Supplementary Data

EMethods

Participants

Participants were recruited through referrals from a university-affiliated autism clinic. All had a full-scale IQ within the normal range as assessed with the Weschler Abbreviated Scales of Intelligence,[1] or the Weschler Intelligence Scale for Children – 4th Edition.[2] Original participants included 22 TD and 22 ASD subjects, but 3 TD and 3 ASD subjects were excluded due to maximum motion >2.5 mm. Volumes with motion > 2mm were removed for 3 ASD subjects (average volumes removed = 12.33) and 2 TD subjects (average volumes removed = 8.67). Nine of the ASD participants were taking psychoactive medications including selective serotonin reuptake inhibitors (N= 1), psychostimulants (N=5), and multiple medications (N=3).

Measures

Screen for Child Anxiety Related Emotional Disorders (SCARED[3]. The SCARED is a 41-item parent report form of child anxiety symptoms. The total score was used as a continuous measure of anxiety symptom severity. The SCARED has good internal consistency, test-retest reliability, and discriminative validity.[3]

Short Sensory Profile (SSP).[4] The SSP is a widely used, parent report measure of sensory dysregulation across a number of modalities. We used the subscales relevant to the auditory and tactile stimuli administered: Auditory/Visual Sensitivity, Auditory Filtering, and Tactile Sensitivity, as well as the Under-responsive/Seeks Sensation subscale. Higher scores on the SSP indicate *lower* impairment. This measure has strong reliability and validity.[5]

Sensory Over-Responsivity (SensOR) Inventory.[6] The SensOR Inventory is a parent checklist of sensory sensations that bother their child. For the purposes of this study, only the auditory and tactile subcales were used. The number of items parents rate as bothering their child has been shown to discriminate between children with and without SOR.[6]

MRI Data Acquisition

Scans were acquired on a Siemens Trio 3 Tesla magnetic resonance imaging scanner. A high-resolution structural T2-weighted echo-planar imaging volume (spin-echo, TR=5000 ms, TE=33 ms, 128x128 matrix, 20cm FOV, 36 slices, 1.56mm in-plane resolution, 3mm thick) was acquired coplanar to the functional scans in order to ensure identical distortion characteristics to the fMRI scan. Each functional run involved the acquisition of 137 EPI volumes (gradient-echo, TR=2500ms, TE=30ms, flip angle=90, 64x64 matrix, 20cm FOV, 33 slices, 3.125mm in-plane resolution, 3mm thick). Auditory stimuli were presented to the participant using magnet-compatible headphones under computer control (Resonance Technologies, Inc.). Participants wore earplugs and headphones to reduce interference of the auditory stimuli from the scanner noise.

Data analysis**:** Analyses were performed using FSL Version 5.0.5 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Preprocessing included motion correction to the mean image, spatial smoothing (Gaussian Kernel FWHM = 5mm), and high-pass temporal filtering (t > 0.01 Hz). Functional data were linearly registered to a common stereotaxic space by first registering to the in-plane T2 image (6 degrees of freedom) then to the MNI152 T1 2mm brain (12 degrees of freedom).

FSL's fMRI Expert Analysis Tool (FEAT), Version 5.98 was used for statistical analyses. Fixed-effects models were run separately for each subject, then combined in a higher-level mixed-effects model to investigate within and between-group differences. Single-subject models included six motion parameters as covariates. Each experimental condition (Auditory, Tactile, or Joint condition) was modeled with respect to the fixation condition during rest. Higher-level group analyses were carried out using FSL's FLAME (FMRIB's Local Analysis of Mixed Effects State) stage 1.[7–9]

Amygdala seed. The amygdala seed region for the PPI analysis was functionally defined by areas of the right amygdala that were active in either group during the Joint condition; the right amygdala was chosen because both groups had significant activation in the right, but not left amygdala.

eResults

Behavioral comparisons of SOR groups: A total of nine children in the ASD group and one child in the TD group had elevated SOR. A one-way analysis of variance (ANOVA) was used to compare the SOR composite and

SCARED anxiety totals for the following three groups: ASD(SOR+), ASD(SOR-), and TD (without SOR). In both cases, the overall F was significant (SOR composite $F(2,34)=65.20$, $p<.001$; SCARED $F(2.34)=20.61$, $p<.001$). Post-hoc LSD tests showed that the ASD(SOR+) group had significantly higher SOR composite scores ($M=1.27$, $SD=.64$) than either the ASD(SOR-) group ($M=-0.29$, $SD=.27$, $p<.001$) or the TD group ($M=-0.55$, $SD=.29$, $p<.001$). Similarly, the ASD(SOR+) group had significantly higher SCARED scores ($M=21$, $SD=8.78$) than either the ASD(SOR-) group ($M=7.40$, $SD=3.50$, $p<.001$) or the TD group ($M=5.11$, $SD=5.83$, $p<.001$). For both the SOR composite and the SCARED scores, there were no significant differences between the ASD(SOR-) and the TD groups.

There were no significant differences between ASD(SOR+) and ASD(SOR-) groups in IQ ($t(17)=-1.01$, $p=.33$), ADOS severity score ($t(17)=-1.11$, $p=.28$), or percentage using medication ($\chi^2(1)=.06$, $p=.81$).

eReferences

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7. Beckmann CF, Jenkinson M, Smith SM. General multilevel linear modeling for group analysis in FMRI. *NeuroImage*. 2003;20(2):1052-1063. doi:10.1016/S1053-8119(03)00435-X.

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eTable 1. MNI coordinates for the auditory condition as compared to baseline.

	TD				ASD			
	MNI Peak (mm)			Max	MNI Peak (mm)			Max
	x	y	z	*Z*	x	y	z	*Z*
Right Precentral Gyrus	44	8	26	3.11				
Right IFG	58	26	26	4.23	46	40	6	3.14
Right Heschl's gyrus	52	-20	8	6.53	48	-16	8	6.36
Left Heschl's gyrus	-44	-20	2	6.44	-52	-22	8	6.14
Right Superior Temporal Gyrus	66	-42	14	5.40	66	-32	6	4.58
Left Superior Temporal Gyrus	-62	-30	10	4.52	-66	-18	-4	3.25
Right Planum Temporale					62	-18	12	6.60
Left Planum Temporale	-48	-36	12	5.39	-36	-36	16	4.57
Right Planum Polare	42	0	-16	3.43				
Right Temporal Pole	54	8	-8	2.73	52	22	-14	3.45
Right Middle Temporal Gyrus	60	-56	10	2.96	48	-40	10	3.59
Right Central Opercular Cortex					60	-6	14	4.01
Right Insula	48	-10	-4	5.51	-54	-6	4	4.31
Left Insula	-32	-34	16	4.85				
Cerebellum					-28	-56	-46	3.79

Note: x, y, and z refer to the left–right, anterior–posterior, and inferior–superior dimensions, respectively; Z refers to the Z-score at those coordinates (local maxima or submaxima Within-group analyses are cluster corrected for multiple comparisons, $Z>2.3$, $p<.05$.

eTable 2. MNI coordinates for the tactile condition as compared to baseline.

	TD				ASD				ASD>TD			
	MNI Peak (mm)			Max	MNI Peak (mm)			Max	MNI Peak (mm)			Max
	x	y	z	*Z*	x	y	z	*Z*	x	y	z	*Z*
Right Postcentral Gyrus	22	-42	68	4.98	24	-38	64	5.63	14	-30	76	3.77
Left Postcentral Gyrus	-56	-22	26	4.63	-26	-40	64	4.01	-54	-22	52	2.86
Right Precentral Gyrus	28	-16	66	3.57	62	6	6	4.33	12	-16	78	3.37
Left Precentral Gyrus	-58	10	26	4.26	-58	4	28	4.59				
Right Middle Frontal Gyrus					32	-4	58	2.77				
Right Inferior Frontal Gyrus	42	-30	24	5.70	48	14	0	2.91				
Left Inferior Frontal Gyrus	-46	12	4	2.85								
Left Frontal Orbital Cortex					-30	16	-20	3.18				
Right Operculum	48	-16	16	4.38	44	-22	18	5.88				
Left Operculum	-46	-36	22	4.05	-44	-30	22	4.49				
Right Insula	36	-16	14	5.40	32	0	12	4.83				
Left Insula	-40	6	-2	3.65	-34	-2	14	4.16				
Right Supramarginal Gyrus	62	-44	26	2.52	66	-22	24	4.81				
Left Supramarginal Gyrus	-56	-46	34	2.88	-58	-28	24	5.90				
Posterior Cingulate					16	-24	42	3.74	16	-20	38	2.68
Right Superior Parietal Lobule					20	-50	72	4.02				
Left Superior Parietal Lobule					-40	-46	64	3.99	-16	-50	74	3.47
Right Planum Temporale	64	-32	20	5.73								
Right Putamen	26	4	-4	3.23	26	6	-4	4.39				
Left Putamen					-24	8	-10	4.72				
Right Thalamus - Pulvinar					14	-22	14	3.67				

Note: x, y, and z refer to the left–right, anterior–posterior, and inferior–superior dimensions, respectively; Z refers to the Z-score at those coordinates (local maxima or submaxima Within-group analyses are cluster corrected for multiple comparisons, $Z>2.3$, $p<.05$; between-group and regression analyses are thresholded at $Z>1.7$, corrected. Between-group analyses are masked by regions of significant activation in either within-group analysis, at the liberal threshold of $Z>1.7$, uncorrected. Regression results show clusters with activation significantly correlated with SOR composite, within the ASD group, over and above age and anxiety symptoms.

eTable 3. MNI coordinates for significant amygdala clusters in each condition compared to baseline.

		Right Amygdala						Left Amygdala					
		MNI Peak (mm)			Max	Size	p-value	MNI Peak (mm)			Max	Size-	p-value
		x	y	z	*Z*	(voxels)		x	y	z	*Z*	#voxels	
Auditory	TD												
	ASD	20	-8	-14	2.89	25	p = 0.08						
	ASD>TD												
Tactile	TD	20	-4	-12	3.61	68	p < 0.001	-22	-10	-12	2.68	59	p < 0.001
	ASD							-22	0	-14	3.58	26	p =.05
	ASD>TD												
	ASD Regress Tactile	22	-4	-14	2.96	92	p < 0.001	-24	-4	-26	2.75	142	p < 0.001
Joint	TD	20	-6	-12	2.24	23	p =.10						
	ASD	22	-12	-10		199	p < 0.001	-32	2	-18	2.90	145	p < 0.001
	ASD>TD							-28	-6	-24	2.62	109	p < 0.001
	ASD Regress Both	20	-4	-14	2.16	29	p =.048						

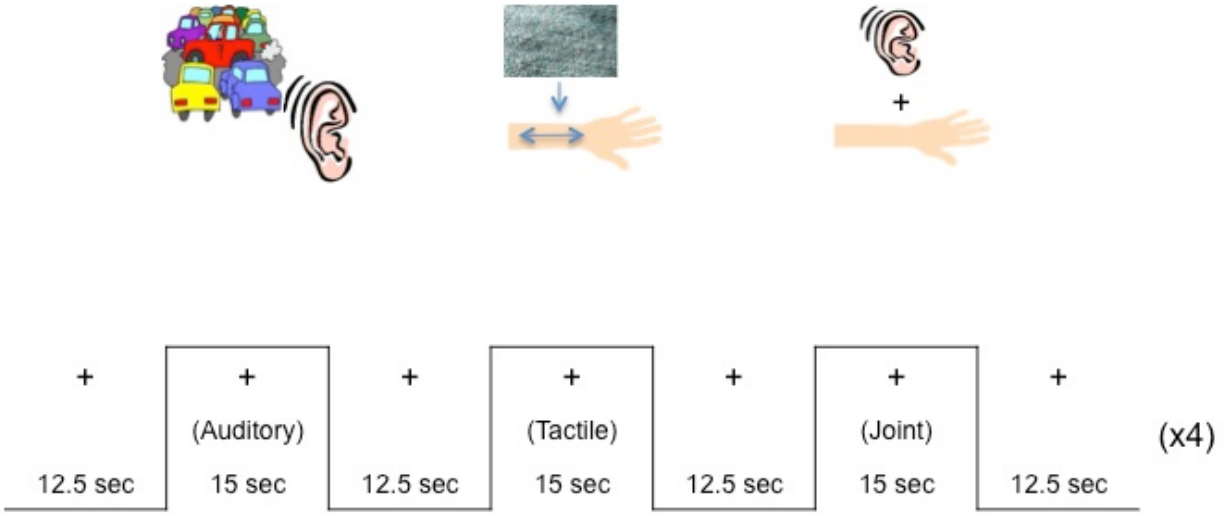
Note: x, y, and z refer to the left–right, anterior–posterior, and inferior–superior dimensions, respectively; Z refers to the Z-score at those coordinates (local maxima). Analyses are cluster-corrected using a small volume correction within the amygdala. Regression results show clusters with activation significantly correlated with SOR composite, within the ASD group, over and above age and anxiety symptoms.

eTable 4. Repeated-measures ANOVA predicting changes in amygdala and sensory cortex activation across the scan by diagnostic status and by SOR category.

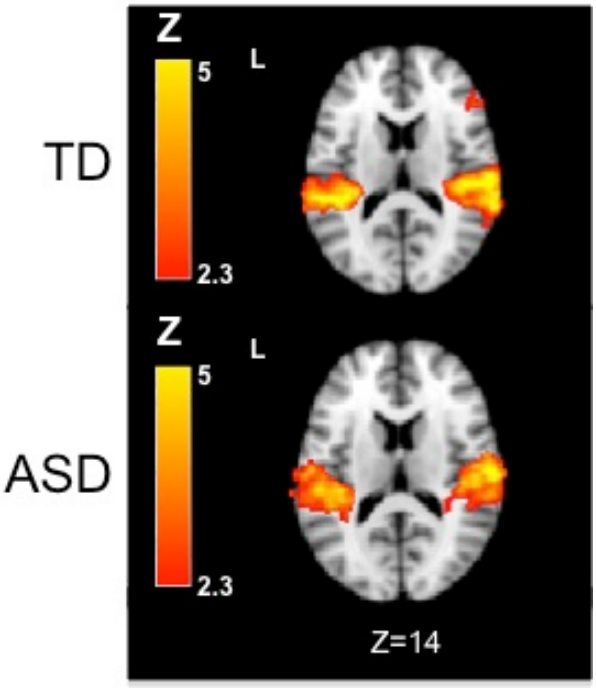
		Right Amygdala		Somatosensory Cortex		Auditory Cortex	
		MS	F	MS	F	MS	F
By Dx	**Main effect of time**						
	Linear	1.27	12.25**	0.79	5.05*	0.93	17.35***
	Quadratic	0.54	7.42*	--	--	0.24	8.52**
	Main effect of dx	0.23	0.34	0.69	1.47	0.02	0.16
	TimeXdx						
	Linear	0.05	0.48	0.00	0.00	0.05	0.88
	Quadratic	0.08	1.15	0.32	3.85+	--	--
	Cubic	0.41	10.58**	--	--	--	--
By SOR	**Main effect of time**						
	Linear	1.00	9.43**	0.78	5.07*	0.98	17.40***
	Quadratic	0.35	4.60*	--	--	0.16	5.35*
	Cubic	0.21	5.22*				
	Main effect of SOR	0.64	2.80+	01.07	2.40	0.03	0.22
	TimeXSOR						
	Linear	0.60	0.56	0.05	0.29	0.03	0.61
	Quadratic	0.04	0.53	--	--	--	--
	Cubic	0.21	5.15*				

+p<.10; *p<.05; **p<.01; ***p<.001.

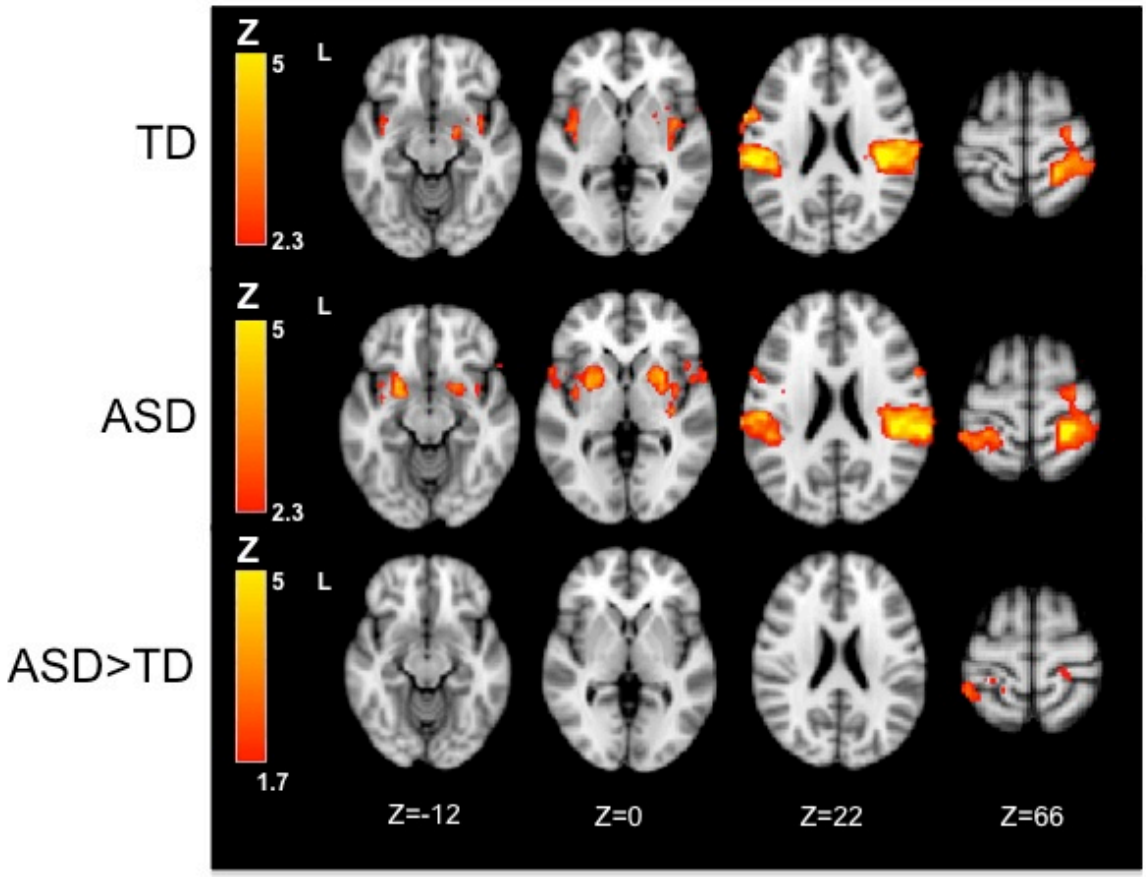
Note: Dx indicates a comparison of the two diagnostic groups, ASD vs. TD. SOR indicates a comparison of the three SOR category groups: ASD-no SOR, ASD-SOR, and TD-no SOR



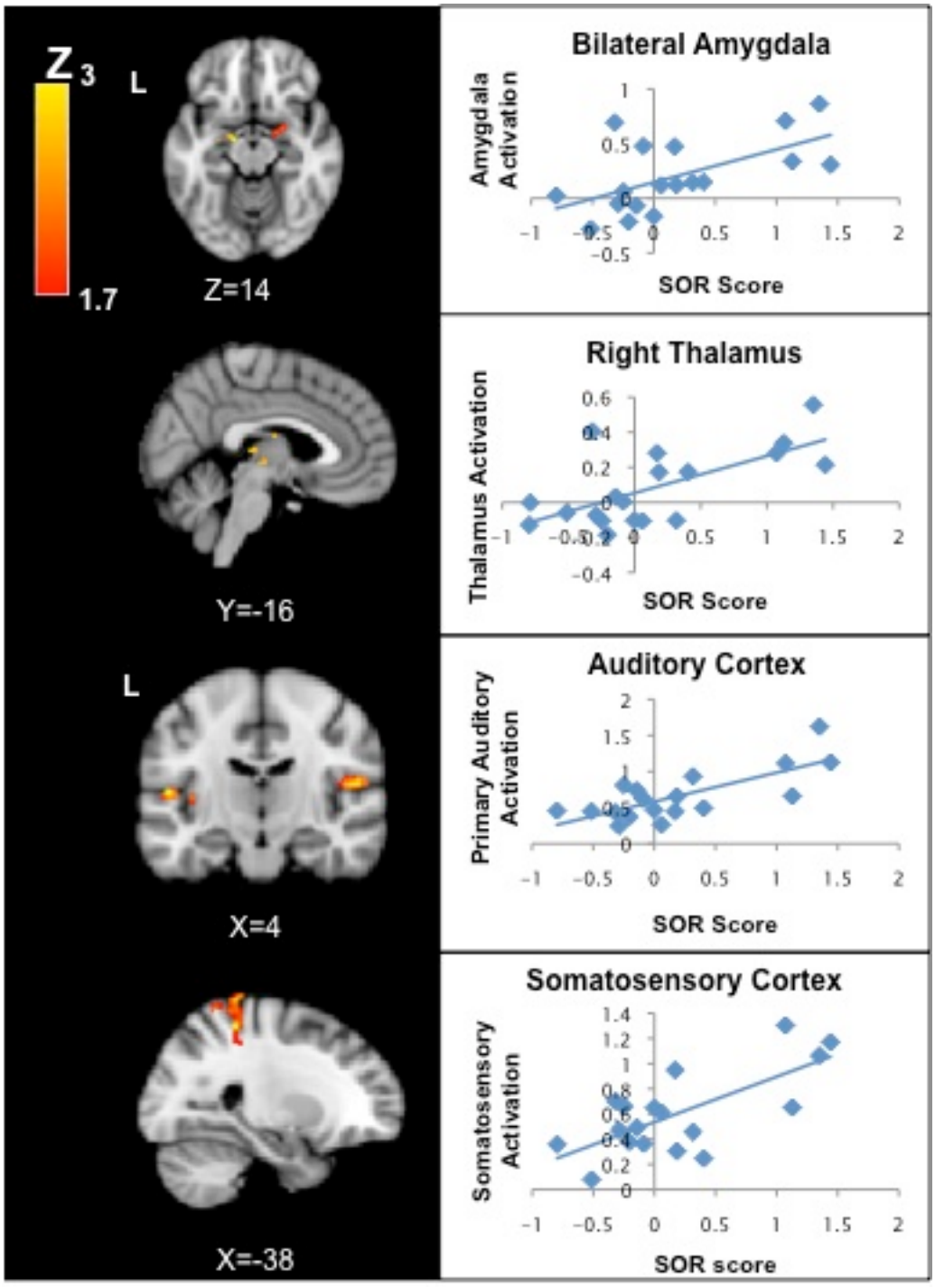
eFigure 1. Experimental design.



eFigure 2. Within-group results: Auditory condition. Within-group contrasts thresholded at Z>2.3, corrected (p<.05).



eFigure 3. Within- and between-group results: Tactile condition. Within-group contrasts thresholded at Z>2.3, corrected (p<.05). Between-group contrasts thresholded at Z>1.7, corrected. Between-group maps are masked by regions active in either within-group condition at Z>1.7, uncorrected.



eFigure 4. SOR severity as a predictor of BOLD response during the Joint condition. The horizontal axis displays the standardized residual SOR composite score after regressing out SCARED total scores and age. The vertical axis displays the parameter estimate extracted from areas of significant activation.