Neural Connectivity Evidence for a Categorical-Dimensional Hybrid Model of Autism Spectrum Disorder

Supplemental Information

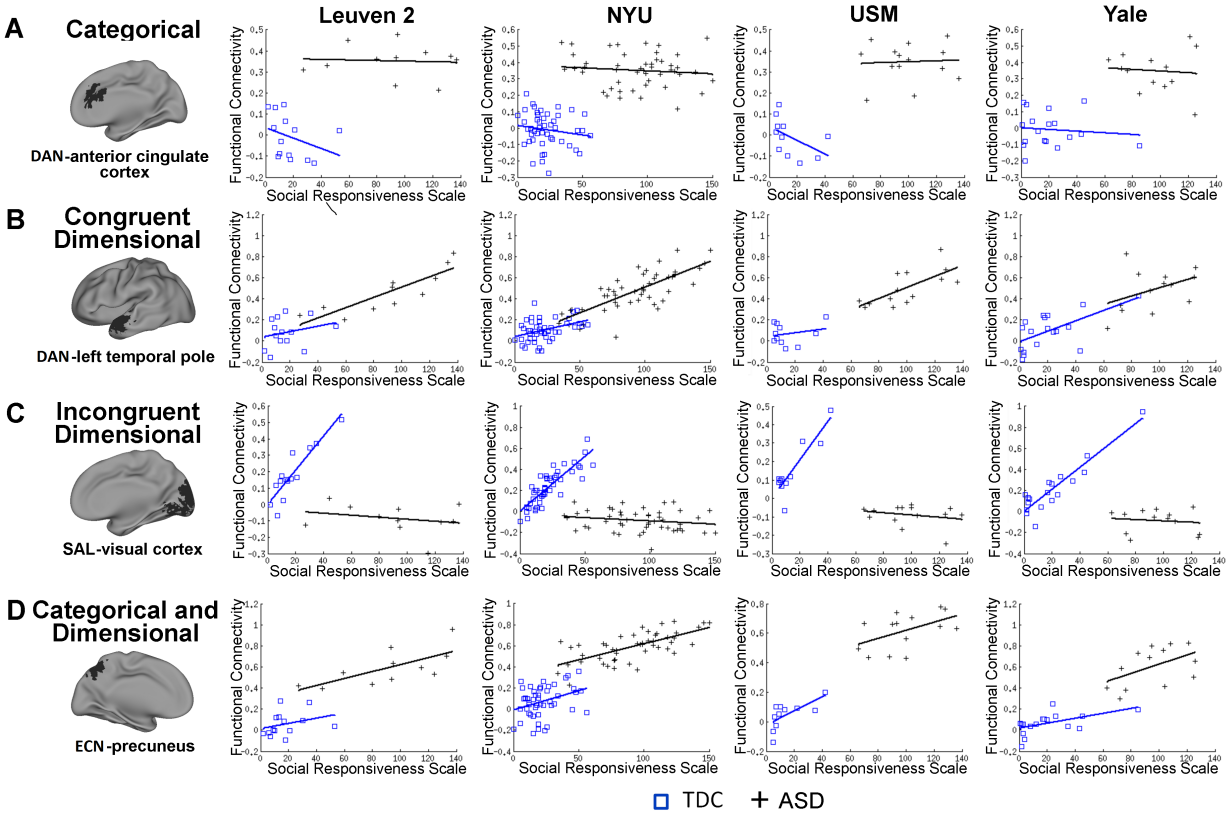

Figure S1. Scatter plots depicting the site-specific relationships between SRS scores and functional connectivity for TDC and ASD groups for selected regions. Least-squares fit lines are plotted for TDC and ASD separately for each of the four sites demonstrating (**A**) categorical effects only, (**B**) dimensional effects only, (**C**) an interaction of categorical and dimensional effects, and (**D**) both dimensional and categorical effects. Plotted functional connectivity values represent residuals after removing nuisance effects as described in the main text. DAN, dorsal attention network; DMN, default mode network; SAL, salience network; ECN, executive control network; NYU, New York University; USM, Utah School of Medicine.

Table S1. Resting-state fMRI scan parameters by site.

	Leuven	**NYU**	**USM**	**Yale**
Scan Duration	6:40	6:00	8:06	6:40
TR (ms)	1667	2000	2000	2000
TE (ms)	33	15	28	25
Flip Angle (°)	90	90	90	60
Voxel Size (mm^3)	3.59 x 3.59 x 4	3 x 3 x 4	3.4 x 3.4 x 3	3.4 x 3.4 x 4
Slices	32	33	40	34
FOV (mm^2)	230 x 230	240 x 192	220 x 220	220 x 220
Acquisition Sequence	ascending	interleaved	interleaved	interleaved

TR, repetition time; TE, echo time; FOV, field of view; mm, millimeters; ASD, autism spectrum disorder; NYU, New York University; USM, Utah School of Medicine.

Table S2. Congruent dimensional effects of ASD symptoms (i.e., SRS score).

	BA	x	y	z	# Voxels	Direction
DA						
medial frontal gyrus	8	9	54	45	509	+
R middle/superior temporal gyrus	21/22	69	-39	9	179	+
L middle temporal gyrus	21	-66	-30	-6	177	+
R putamen, thalamus		12	-69	-36	347	-
L putamen		-21	0	3	176	-
DM						
R insula/precentral gyrus	13, 44	45	-3	21	191	+
R inferior frontal gyrus	45	48	30	9	145	+
R precentral gyrus	6	36	3	27	91	+
SAL						
precuneus	7	-15	-66	33	361	+
R lingual gyrus	19	27	-72	0	146	+
posterior cingulate cortex	29, 30	-3	-48	21	138	+
CON						
medial frontal gyrus	8	6	30	48	250	+
L middle frontal gyrus	10	-36	60	12	161	+
R lingual gyrus	18	39	-93	-3	156	+
R middle frontal gyrus	8	38	28	42	113	+
posterior cingulate cortex	29	0	-39	21	100	+
R postcentral gyrus, inferior frontal gyrus, insula	40, 13	53	-29	45	747	-
R precentral gyrus	4	24	-21	65	307	-
L precuneus, superior parietal lobule	7	-24	-54	36	142	-

Coordinates reported in Montreal Neurological Institute (MNI) standard space.

L, left; R, right; BA, Brodmann area; DA, dorsal attention network; DM, default mode network; SAL, salience processing network; CON, executive control network; ASD, autism spectrum disorder; TDC, typically-developing children.

"+": positive relationships; "-": negative relationships.

Table S3. Categorical differences in functional connectivity values associated with an ASD diagnosis but not explained by ASD-related symptom severity (i.e., SRS score).

	BA	x	y	z	# Voxels	Contrast
DA						
L, R precuneus	7	-15	-75	48	673	ASD > TDC
L, R cerebellum		12	-69	-36	523	ASD > TDC
R middle frontal, precentral gyrus	6	39	-3	36	266	ASD > TDC
R cerebellum		21	-51	-18	110	ASD > TDC
L inferior parietal lobule	40	-36	-48	45	110	ASD > TDC
L superior temporal gyrus, angular gyrus	41, 39	-48	-33	12	706	TDC > ASD
L middle/medial frontal gyrus	9, 10	-21	60	18	517	TDC > ASD
L superior frontal gyrus	6	-9	21	60	188	TDC > ASD
L middle/superior temporal gyrus	21, 22	-54	6	-33	151	TDC > ASD
R superior temporal gyrus	22	60	-15	3	144	TDC > ASD
R precentral gyrus	4	36	-18	57	142	TDC > ASD
L fusiform gyrus	37	-45	-48	-15	115	TDC > ASD
R medial frontal gyrus	10	18	42	12	98	TDC > ASD
R superior frontal gyrus	9	18	51	27	98	TDC > ASD
DM						
L supramarginal gyrus	40	-30	-48	36	328	ASD > TDC
R superior/middle frontal gyrus	9, 46	45	42	30	319	ASD > TDC
L middle frontal gyrus	9, 45	-36	33	21	273	ASD > TDC
R insula, precentral gyrus	13, 44	48	6	6	177	ASD > TDC
R inferior parietal lobule	40	60	-36	21	105	ASD > TDC
SAL						
anterior cingulate cortex	32	-6	6	42	169	ASD > TDC
L postcentral gyrus	3	-45	-18	57	192	TDC > ASD
R medial frontal gyrus	6	12	-21	54	158	TDC > ASD
L middle frontal gyrus	10	-27	60	6	98	TDC > ASD
CON						
L cerebellum		-12	-59	40	300	ASD > TDC
R superior frontal gyrus	10	21	45	24	150	TDC > ASD
L middle frontal gyrus	9	-27	36	36	135	TDC > ASD
R precentral gyrus	44	48	6	9	126	TDC > ASD
L postcentral gyrus	3	-57	-21	39	110	TDC > ASD
medial frontal gyrus	10	3	57	18	101	TDC > ASD

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Table S4. Significant categorical-by-dimensional interaction effects of ASD.

	BA	x	y	z	# Voxels	Direction
DA						
anterior cingulate cortex	32	-9	15	42	211	+
L parahippocampal gyrus, insula	21	-39	-6	9	156	+
Thalamus		11	-24	8	147	+
R cerebellum		27	-48	-30	141	+
L caudate		-15	3	24	98	+
posterior cingulate cortex	23	6	-54	18	175	-
R precentral gyrus	4	30	-27	58	151	-
L middle temporal gyrus	21	-51	3	-33	120	-
R middle temporal gyrus	20	54	-36	9	98	-
DM						
R parahippocampal gyrus		21	-3	-9	180	+
R middle frontal gyrus	10	42	42	-6	154	+
R inferior frontal gyrus	45	46	22	18	97	+
L superior frontal gyrus	9	-39	45	30	97	+
L precuneus	7	-12	-63	36	152	-
L superior temporal gyrus	22	-45	-56	16	112	-
SAL						
L insula	13	-30	9	12	190	+
L, R superior frontal gyrus	8	6	18	51	125	+
L middle occipital gyrus	18	-30	-90	13	106	+
precuneus	7	-9	-63	45	576	-
precuneus	31	-3	-69	18	106	-
R angular gyrus	39	41	-56	30	104	-
CON						
R cerebellum		36	-69	-33	250	+
L middle frontal gyrus, precentral gyrus	6	-42	-15	60	150	+

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L, left; R, right; BA, Brodmann area; DA, dorsal attention network; DM, default mode network; SAL, salience processing network; CON, executive control network; ASD, autism spectrum disorder; TDC, typically-developing children.

“+” indicates those regions for which the relationship between functional connectivity and symptoms was increased in slope (i.e., either become more positive or change from negative to positive) for ASD versus TDC. “-” indicates regions with a decrease in slope (i.e., either become more negative or change from positive to negative) relationship between functional connectivity and symptoms for ASD versus TDC.