Data supplement for Green et al., Distinct Patterns of Neural Habituation and Generalization in Children and Adolescents With Autism With Low and High Sensory Overresponsivity. Am J Psychiatry (doi: 10.1176/appi.ajp.2019.18121333)

SUPPLEMENTARY METHODS

Participants

The final sample included 27 typically developing (TD) and 42 autism spectrum disorder (ASD) participants. Participants were recruited through referrals from a university-affiliated autism clinic. Original participants included 31 TD and 52 ASD subjects, but 1 TD and 6 ASD subjects were excluded due to mean absolute motion >1.0mm and mean relative motion > 0.30mm. An additional 1 TD participant was excluded from Exposure analyses only and 1 TD and 1 ASD excluded from Generalization analyses only, due to motion. Outlier motion volumes were identified using the FSL tool fsl_motion_outliers and were covaried out in the single-subject level analyses. Two additional TD participants were excluded: 1 due to computer malfunction and 1 due to structural brain abnormalities. Three additional ASD participants were excluded: 1 due to computer malfunction, 1 due to a coil artifact, and 1 who did not complete the fMRI task.

Stimuli. Auditory and tactile stimuli used in the fMRI Exposure and Generalization paradigms were designed to be mildly aversive. Auditory stimuli included two types of noise, one “pink” (weighted towards lower frequencies) and one “violet” (weighted towards higher frequencies). Participants heard auditory stimuli through noise-canceling headphones (Resonance Technologies, Inc.) which were calibrated to specifically reduce the noise of the EPI sequence used. Tactile stimuli were a scratchy bath glove and a kitchen sponge, each attached to a wooden dowel so that they could be rubbed on the participant’s arm without the experimenter touching the participant. Tactile stimuli were rubbed from the participants’ inner left wrist to the crease of the elbow at a rate of 1 stroke/sec. The experimenter watched a countdown timer to ensure timing was standardized across participants. Pressure was standardized through extensive reliability training and the experimenter tested their pressure with a trained research assistant prior to each administration. Participants received one type of noise and tactile stimulus during Exposure and the other type during Generalization. The stimuli received in the Exposure vs. Generalization phases were counterbalanced among participants. Stimuli were matched during pilot testing where neurotypical adults rated each of multiple auditory and tactile stimuli on aversiveness from 0-10, and stimuli used were rated a 4 out of 10 on average.

fMRI Data Analysis

ROIs for habituation analyses. Right and left postcentral gyrus, Heschl’s gyrus, and orbitofrontal cortex, and primary visual cortex (V1) ROI masks were structural masks created from the Harvard-Oxford probabilistic atlas and thresholded at 75%. The V1 mask was created by adding together occipital pole and calcarine cortex masks. The vmPFC mask was a Neurosynth map created by averaging functional activation in the vmPFC region across all studies in the Neurosynth database. Structural masks allowed for easy comparison among regions as well as allowing us to examine inhibition in regions that were not significantly activated across most participants (i.e. left postcentral gyrus; V1). Note that average initial activation in right postcentral gyrus may appear low due to the large size of the ROI and the fact that most participants activated only a small portion of it. We were also interested in comparing SOR subgroup activation in the gyrus as a whole because it highlighted group differences in spread of activation (i.e. high SOR participants may activate a greater spatial extent of postcentral gyrus as opposed to showing greater levels of activation in a small region). On the other hand, we used functional amygdala masks by drawing 4mm spheres around the peak Exposure coordinates for each group, then adding the spheres together. We chose these functional amygdala masks to be most consistent with our PPI analysis which also used the same amygdala seeds. However, for the purposes of comparison, we show in Figures S4 and S5 the right postcentral analysis using a sphere around the peak areas of activation as well as amygdala analyses using structural Harvard-Oxford masks thresholded at 75%. The pattern of results remained significant regardless of the type of mask used.

Habituation analyses outlier adjustment. Because individual blocks are highly prone to outliers, each block was examined for extreme outliers (1.5*interquartile range), which were then adjusted to be 0.1 higher or lower than the next most extreme value (this maintains the rank order while reducing the influence of outliers on group differences). One TD was excluded from the Generalization analyses for the amygdala ROI as this subject was an extreme outlier for more than half of the blocks.

SUPPLEMENTARY RESULTS

Full habituation repeated-measures ANOVA results:

Postcentral gyrus. Activation in postcentral gyrus decreased linearly across the Exposure phase, and there was a significant TimeXSOR interaction showing that change across the scan differed by SOR group. There was also a main effect of laterality, indicating that right postcentral gyrus was significantly more active than left postcentral gyrus for all groups (consistent with participants receiving the tactile stimulus on their left arms). There were no other significant main effects or interactions. A post-hoc analysis showed that only the SOR-low group had significant decreases in postcentral gyrus across time ($F(1,20)=14.68$, $p=.001$). From the late Exposure phase through the Generalization phase, there were no overall significant changes in postcentral gyrus activation, but there was a significant quadratic TimeXSOR interaction as well as a significant quadratic TimeXSORXlaterality interaction, indicating that the group differences in change over time were greater for the left than for the right postcentral gyrus. There was also a trend-level TimeXIQ interaction ($p=.08$). Posthoc analyses showed that there was significant quadratic change over time for the SOR-high group in the bilateral postcentral gyrus ($F(1,20)=8.79$, $p=.008$). The TimeXIQ quadratic interaction was also significant only for the TD group ($F(1,23)=5.86$, $p=.02$), indicating that TD youth with lower IQs were more likely to decrease and then increase postcentral activation.

Heschl's gyrus. Activation in primary auditory cortex did not significantly change across the Exposure phase, but there was a trend-level TimeXSOR interaction suggesting that it changed differently for the different SOR groups. There was also a significant TimeXlaterality interaction, as auditory cortex decreased more quickly in the left compared to the right cortex, and a significant main effect of IQ, as higher IQ was associated with higher overall auditory cortex activation across all three groups. Post-hoc analyses showed that auditory cortex decreased significantly across the exposure phase only for the SOR-low group (F(1,20)=12.43, p=.002), and the TD group (F(1,25)=9.88, p=.004), but not for the SOR-high group. In the late Exposure to Generalization phase, there was an overall trend towards decreasing auditory cortex activation, and a trend-level TimeXSORXlaterality interaction as well as a trend-level TimeXSORXIQ interaction. Post-hoc analyses showed that there were greater SOR-group differences in auditory cortex change as IQ increased. Additionally, in both right and left Heschl's gyrus, only the TD group showed a significant quadratic effect of time (F(1,24)=5.50,p=.03). However, there were no group differences in change over time in the left Heschl's gyrus as both the SOR-low (F(1,19)=3.44, p=.08) and the SOR-high (F1,20)=4.21, p=.05) groups had trend-level quadratic change over time.

Primary visual cortex (V1). In the Exposure phase, there were no overall effects of time in primary visual cortex, nor were there any significant TimeXSOR interactions. There was a trend-level main effect of SOR (p=.06). Post-hoc analyses showed that V1 had significantly greater activation in the SOR-high group compared to both the SOR-low group (p=.046) and the TD group (p=.04). The SOR-high group showed significant V1 increases across the Exposure phase (F(1,20)=7.03, p=.02), whereas the SOR-low group did not have significant change over time in V1 and the TD group had trend-level quadratic change (i.e. went up and then down; F(1,25=3.47, p=.07). For the late Exposure through Generalization phase, there was a significant quadratic main effect of time, as well as a TimeXSOR interaction and a TimeXSORXIQ interaction. Posthoc analyses showed that the SOR-low group had trend-level linear increases in V1 (F(1,19)=4.38, p=.05), the SOR-high group had significant linear decreases (F(1,20)=4.94, p=.04), and the TD group did not have significant changes in V1 activation across the generalization period. Additionally, SOR-group differences in V1 change increased as IQ decreased.

Amygdala. In bilateral amygdala, there were significant linear and quadratic main effects for time, indicating that the amygdala response decreased significantly across the Exposure phase, and the rate of decrease slowed over time. There was also a significant timeXSOR interaction, indicating that the linear slope differed by SOR category. There was a significant main effect for lateralization indicating that overall, there was greater activation in the right compared to the left amygdala. There was also a significant lateralizationXSOR effect. There were no other significant main effects or interactions. A post-hoc analysis indicated that the linear decrease in amygdala response was significant for the SOR-low group (F(1,20)=8.23, p=.01), and the TD group (F(1,25)=19.18, p<.001), but not for the SOR-high group (F(1,20)=0.23, p=.64). Furthermore, the effect of laterality was significant only for the TD group, for which the right amygdala had significantly greater overall activation compared to the left amygdala (F(1,25)=31.22, p<.001).

From the late Exposure phase to the Generalization phase, there was no main effect of time, but there was a trend-level TimeXSOR interaction for the quadratic slope (p=.07). There was also a main effect of SOR. Post-hoc analyses showed that the quadratic slope was significant only for the TD group (F(1)=4.61, p=.04), indicating that the TD group showed a significant increase in amygdala from the end of the exposure phase to the beginning of the generalization phase, and then decreased again at the end of the generalization phase (F(1,24)=5.78, p=.02). A Tukey's HSD post-hoc test on SOR category differences indicated that the ASD-high group had significantly higher amygdala response than the SOR-low group across the end of the exposure phase through the generalization phase (p=.045).

Prefrontal cortex. Overall, the OFC decreased significantly across the Exposure period, but there was a significant TimeXSOR interaction indicating that change over time differed by SOR group. There was also a significant TimeXLaterality interaction. Post-hoc analysis showed that the SOR-low group (F(1,20)=7.89, p=.01) and the TD group (F(1,25)=7.38, p=.01) had significant linear decreases in OFC across the scan, whereas the SOR-high group had no significant change over time. These decreases over time were greater in the left compared to the right OFC. The vmPFC showed the same pattern, with significant overall decreases (F(1,65)=5.94, p=.02), and a trend-level TimeXSOR interaction (F(2,65)=2.83, p=.07). Like in the OFC, this interaction was accounted for by decreases in the SOR-low (F(1,20)=4.15, p=.055) and TD (F(1,25)=5.93, p=.02) but not the SOR-high group. From the late Exposure to the Generalization phase, OFC activation had a significant overall quadratic effect, indicating that all participants increased OFC activation in response to the new stimulus and subsequently decreased it. There were no significant group differences in OFC change over time, but there was a trend-level main effect of SOR. A post-hoc analysis indicated significantly greater OFC activation in the SOR-high compared to the SOR-low group (p=.03). The vmPFC showed a similar pattern of activation in the Generalization phase, but the overall change in activation, TimeXSOR interaction, and main effect of SOR did not reach significance.

Functional connectivity

Within the ASD group, SOR was correlated with significant changes between right amygdala and left OFC (cluster size=862 voxels; peak coordinates=38, 34, -24) from the first to second half of the exposure phase. We extracted parameter estimates from the region of the left OFC found to be significant in the initial bottom-up analysis and conducted a repeated-measures ANOVA with SOR group as a between-groups factor and Time (First half vs. Second half of Exposure) as within-subjects factor. Two extreme outliers (1.5*interquartile range), both in the ASD group, were excluded for these analyses. By default (given how the whole-brain analysis was configured), there was a significant SOR*Time effect (F(1,63)=7.32, p=.001). Post-hoc analysis showed that the SOR-low group had a significant change from positive to negative connectivity across the Exposure phase (F(1,20)=17.30, p=.001), whereas the SOR-high group initially had negative connectivity values which then changed to non-significant connectivity by the second half of the Exposure phase, though this change did not reach significance (F(1,20)=1.87, p=.19). The TD group also did not show significant changes in connectivity (F(1,25)=1.17,p=.29).

Whole-brain Auditory and Tactile condition results. In the Exposure phase, there were no brain areas where activation was greater in ASD than TD during Auditory (only) Exposure, but the TD group had higher activation than the ASD group in the left thalamus and subgenual callosal cortex. In the second 6-min period of new but similar stimuli (Generalization), there were no significant group differences for Auditory Generalization. During initial Tactile Exposure, the ASD group had greater activation in bilateral parietal lobule/postcentral gyrus, insula, and putamen, and anterior cingulate. During Tactile Generalization, the ASD group had greater activation in right parietal lobule/postcentral gyrus and left precentral gyrus. See Tables S2–S7 and Figures S1–S3.

TABLE S1. Group differences in motion across different scan segments.

	High-SOR ASD	Low-SOR ASD	TD	F or χ^2
Mean absolute motion Exposure – Early*	0.46 (.22)	0.42 (.21)	0.57 (.51)	1.15
Mean absolute motion Exposure – Middle*	0.39 (.26)	0.29 (.16)	0.41 (.55)	0.61
Mean absolute motion Exposure – Late*	0.58 (.49)	0.44 (.35)	0.55 (.47)	0.56
Mean absolute motion Generalization – Early*	0.52[a] (.34)	0.28[a] (.14)	0.37 (.23)	4.50*
Mean absolute motion Generalization – Late*	0.46 (.21)	0.37 (.27)	0.41 (.28)	0.68
Mean relative motion Exposure – Early	0.14 (.05)	0.12 (.05)	0.13 (.07)	0.52
Mean relative motion Exposure – Middle	0.14 (.06)	0.12 (.04)	0.14 (.08)	0.93
Mean relative motion Exposure – Late	0.15 (.07)	0.13 (.08)	0.14 (.08)	0.44
Mean relative motion Generalization - Early	0.15 (.07)	0.12[b] (.05)	0.12[b] (.04)	2.65+
Mean relative motion Generalization - Late	0.15 (.06)	0.15 (.08)	0.13 (.05)	0.56

+p<.10, *p<.05.

*Each segment consists of two 15-sec blocks, consistent with how the ROI habituation analyses are broken up. Exposure early, middle, and late segments consist of the first two, middle two, and last two blocks respectively in the exposure phase, and Generalization early and late segments consist of the first two and last two blocks in the generalization phase.

[a]Denotes the two groups that are significantly different from each other. If no notation in any groups, all three groups are significantly different from each other.

[b]Denotes that these two groups are marginally significant from each other (p<.10).

Note: N= 21 high-SOR ASD, 21 low-SOR ASD, and 27 TD for Exposure analyses; N=21 high-SOR ASD, 20 low-SOR ASD, 26 TD for Generalization analyses.

TABLE S2. MNI coordinates for initial Exposure auditory condition as compared to baseline.

	TD					ASD					TD>ASD				
		MNI Peak (mm)			Max		MNI Peak (mm)			Max		MNI Peak (mm)			Max
	Voxels	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***
Right Planum Temporale/Heschl's Gyrus/Superior Temporal Gyrus	1690	52	-28	10	6.01	3798	48	-20	6	7.49					
Right Hippocampus							34	-12	-18	3.85					
Left Planum Temporale/Heschl's gyrus/ Superior Temporal Gyrus	1958	-48	-30	6	6.12	3140	-46	-32	8	7.74					
Left Hippocampus		-36	-36	-6	2.92		-32	-28	-8	3.61					
Occipital Pole						1696	-12	-96	14	4.76					
Right Cerebellum	624	18	-92	-32	4.49	16	52	-54	-44	3.84					
Left Cerebellum	326	-12	-82	-50	4.09	2874	-24	-80	-44	4.89					
Left Orbitofrontal Cortex/Frontal Pole	6	-50	26	-14	3.10	420	-34	38	-16	3.22					
Left Frontal Pole	330	-18	62	12	4.30										
Brainstem	171	8	-38	-14	5.67										
Left Temporal Pole	147	-42	26	-24	5.01										
Left Parahippocampal Gyrus	136	-18	-24	-16	4.72										
Left Inferior Frontal Gyrus, Pars Triangularis	112	-52	26	0	3.39										
Right Middle Temporal Gyrus/Superior Temporal Gyrus	21	70	-40	-6	3.05										
Left Middle Temporal Gyrus	15	-66	-44	-14	3.58										
Left Lingual Gyrus	8	-2	-80	-8	3.00	24	-8	-86	-6	3.00					
Left Caudate	17	-18	24	10	3.01										
Left Subcallosal Cortex/vmPFC											213	-2	14	-16	3.09
Left Ventral Posterior Lateral Thalamic Nucleus												-18	-24	-2	3.11

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.

TABLE S3. MNI coordinates for initial Exposure tactile condition as compared to baseline fixation.

	TD					ASD					ASD>TD				
		MNI Peak (mm)			Max		MNI Peak (mm)			Max		MNI Peak (mm)			Max
	Voxels	x	y	z	*Z*	Voxels	x	y	z	*Z*	Voxels	x	y	z	*Z*
Right Parietal Operculum/Insula	1543	46	-26	24	6.13	6295	50	-32	24	8.01	182	44	-12	18	3.45
Right Insula		42	-2	8	3.91		38	-6	-6	6.73					
Right Thalamus (Ventral Lateral Nucleus)							18	-16	10	4.32	45	12	-16	12	2.58
Right Thalamus (Reticular Thalamic/Ventral Lateral Nucleus)							16	-14	14	4.30					
Right Putamen							26	8	-2	4.30	8	24	-6	14	3.30
Right Amygdala							28	2	-16	4.09					
Left Superior Temporal Gyrus/Operculum	791	-50	-30	20	5.65	6329	-60	4	2	7.25	134	-58	-22	8	3.42
Left Postcentral/Supramarginal Gyrus							-62	-20	42	6.69	562	-68	-18	26	3.29
Left Insula	169	-40	-14	0	4.37		-40	-4	-6	6.60	8	-34	-20	2	3.12
Left Putamen							-26	-2	-10	3.97	568	-24	6	12	3.36
Left Amygdala							-24	2	-20	3.17					
Right Postcentral/Supramarginal Gyrus	724	30	-40	68	5.05	3588	24	-44	66	7.58	2493	70	-14	28	3.74
Right Precentral Gyrus		26	-16	74	4.47	69	62	12	26	3.71	332	14	-16	74	3.86
Left Precentral Gyrus											193	-30	-10	62	3.59
Right Cerebellum						1792	16	-74	-52	5.48	992	26	-60	-46	3.43
Left Cerebellum	1221	-18	-66	-54	4.89	2865	-20	-66	-52	6.42	1040	-22	-32	-28	3.50
Right Superior Frontal Gyrus						800	6	54	24	4.43					
Left Superior Frontal Gyrus						359	-6	28	58	4.30					
Right Frontal Pole						18	18	54	32	3.13					
Left Frontal Pole						384	-24	48	32	4.19	673	-50	44	18	3.65
Left Lateral Occipital Cortex						262	-58	-66	18	4.33	492	-44	-82	30	3.18
Right Temporal Pole						94	44	26	-24	3.89					
Left Temporal Pole						72	-52	20	-16	3.87	56	-48	18	-16	3.39
Left Globus Pallidus/Thalamic Reticular Nucleus						16	-16	-4	8	3.02					
Left Middle Temporal Gyrus						12	-64	-52	0	3.30	62	-26	22	-2	4.27
Anterior Cingulate											494	0	40	4	3.41
Anterior/Posterior Cingulate											426	-2	-10	32	4.10
Left Superior Parietal Lobule											2215	-14	-52	62	3.77
Inferior Frontal Gyrus, Pars Triangularis											52	-48	20	0	3.72
Left Inferior Temporal Gyrus											47	-62	-38	-20	3.88
Medial Frontal Cortex											25	2	32	-26	2.74
Paracingulate Gyrus											92	-2	18	42	3.70
Left Parahipppocampal Gyrus											13	-28	-30	-16	3.73

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.

TABLE S4. MNI coordinates for initial Exposure joint auditory+tactile condition as compared to baseline fixation.

	TD					ASD					ASD>TD				
		MNI Peak (mm)			Max		MNI Peak (mm)			Max		MNI Peak (mm)			Max
	Voxels	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***
Right Superior Temporal Gyrus/Heschl's Gyrus	4545	52	-26	12	6.66	7601	46	-26	14	9.69	653	58	4	-12	3.29
Right Putamen		30	0	-4	6.28		24	-6	8	4.08					
Right Insula/Operculum		38	-18	16	5.63										
Right Ventral Lateral Posterior Thalamic Nucleus							16	-20	8	3.87	6	26	0	-28	2.6
Right Amygdala		22	-2	-16	4.76	10	22	-10	-12	2.91					
Left Superior Temporal Gyrus/Heschl's Gyrus/Operculum	3157	-50	-24	14	8.85	6197	-48	-30	12	8.44					
Left Amygdala							-26	0	-18	3.52	83	-28	-4	-18	2.77
Left Insula	41	-36	-2	14	3.74										
Right Postcentral Gyrus	868	36	-36	62	4.86	2321	30	-38	60	7.17	376	20	-46	52	3.07
Left Superior Parietal/Postcentral Gyrus											75	-40	-42	66	2.61
Right Cerebellum						2293	12	-72	-52	7.04	220	30	-58	-56	3.37
Left Cerebellum	562	-20	-66	-52	4.44	3464	-20	-58	-56	6.45	71	-6	-70	-38	3.11
Cerebellum						120	2	-86	-30	4.09					
Right Inferior Frontal Gyrus, Pars Triangularis/Frontal Pole						462	44	38	-4	4.51					
Right Ventral Lateral Posterior Thalamic Nucleus	245	16	-24	4	6.14										
Brainstem						116	-8	-34	-44	5.36	165	0	-44	-54	3.22
Right Orbitofrontal Cortex						61	22	24	-18	3.53	8	22	24	-20	3.01
Left Orbitofrontal Cortex						41	-24	36	-10	3.48					
Left Superior Frontal Gyrus						11	-16	58	20	3.49	48	-24	44	34	3.09
Paracingulate/Anterior Cingulate						10	10	46	12	2.93	10	12	42	20	3.17
Right Anterior Cingulate											23	10	-8	42	2.99
Left Anterior Cingulate						7	-10	42	6	2.92					
Right Hippocampus	10	30	-18	-12	3.23										
Left Hippocampus											134	-34	-28	-8	3.53
Right Frontal Medial Cortex											391	12	36	-20	3.42
Left Frontal Medial Cortex											7	-10	50	-12	2.93
Right Middle Frontal Gyrus											45	40	44	20	3.09
Left Middle Frontal Gyrus											354	-38	30	24	3.68
Right Precentral Gyrus											238	14	-20	72	3.88
Left Lingual Gyrus											161	-10	-54	-4	3.56
Left Parahippocampal Gyrus											65	-20	-28	-18	3.23

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.

TABLE S5. MNI coordinates for Generalization auditory condition as compared to baseline fixation.

	TD					ASD				
		MNI Peak (mm)			Max		MNI Peak (mm)			Max
	Voxels	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***
Right Superior Temporal Gyrus/Heschl's Gyrus	1973	48	-30	10	6.73	2521	48	-22	6	6.78
Left Superior Temporal Gyrus/Heschl's Gyrus	2251	-58	-24	8	6.24	3069	-42	-30	8	7.55
Right Frontal Pole/Orbitofrontal Cortex	371	44	38	-6	4.83	146	44	38	-22	3.95
Left Frontal Pole/Orbitofrontal Cortex	505	-34	44	-10	4.64	142	-44	30	-24	4.39
Left Cerebellum	306	-28	-62	-48	5.15	76	-20	-72	-30	3.65
Frontal Medial Cortex						292	0	22	-32	4.92
Brainstem	188	8	-38	-10	5.28					
Right Orbitofrontal Cortex	45	18	34	-22	3.38					
Left Orbitofrontal Cortex	187	-28	24	-24	4.76	38	-26	18	-26	3.18
Left Inferior Frontal Gyrus, Pars Triangularis	112	-42	30	2	3.98					
Right Temporal Pole						13	52	8	-10	3.26

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.

TABLE S6. MNI coordinates for Generalization tactile condition as compared to baseline fixation.

	TD					**ASD**					**ASD>TD**				
		MNI Peak (mm)			**Max**		**MNI Peak (mm)**			**Max**		**MNI Peak (mm)**			**Max**
	Voxels	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***
Right Parietal Operculum	2271	50	-28	20	5.61	2171	42	-22	18	7.48					
Right Amygdala		24	-2	12	4.28										
Right Putamen		28	8	-4	4.01										
Left Parietal Operculum	1076	-58	-30	20	4.68										
Right Central Operculum/Inferior Frontal Gyrus Pars Opercularis	138	62	12	8	3.72										
Left Central Operculum/Inferior Frontal Gyrus Pars Opercularis						334	-60	2	4	5.05					
Left Amygdala	8	-26	0	-22	3.30										
Right Postcentral gyrus	348	34	-40	72	4.18	1191	24	-42	66	6.07	29	12	-44	78	3.08
Right Precentral Gyrus		30	-22	72	3.22		22	-18	74	4.30	72	16	-18	74	2.82
Left Postcentral Gyrus/Superior Parietal Lobule											85	-28	-44	70	2.67
Left Precentral Gyrus	14	-58	8	8	2.92										
Right Insula/Putamen						34	32	0	10	3.47					
Left Insula	243	-40	-10	0	4.27	1534	-38	-18	8	5.84					
Right Cerebellum						427	14	-82	-26	5.64	1323	34	-50	-36	3.46
Left Cerebellum						600	-22	-58	-50	6.36	151	50	-54	-36	4.12
Right Frontal Pole						282	52	44	-14	4.64					
Left Superior Temporal Gyrus/Central Opercular Cortex	24	-60	0	0	3.03										
Right Inferior Frontal Gyrus, Pars Opercularis/Planum Polare	20	54	16	0	3.06										
Left Temporal Pole	14	-52	16	-10	2.90										

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.

TABLE S7. MNI coordinates for Generalization joint auditory+tactile condition as compared to baseline fixation.

	TD					ASD					ASD>TD				
		MNI Peak (mm)			Max		MNI Peak (mm)			Max		MNI Peak (mm)			Max
	Voxels	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***	**Voxels**	**x**	**y**	**z**	***Z***
Right Superior Temporal Gyrus/Heschl's Gyrus/Operculum	3990	44	-30	16	6.94	4152	46	-32	22	7.45					
Right Amygdala		16	0	-18	2.77		32	4	-16	3.66					
Left Superior Temporal Gyrus/Heschl's Gyrus/Operculum	2982	-56	-26	8	6.79	3922	-50	-26	10	6.12					
Right Cerebellum						1111	36	-80	-32	4.72					
Left Cerebellum	390	-22	-56	-54	4.38	1377	-20	-64	-46	5.20	26	-6	-60	-26	3.28
Right Postcentral Gyrus/Superior Parietal Lobule						1181	26	-40	62	5.86	352	28	-48	68	2.66
Right Precentral Gryus							26	-20	70	3.64	171	18	-18	74	3.74
Right Ventral Posterior Lateral Thalamic Nucleus						6	22	-26	4	3.25					

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.

FIGURE S1. Within- and between-group results: Auditory 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.

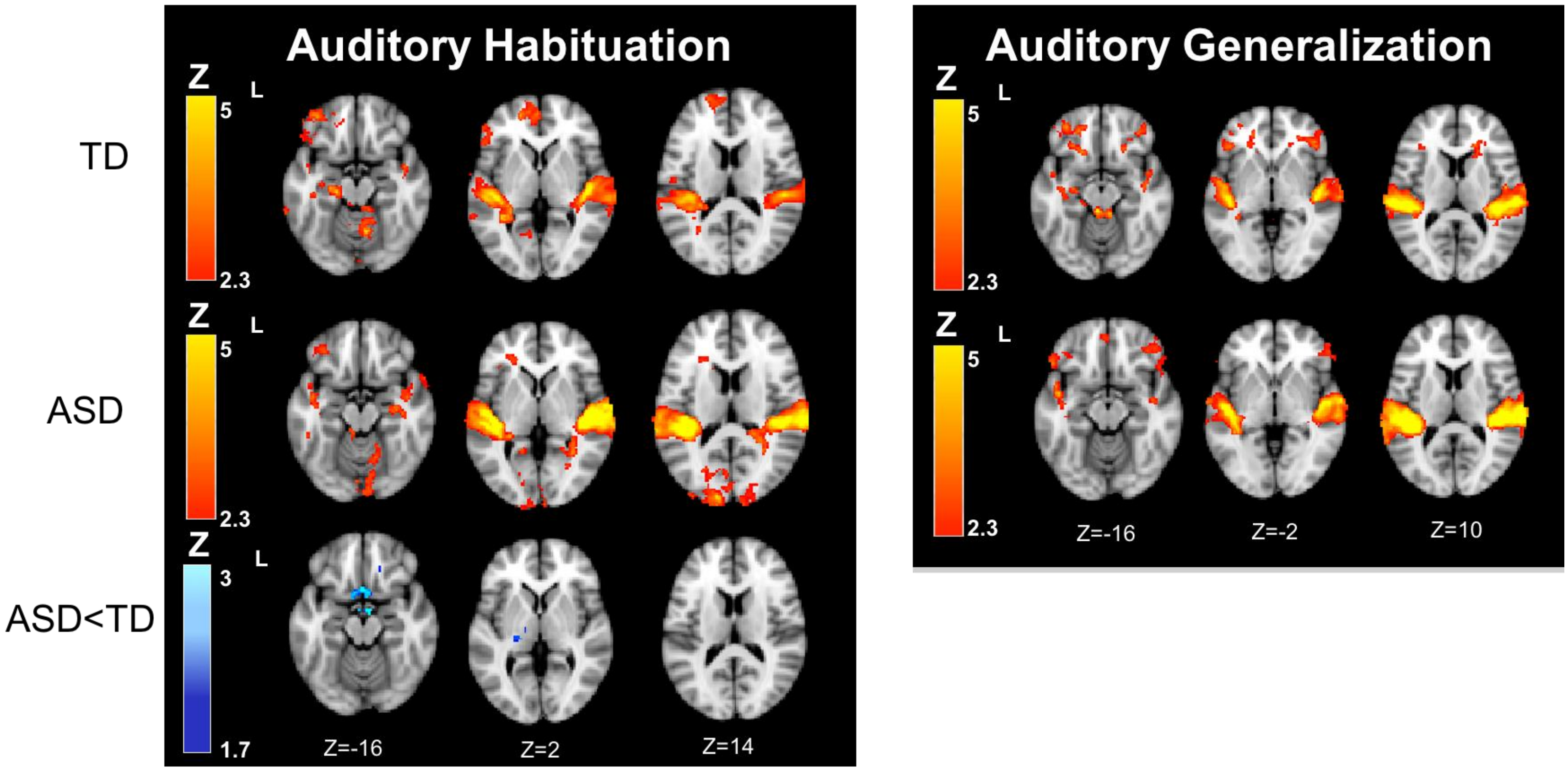


FIGURE S2. Within- and between-group results: Tactile condition. Within-group contrasts thresholded at Z>2.3, corrected (p<.05). Between-group contrasts thresholded at Z>1.7, corrected. Between-group maps are masked by regions active in either within-group condition at Z>1.7, uncorrected.

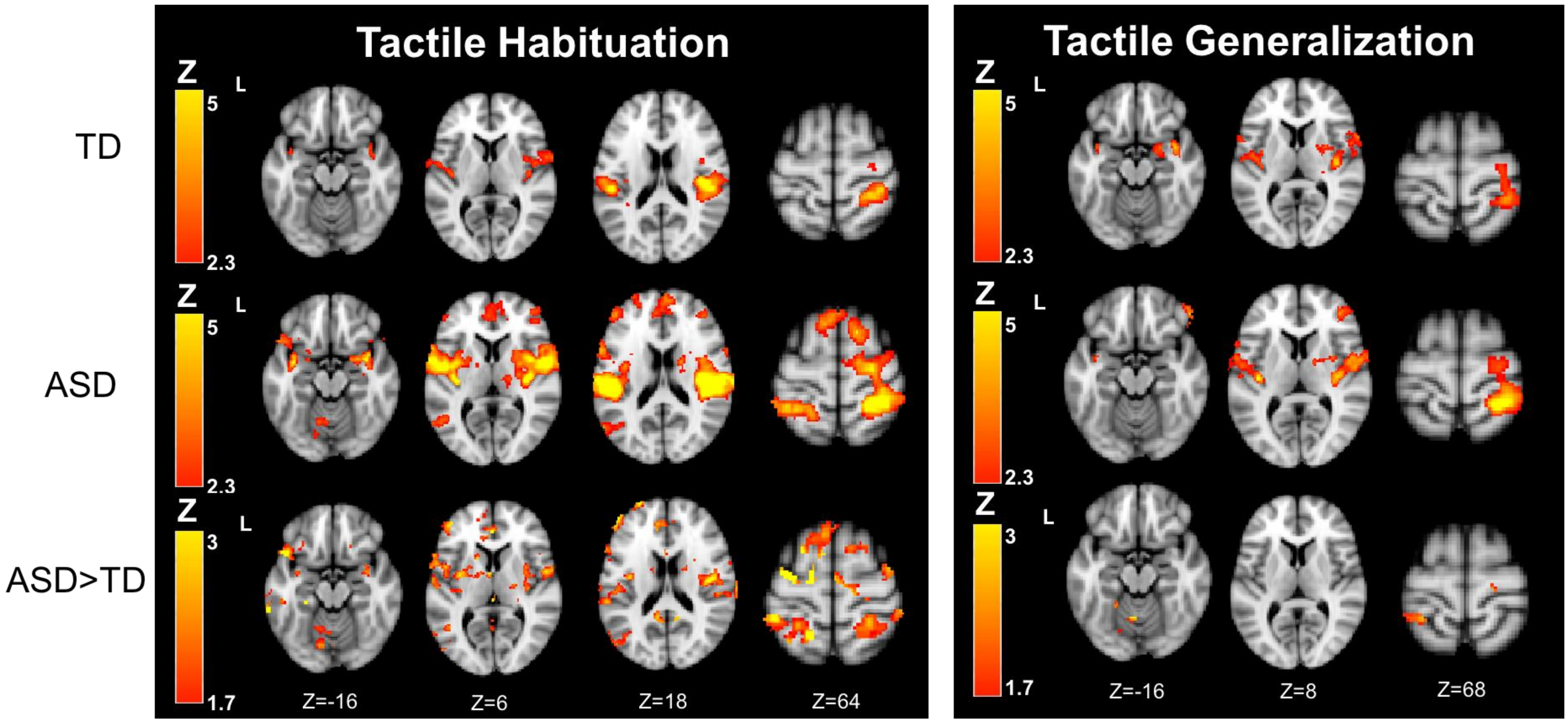


FIGURE S3. Within- and between-group results: Joint auditory+tactile condition. Within-group contrasts thresholded at Z>2.3, corrected (p<.05). Between-group contrasts thresholded at Z>1.7, corrected. Between-group maps are masked by regions active in either within-group condition at Z>1.7, uncorrected.

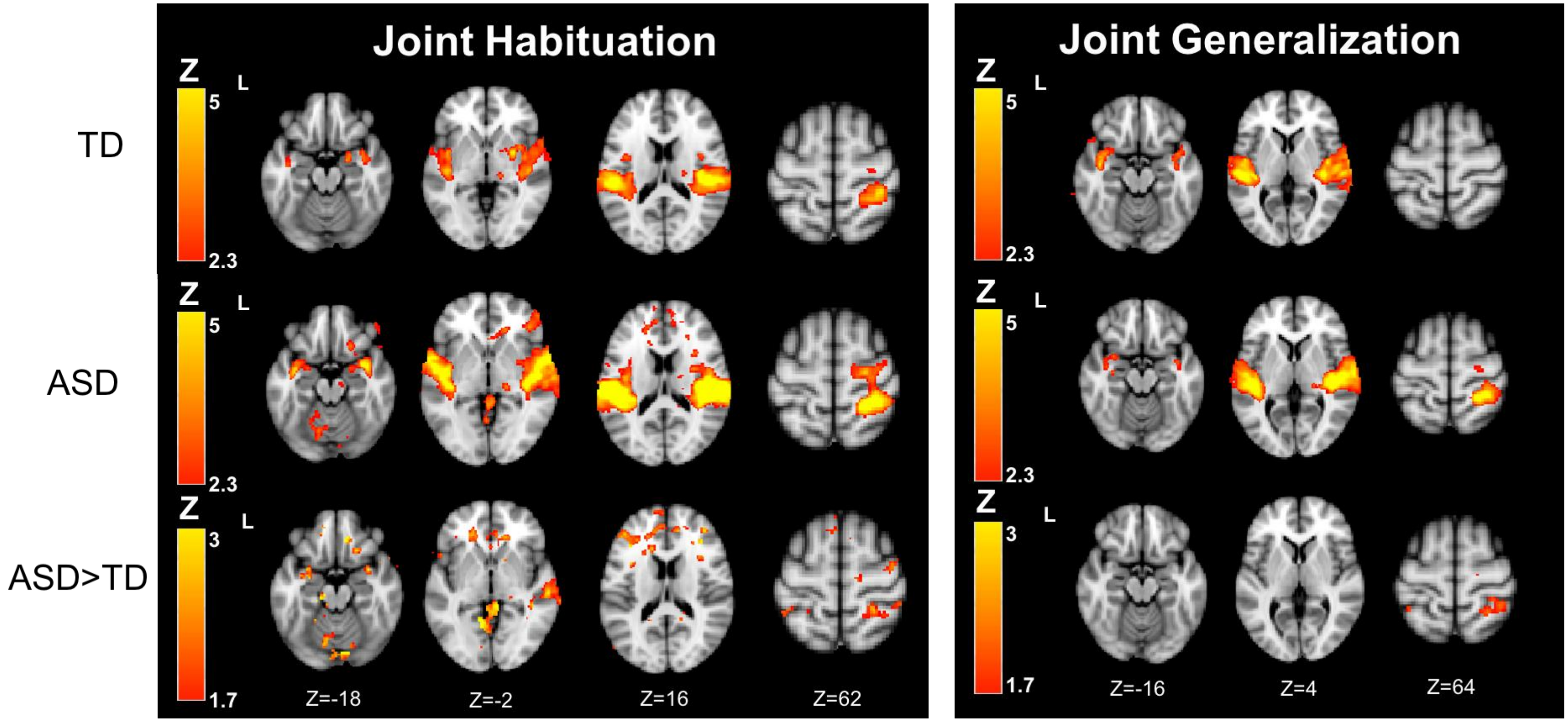
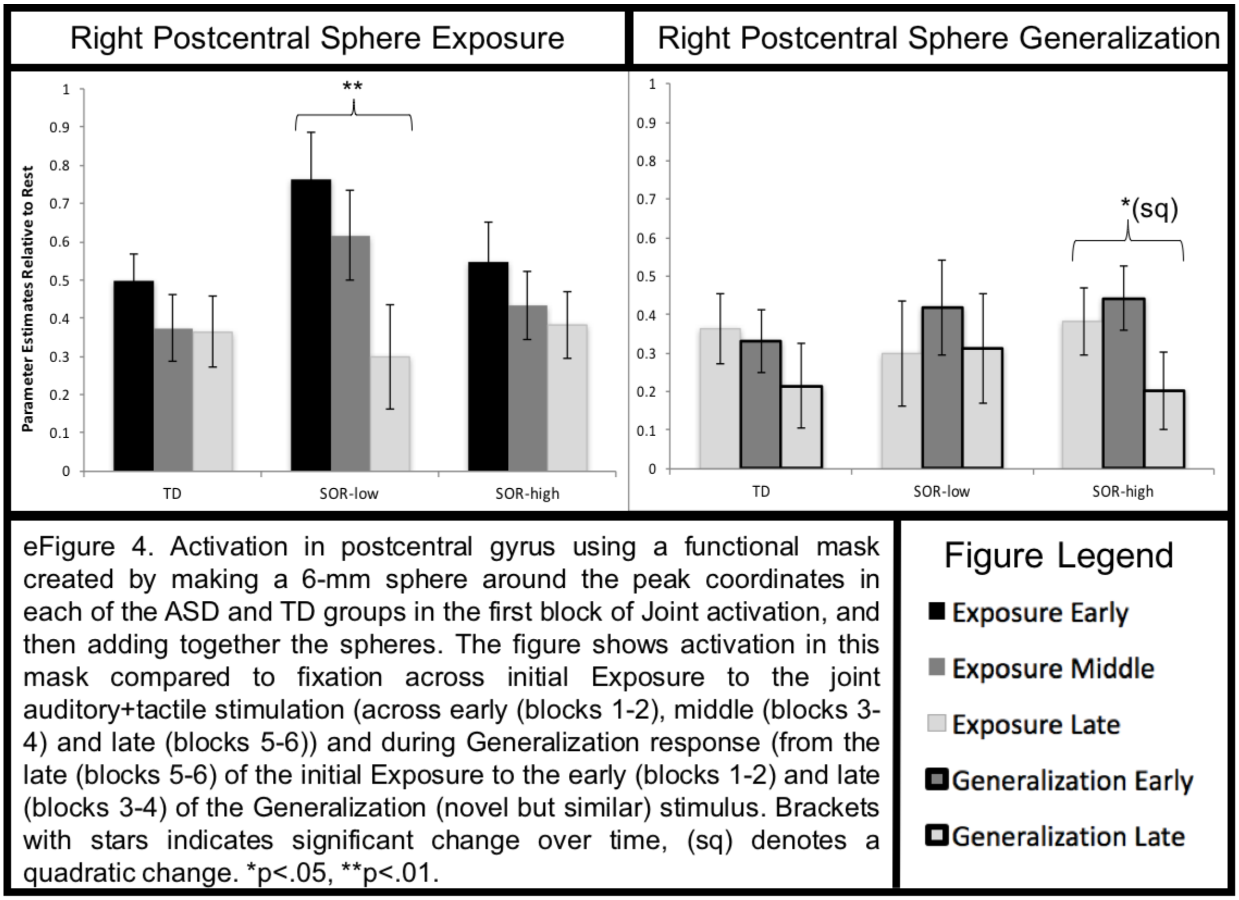
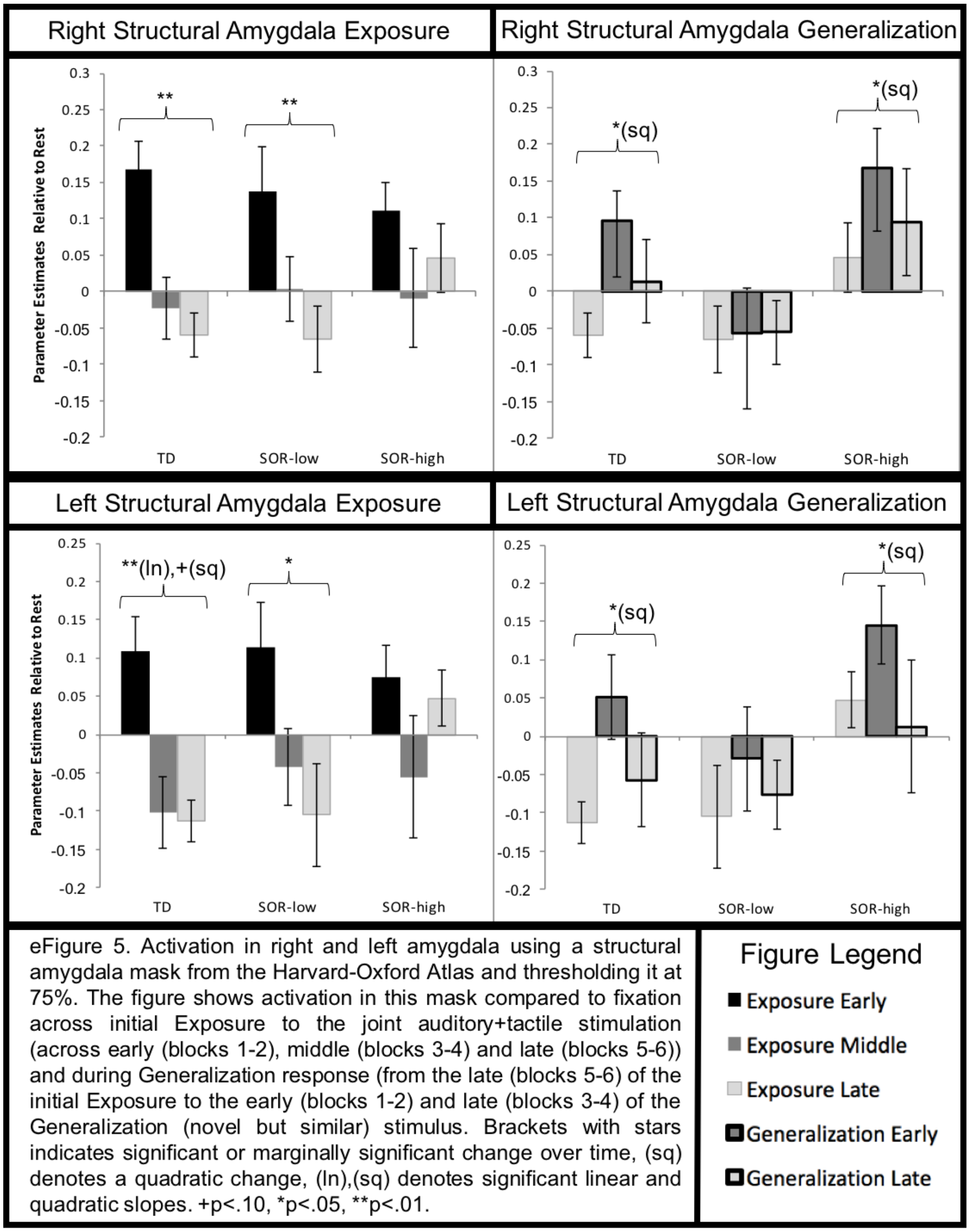


FIGURE S4. Activation in postcentral gyrus using a functional mask created by making a 6-mm sphere around the peak coordinates in each of the ASD and TD groups in the first block of Joint activation, and then adding together the spheres. The figure shows activation in this mask compared to fixation across initial Exposure to the joint auditory+tactile stimulation (across early (blocks 1-2), middle (blocks 3-4) and late (blocks 5-6)) and during Generalization response (from the late (blocks 5-6) of the initial Exposure to the early (blocks 1-2) and late (blocks 3-4) of the Generalization (novel but similar) stimulus. Brackets with stars indicates significant or marginally significant change over time, (sq) denotes a quadratic change. +p<.10, **p<.01.



eFigure 4. Activation in postcentral gyrus using a functional mask created by making a 6-mm sphere around the peak coordinates in each of the ASD and TD groups in the first block of Joint activation, and then adding together the spheres. The figure shows activation in this mask compared to fixation across initial Exposure to the joint auditory+tactile stimulation (across early (blocks 1-2), middle (blocks 3-4) and late (blocks 5-6)) and during Generalization response (from the late (blocks 5-6) of the initial Exposure to the early (blocks 1-2) and late (blocks 3-4) of the Generalization (novel but similar) stimulus. Brackets with stars indicates significant change over time, (sq) denotes a quadratic change. *p<.05, **p<.01.

FIGURE S5. Activation in right and left amygdala using a structural amygdala mask from the Harvard-Oxford Atlas and thresholding it at 75%. The figure shows activation in this mask compared to fixation across initial Exposure to the joint auditory+tactile stimulation (across early (blocks 1-2), middle (blocks 3-4) and late (blocks 5-6)) and during Generalization response (from the late (blocks 5-6) of the initial Exposure to the early (blocks 1-2) and late (blocks 3-4) of the Generalization (novel but similar) stimulus. Brackets with stars indicates significant or marginally significant change over time, (sq) denotes a quadratic change, (ln&sq) denotes significant linear and quadratic slopes. +p<.10, *p<.05, **p<.01.



eFigure 5. Activation in right and left amygdala using a structural amygdala mask from the Harvard-Oxford Atlas and thresholding it at 75%. The figure shows activation in this mask compared to fixation across initial Exposure to the joint auditory+tactile stimulation (across early (blocks 1-2), middle (blocks 3-4) and late (blocks 5-6)) and during Generalization response (from the late (blocks 5-6) of the initial Exposure to the early (blocks 1-2) and late (blocks 3-4) of the Generalization (novel but similar) stimulus. Brackets with stars indicates significant or marginally significant change over time, (sq) denotes a quadratic change, (ln),(sq) denotes significant linear and quadratic slopes. +p<.10, *p<.05, **p<.01.