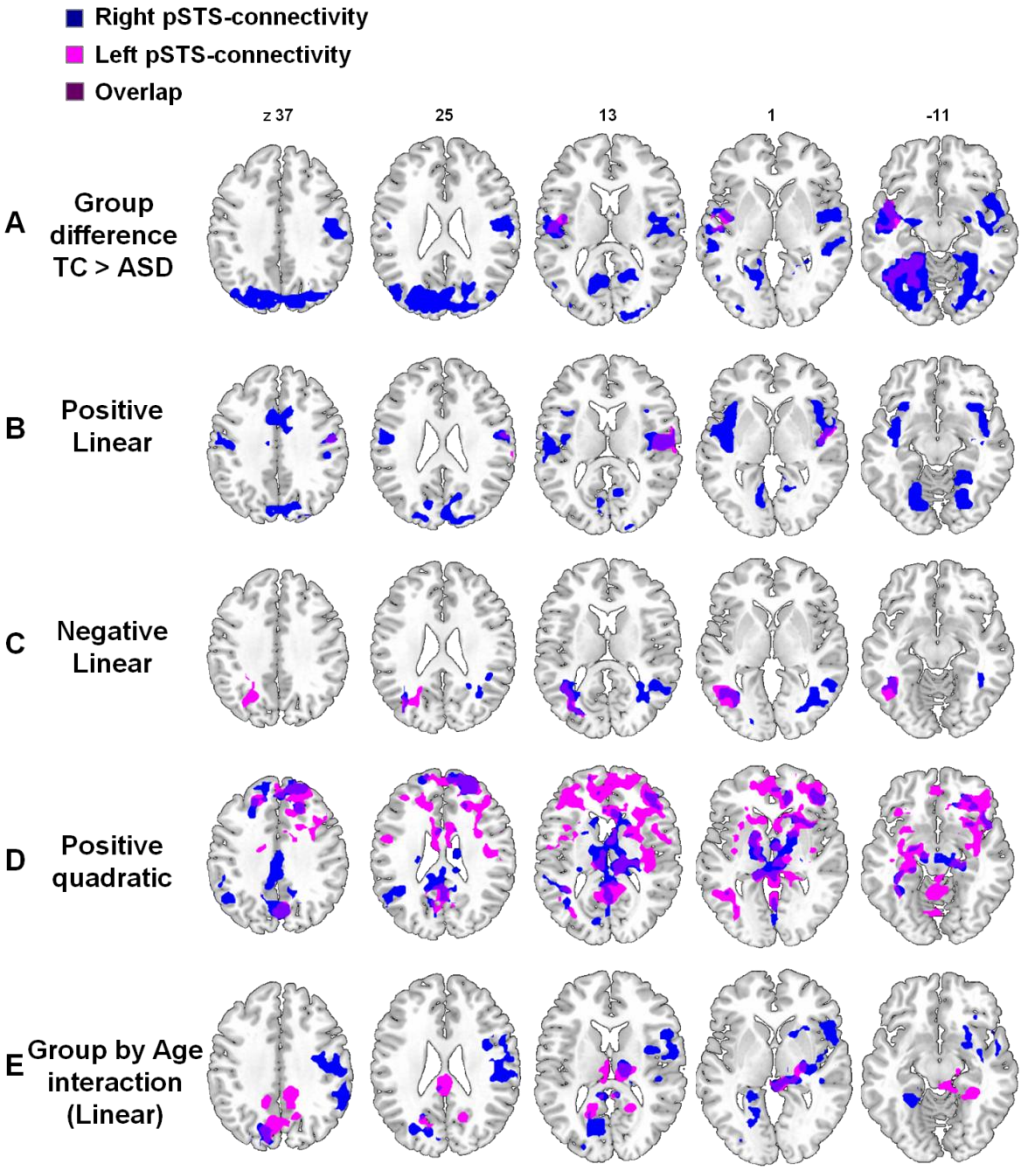
Panel B. No relationship was observed between age and mean FD (computed per Power et al., 2012) either across all participants (black regression line) [β= -0.04; $t_{(213)}$= -0.52; p= 0.60] or within each group [in pink, ASD: β= -0.10; $t_{(104)}$= -0.99; p= 0.32] [in grey, TC: β= 0.07; $t_{(107)}$= 0.73; p= 0.46].

No quadratic relationships were shown between these variables within or across groups [ASD: β= 0.16; $t_{(104)}$= 0.29; p= 0.77] [TC: β= -0.32; $t_{(107)}$= -0.57; p= 0.57] [All: β= 0.07; $t_{(213)}$= -0.18; p= 0.86] (regression lines not displayed).



Supplementary Figure 2. Intrinsic functional connectivity (iFC) of the left posterior superior temporal sulcus (pSTS) seed.

Results obtained for left pSTS-iFC (purple) were overall similar to those found for right pSTS-iFC (blue), albeit often to a lesser extent (min Z>2.3; cluster significance: p<.05, corrected). Specifically, group differences in left pSTS-iFC (**panel A**) were found only within regions of the left hemisphere, encompassing left fusiform gyrus and left anterior superior temporal gyrus extending into insula. Linear increases with age (**panel B**) were only observed for iFC between left pSTS and right insula. Linear decreases with age (**panel C**) were observed for 'local' iFC within left pSTS itself. Similar to right pSTS, left pSTS also showed a positive quadratic relationship (U-shaped) (**panel D**) with regions of the default mode network (DMN), indicating a decrease in left pSTS-DMN iFC during adolescence/young adulthood. Analysis of linear group-by-age interaction effects (**panel E**) identified clusters in left fusiform gyrus, and right thalamus, which overlapped with clusters identified for right pSTS-iFC. Significant clusters are overlaid on axial images generated with MRIcroN (http://pwww.mricro.com/).



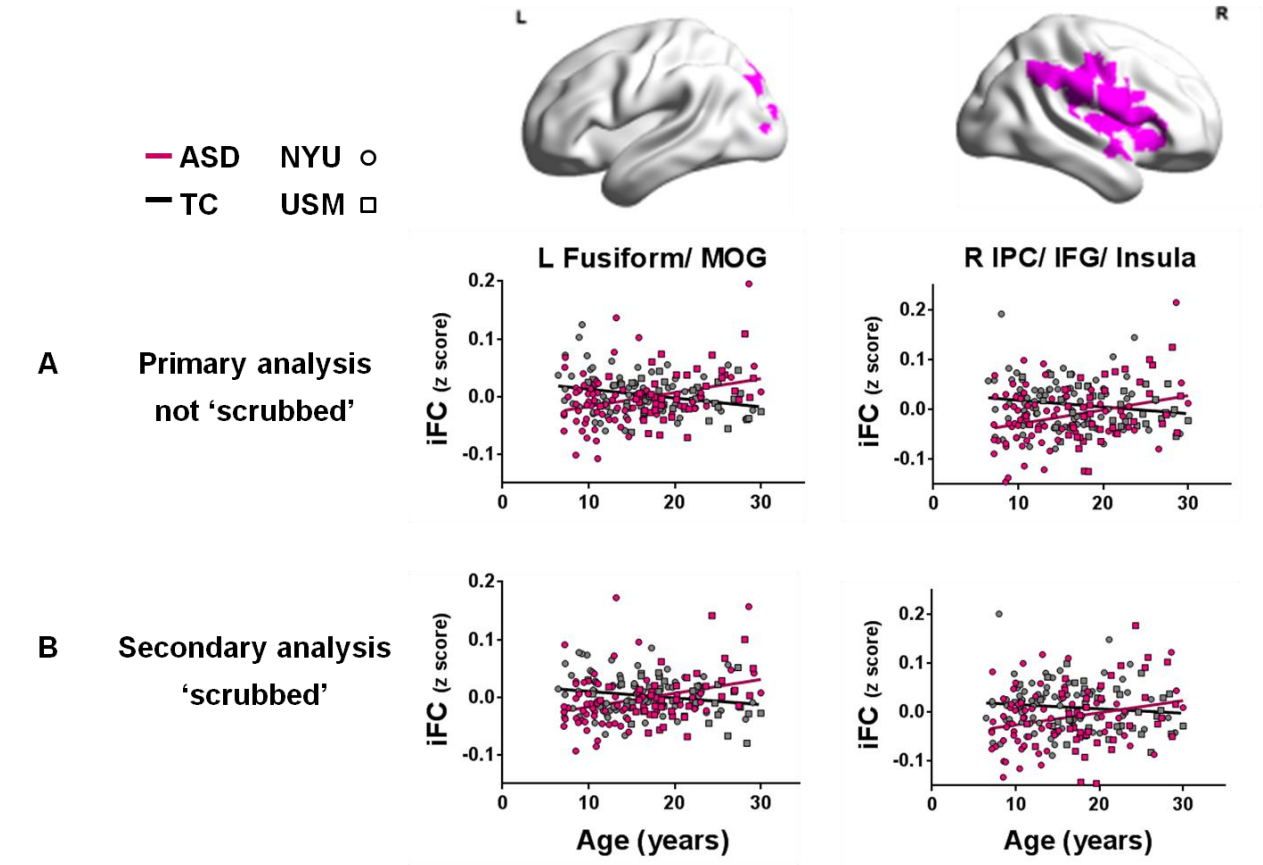
Supplementary Figure 3. Secondary analyses on 'scrubbed' data.

One approach to head motion correction involves the removal of motion-affected frames at the individual subject level ("scrubbing") (Power *et al*., 2012). While primary analyses accounted for the potentially confounding effect of micro-movements by including mean frame-wise displacement as a group-level covariate, we also examined whether our findings were robust to alternate correction strategies in supplementary analyses.

We computed intrinsic functional connectivity (iFC) of the right pSTS for data 'scrubbed' at 0.2 mm, and verified the pattern of group-by-age interaction effects (purple clusters) for the clusters identified in primary analyses.

Panel A depicts the primary analysis results (not 'scrubbed' data).

Panel B displays the secondary analysis results ('scrubbed'). The scatter plots illustrate the individual participants' iFC-scores as a function of age, separately for the ASD (pink) and TC groups (grey). NYU participants are displayed as circles; USM participants as squares.

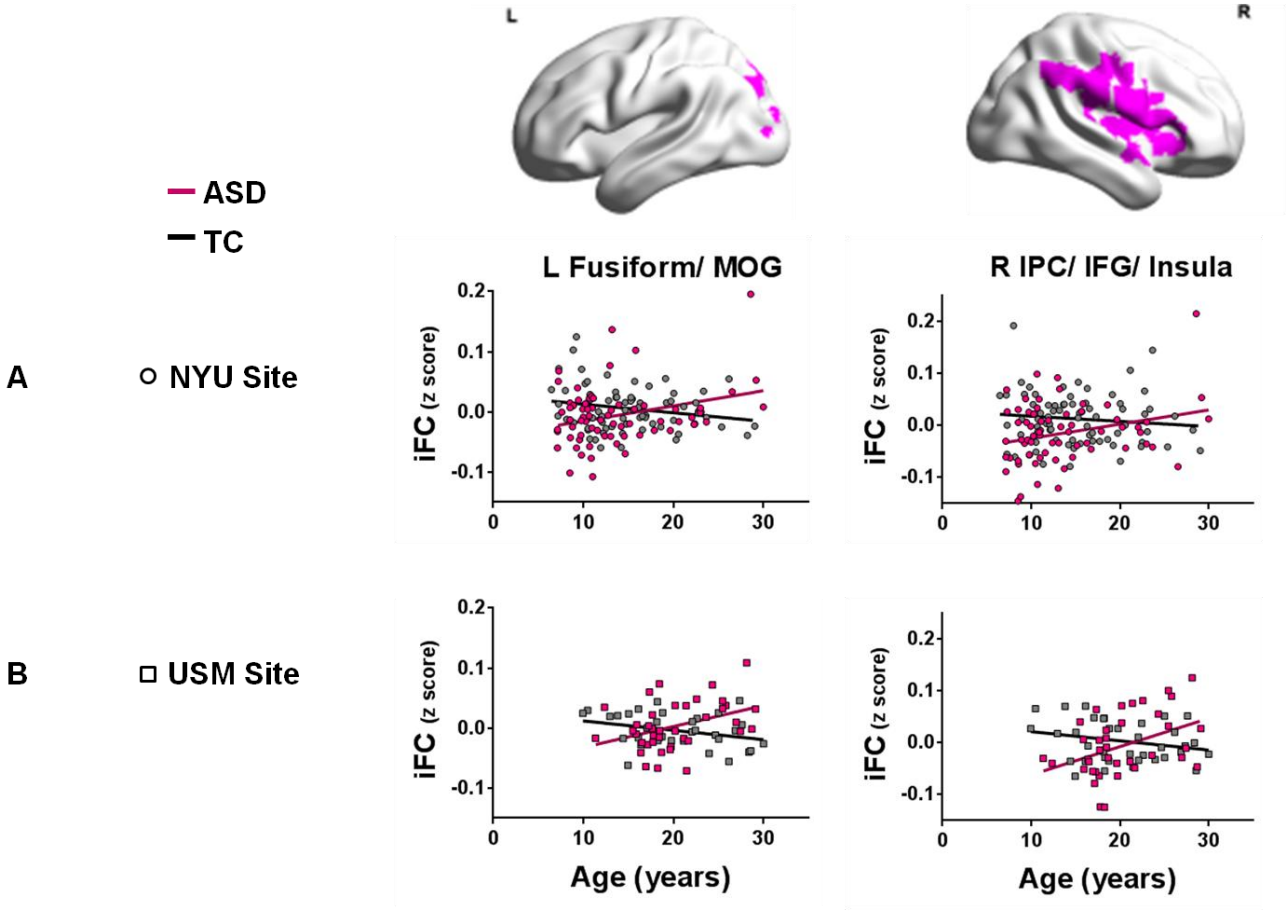


Supplementary Figure 4. Secondary analyses for each site separately.

Primary findings were identified across participants of two sites of the ABIDE repository (NYU and USM). Here, we verified the pattern of group-by-age interaction effects (purple clusters) in pSTS-iFC within each site separately for the clusters identified in primary analyses.

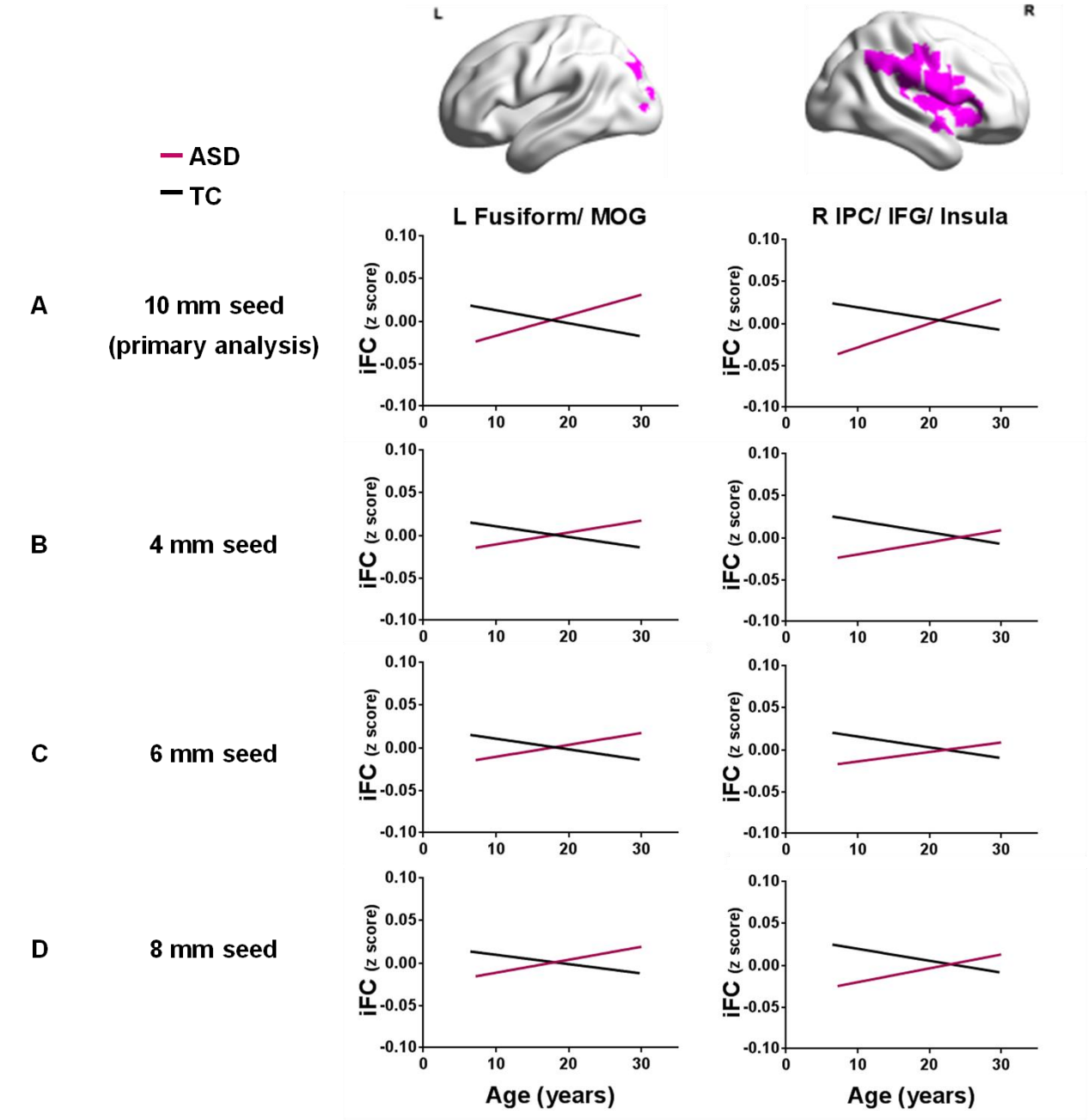
Panel A depicts the results for the participants of the NYU site.

Panel B displays results for the participants of the USM site. The scatter plots show iFC as a function of age, separately for the ASD (pink) and TC groups (grey). NYU participants are displayed as circles; USM participants as squares.



Supplementary Figure 5. Secondary analyses using seeds with different radii.

Primary intrinsic functional connectivity (iFC) analyses were performed using a 10 mm radius spherical seed for the right posterior superior temporal sulcus (pSTS). In the secondary analyses, we computed pSTS-iFC using seeds with different radii (4 mm, 6 mm, 8 mm) and verified the pattern of group-by-age interaction effects (pink clusters). **Panel A** depicts the primary analysis results, obtained using the 10 mm radius seed. **Panels B, C and D**, display secondary analyses results, obtained using pSTS-seeds with a radius of 4 mm, 6 mm, and 8 mm, respectively. Linear trend lines are shown as a function of age, separately for the ASD (pink) and TC groups (grey). L, left hemisphere; R, right hemisphere.



Supplementary Figure 6. Secondary analyses using subsamples of TC and ASD participants pair-wise matched on age and IQ.

Individuals with ASD in the primary analyses showed significantly lower full-scale IQ (FSIQ) and verbal IQ (VIQ), as well as non-significantly lower performance IQ (PIQ) (Table 1).

Here, we verified the pattern of group-by-age interaction effects (purple clusters) in pSTS-iFC within subsamples of TC and ASD participants that are pair-wise matched on age and IQ (VIQ and PIQ).

Panel A lists the group characteristics of the matched samples.

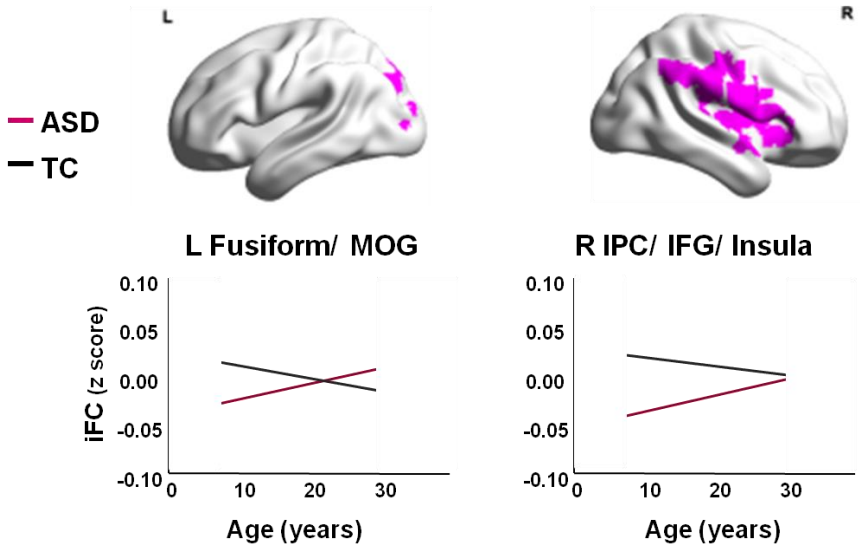
Panel B displays the secondary analyses results obtained using the matched subsamples of TC and ASD participants. Linear trend lines are shown as a function of age, separately for the ASD (pink) and TC groups (grey). Overall, the pattern of results obtained was consistent with our main findings. Note however, that the interaction effect only reached significance for the left fusiform gyrus/ MOG cluster, ($p < 0.05$), while for the right IPC/ IFG/ insula cluster, the group-by-age interaction was marginally significant within the IQ-matched subsample ($p = 0.09$). L, left hemisphere; R, right hemisphere.

Panel A.

	ASD (n = 55)				TC (n = 55)					
	mean	SD	min	max	mean	SD	min	max	t-value	p
Age at scan (years)	16.0	5.4	7.1	30.0	16.4	5.4	7.2	28.2	0.40	0.69
Full-scale IQ	111.1	13.3	84.0	142.0	111.3	14.0	83.0	144.0	0.06	0.96
Verbal IQ	107.7	14.6	71.0	136.0	109.5	14.5	80.0	141.0	0.65	0.52
Performance IQ	112.3	15.5	81.0	149.0	110.5	13.2	83.0	138.0	-0.66	0.51
Head Motion (mean FD)	0.15	0.08	0.05	0.39	0.13	0.08	0.05	0.37	-1.01	0.32

ASD, autism spectrum disorder; TC, typical controls; IQ, intelligence quotient; mean FD, mean framewise displacement; SD, standard deviation; min, minimum; max, maximum.

Panel B.



Supplementary Table 1. Group characteristics separately for the NYU and USM ABIDE samples.

	NYU								USM							
	ASD (n = 67)				**TC (n =74)**				**ASD (n = 39)**				**TC (n = 35)**			
Sex	all males				all males				all males				all males			
Handedness (right/left)*	52/14				72/2				34/5				33/2			
Eye status (open/closed)	59/8				62/12				39/0				35/0			
DSM-IV-TR Diagnosis (Autism/Asperger/PDD-NOS)	45/17/5				-				38/0/1				-			
Medication status (n on meds)	15															
Medication status (n on meds at scan)**	5				-				-				-			
Comorbidity***	21				-				15				-			
	mean	**SD**	**min**	**max**	**mean**	**SD**	**min**	**max**	**mean**	**SD**	**min**	**max**	**mean**	**SD**	**min**	**max**
ADOS Scores**																
Total Score (Social+Communication)	11.4	4.2	5.0	22.0	-	-	-	-	13.3	3.6	6.0	21.0	1.3	1.3	0.0	4.0
Social	3.6	1.6	0.0	8.0	-	-	-	-	4.6	1.5	2.0	7.0	0.6	0.6	0.0	2.0
Communication	7.7	3.0	2.0	14.0	-	-	-	-	8.7	2.6	4.0	14.0	0.8	0.9	0.0	3.0
RRB	2.4	1.5	0.0	7.0	-	-	-	-	1.9	1.9	0.0	8.0	0.2	0.5	0.0	3.0
ADI-R Total Scores***																
Social	19.0	5.4	7.0	28.0												
Communication	15.6	4.1	8.0	25.0												
RRB	5.7	2.6	0.0	12.0												
Onset	3.4	1.3	1.0	5.0												
SRS Raw Total Scores	90.5	30.8	34.0	164.0	21.8	13.3	0.0	56.0	89.6	32.7	6.0	151.0	15.1	12.6	0.0	51.0
Age at scan (years)	13.6	5.8	7.1	30.0	15.2	5.3	6.5	29.0	20.2	4.4	11.4	29.1	20.3	5.4	10.0	30.0
Full-scale IQ	108.6	16.3	76.0	148.0	113.4	13.3	80.0	142.0	99.7	16.0	73.0	132.0	115.0	14.7	89.0	148.0
Verbal IQ	105.6	15.4	73.0	137.0	113.2	12.8	80.0	141.0	95.8	18.1	55.0	122.0	112.5	14.7	87.0	140.0
Performance IQ	110.4	17.5	72.0	149.0	110.4	14.1	67.0	137.0	103.6	16.6	72.0	133.0	114.1	13.7	90.0	155.0
Head Motion (mean FD)	0.15	0.08	0.05	0.40	0.11	0.06	0.05	0.37	0.18	0.10	0.05	0.41	0.16	0.08	0.06	0.33

NYU, New York University; USM, University of Utah - School of Medicine; ASD, autism spectrum disorder; TC, typical controls; PDD-NOS, pervasive developmental disorder not otherwise specified; ADOS, Autism Diagnostic Observation Schedule; RRB, Restricted Repetitive Behaviors; ADI-R, Autism Diagnostic Interview–Revised; SRS, Social Responsiveness Scale; IQ, intelligence quotient; mean FD, mean framewise displacement; SD, standard deviation; min, minimum; max, maximum.
*Handedness label was not available for one participant with ASD.
**Fluoxetine (n=2), Guanfacine (n=2); Methylphenidate (n=1). Note that for one participant, information on medication status at time of scan was not available.

***Attention Deficit Hyperactivity Disorder (not otherwise specified (n=3); hyperactive (n=1); Inattentive (n=4); Combined (n=4)); Specific phobia (n=7); Mood Disorder (n=6); Dysthymia (n=5); Enuresis (n=5); Encopresis (n=3); Anxiety Disorder not otherwise specified (n=2); Diurnal & Nocturnal Enuresis (n=2); Generalized Anxiety Disorder (n=2); Social Phobia (n=2); Tic Disorder (n=2); Depressive Disorder (n=1); Disruptive disorder (n=1); Separation Anxiety (n=1); Agoraphobia (n=1).
****These scores are based on the algorithm for ADOS module 4 (n=39), module 3 (n=65), module 2 (n=2) (Lord *et al*., 1999). Since we included module 4, the more recent scores per Gotham *et al*., 2009 were not used as they are only available for Modules 1, 2 and 3.
Differences between sites were apparent in terms of ADOS Communication scores, mean age at scan, Full-scale IQ, Verbal IQ and mean FD [$p < 0.05$]. No differences between sites were shown for ADOS Social scores, ADOS RRB scores, Performance IQ or SRS-scores, [$p > 0.05$]. ***** ADI-R scores were obtained for all participants with ASD, but scores were made available in the online ABIDE repository only by the NYU site, not by the USM site.

Supplementary Table 2. Intrinsic functional connectivity of the right posterior superior temporal sulcus (pSTS). List of clusters showing significant group effects, relationships with age (linear/quadratic), or group x age interaction effects (linear/quadratic).

Analysis	Cluster Size (# Voxels)	Cluster Region(s)	Z score	Peak MNI x	Peak MNI y	Peak MNI z	Distance
Group Difference TC > ASD	7449	Left Fusiform Gyrus	4.5	-24	-38	-18	77.52
		Left Inferior Occipital Gyrus	4.47	-42	-74	-12	
		Left Inferior Temporal Gyrus	4.42	-36	-40	-16	
		Right Cuneus	4.38	12	-84	40	
		Left Fusiform Gyrus	4.46	-22	-46	-14	
		Left Lingual Gyrus	4.13	-28	-50	-4	
		Left Superior Parietal Lobule	4.03	-20	-76	44	
	2598	Right Postcentral Gyrus	4.19	50	-12	28	53.75
		Right Insula Lobe	3.86	46	-6	6	
		Right Rolandic Operculum/ Inferior Parietal Cortex	3.75	48	-14	22	
		Right Superior Temporal Gyrus	3.55	60	0	2	
		Right Postcentral Gyrus/ BA 6	3.49	52	-18	48	
		Right Amygdala	3.4	24	-4	-14	
	1493	Left Superior Temporal Gyrus	4.82	-48	2	-10	114.30
		Left Middle Temporal Gyrus	4.53	-54	-12	-8	
		Left Amygdala	3.3	-22	-8	-12	
		Left Rolandic Operculum/ Inferior Parietal Cortex	3.27	-50	-16	14	
		Left Postcentral Gyrus/ BA 6 - BA 44	2.96	-54	-4	20	
		Left Insula Lobe	2.92	-36	-4	-8	
	1309	Right Fusiform Gyrus	3.97	30	-44	-10	27.22
		Right Inferior Temporal Gyrus	2.99	44	-50	-16	
		Right Inferior Occipital Gyrus	2.99	44	-64	-16	
		Right Lingual Gyrus	2.89	16	-42	-8	
		Right ParaHippocampal Gyrus	2.87	34	-26	-18	
Group Difference ASD > TC		-	-	-	-	-	
Positive Linear Relationship with Age	2548	Left Insula Lobe	4.59	-42	-10	4	102.08
		Left Superior Temporal Gyrus	3.88	-44	-4	-12	
		Left Rolandic Operculum	3.79	-56	-8	8	
		Left Postcentral Gyrus/ BA 6	3.72	-52	-10	50	
		Left Postcentral Gyrus/ Inferior Parietal Cortex	3.71	-60	-20	16	
	2222	Right Insula Lobe	4.41	44	4	-12	66.03
		Right Rolandic Operculum	3.92	62	-10	10	
		Right Superior Temporal Gyrus	3.76	46	-12	-2	
		Right Postcentral Gyrus	3.23	62	-10	28	
		Right Precentral Gyrus	3.22	40	-16	42	
	1730	Right Cuneus	3.76	4	-80	36	57.21
		Right Superior Occipital Gyrus	3.44	18	-90	30	
		Right Fusiform Gyrus	3.26	28	-72	-14	
		Right Lingual Gyrus	3.2	18	-50	-8	
		Right Calcarine Gyrus	3.13	10	-60	10	
	1287	Right Middle Cingulate Cortex	4.63	4	6	44	88.35
		Left SMA/ BA 6	3.04	-12	-6	64	
	1007	Left Fusiform/ Lingual Gyrus	3.93	-22	-72	-10	71.42
		Left Cuneus	3.38	-16	-70	20	
		Left Calcarine Gyrus	2.9	-12	-60	4	
		Left Fusiform Gyrus	2.79	-30	-64	-18	

Negative Linear Relationship with Age	1176	Right Middle Temporal Gyrus - pSTS	3.8	48	-52	10	10.05
	1039	Left Middle Occipital Gyrus	3.54	-36	-74	20	85.68
		Left Inferior Temporal Gyrus	3.37	-48	-52	-6	
		Left Middle Temporal Gyrus	2.55	-46	-62	-2	
Positive Quadratic Relationship with Age	8760	Right Thalamus	4.35	10	-28	12	49.57
		Left Thalamus	4.27	-16	-14	0	
		Right Temporal Pole	3.8	50	16	-16	
		Left SupraMarginal Gyrus	3.46	-50	-30	30	
		Left Angular Gyrus	3.35	-46	-56	34	
		Left Anterior Cingulate Cortex	3.18	-4	8	28	
		Right Precuneus	2.95	16	-52	34	
		Right Posterior Cingulate Cortex	2.65	12	-48	24	
	2064	Right Middle Frontal Gyrus	4.32	24	52	26	116.43
		Right Superior Frontal Gyrus	4.09	20	32	38	
		Left Superior Medial Gyrus	3.74	-2	44	44	
		Left Superior Frontal Gyrus	3.4	-22	34	34	
		Left Middle Frontal Gyrus	3.33	-30	28	48	
		Left Superior Frontal Gyrus	3.28	-14	52	38	
Group x Age Linear	4047	Right Postcentral Gyrus / Inferior Parietal Cortex	4.15	50	-14	32	53.94
		Right Thalamus	3.95	20	-28	4	
		Right Inferior Frontal Gyrus (p. Opercularis)	3.74	50	14	6	
		Right Precentral Gyrus/ BA 44	3.63	56	2	22	
		Right Rolandic Operculum	3.5	56	-6	16	
	1570	Left Fusiform Gyrus	3.14	-26	-38	-20	79.93
		Left Cuneus	3.06	-12	-80	18	
		Left Calcarine Gyrus	3.02	-18	-76	14	
		Left Lingual Gyrus	2.97	-26	-52	-2	
Group x Age Quadratic	629	Left Middle Occipital Gyrus	3.49	-38	-80	36	93.00
		Left Angular Gyrus	3.36	-38	-58	30	

Within-cluster peaks were identified using the Anatomy Toolbox, version 1.7. Cluster size is reported in number of voxels (2 x 2 x 2 mm) and stereotaxic coordinates for the peaks detected are reported according to the Montreal Neurological Institute (MNI152) space. The last column displays for each cluster the Euclidian distance between the cluster's peak coordinate and the center coordinate of the right pSTS seed (47, -60, 4).