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## Neurobiology of Sensory Overresponsivity in Youth With Autism Spectrum Disorders

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### Abstract

**IMPORTANCE**—More than half of youth with autism spectrum disorders (ASDs) have sensory overresponsivity (SOR), an extreme negative reaction to sensory stimuli. However, little is known about the neurobiological basis of SOR, and there are few effective treatments. Understanding whether SOR is due to an initial heightened sensory response or to deficits in regulating emotional reactions to stimuli has important implications for intervention.

**OBJECTIVE**—To determine differences in brain responses, habituation, and connectivity during exposure to mildly aversive sensory stimuli in youth with ASDs and SOR compared with youth with ASDs without SOR and compared with typically developing control subjects.

**DESIGN, SETTING, AND PARTICIPANTS**—Functional magnetic resonance imaging was used to examine brain responses and habituation to mildly aversive auditory and tactile stimuli in 19 high-functioning youths with ASDs and 19 age- and IQ-matched, typically developing youths (age range, 9-17 years). Brain activity was related to parents' ratings of children's SOR symptoms.

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Functional connectivity between the amygdala and orbitofrontal cortex was compared between ASDs subgroups with and without SOR and typically developing controls without SOR. The study dates were March 2012 through February 2014.

**MAIN OUTCOMES AND MEASURES**—Relative increases in blood oxygen level–dependent signal response across the whole brain and within the amygdala during exposure to sensory stimuli compared with fixation, as well as correlation between blood oxygen level–dependent signal change in the amygdala and orbitofrontal cortex.

**RESULTS**—The mean age in both groups was 14 years and the majority in both groups (16 of 19 each) were male. Compared with neurotypical control participants, participants with ASDs displayed stronger activation in primary sensory cortices and the amygdala ( $P < .05$ , corrected). This activity was positively correlated with SOR symptoms after controlling for anxiety. The ASDs with SOR subgroup had decreased neural habituation to stimuli in sensory cortices and the amygdala compared with groups without SOR. Youth with ASDs without SOR showed a pattern of amygdala downregulation, with negative connectivity between the amygdala and orbitofrontal cortex (thresholded at  $z > 1.70$ ,  $P < .05$ ).

**CONCLUSIONS AND RELEVANCE**—Results demonstrate that youth with ASDs and SOR show sensorilimbic hyperresponsivity to mildly aversive tactile and auditory stimuli, particularly to multiple modalities presented simultaneously, and show that this hyperresponsivity is due to failure to habituate. In addition, findings suggest that a subset of youth with ASDs can regulate their responses through prefrontal downregulation of amygdala activity. Implications for intervention include minimizing exposure to multiple sensory modalities and building coping strategies for regulating emotional response to stimuli.

Overresponsivity to sensory stimuli is a common symptom of autism spectrum disorders (ASDs) that is understudied, likely because it was only recently added to *DSM-5* diagnostic criteria.<sup>1</sup> At least 56% to 70% of youth with ASDs meet criteria for sensory overresponsivity (SOR),<sup>2,3</sup> which includes severe negative responses to stimuli (eg, noisy environments, scratchy clothing, and being touched) that do not elicit such responses in individuals without SOR.<sup>4</sup> Sensory overresponsivity is associated with greater functional impairment in individuals with ASDs, deficits in social and adaptive skills, and anxiety.<sup>4-6</sup> Little is known about the neurobiological basis of SOR. However, electroencephalography studies<sup>7,8</sup> have demonstrated deficits in sensory gating and selective attention of sensory input, suggesting that individuals with ASDs may become easily overwhelmed by irrelevant or multiple stimuli. Most important, ASDs represent a heterogeneous disorder, and only some diagnosed individuals have SOR. An electrodermal study<sup>9</sup> found that high-functioning youth with ASDs showed high arousal and slow habituation or low arousal and fast habituation.

While research on the neurological basis of SOR is new, results of a recent functional magnetic resonance imaging (fMRI) study<sup>10</sup> suggest that SOR is related to hyperactivity in brain areas involved in primary sensory processing, emotion regulation, and response to threat. The authors found that youth with ASDs had overactivation in limbic areas, primary sensory cortices, and orbitofrontal cortex (OFC) compared with typically developing (TD) control subjects in response to mildly aversive visual and auditory stimuli. Furthermore, activity in these regions correlated with parents' reports of SOR. Limbic overactivation is

consistent with the co-occurrence of SOR and anxiety<sup>11</sup> as well as with amygdala hyperactivity in response to faces in children with ASDs.<sup>12,13</sup> Notably, overreactivity observed in individuals with ASDs was most evident when auditory and visual stimuli occurred simultaneously, consistent with the sensory gating hypothesis and with neurophysiological multisensory integration investigations.<sup>14</sup>

In the present study, we examined responses to tactile and auditory stimuli. Overresponsivity to these stimuli has been found to best distinguish individuals with and without SOR.<sup>15-17</sup> These stimuli are also among those most often reported as aversive for children with ASDs.<sup>17,18</sup> Evidence from a 2008 fMRI study<sup>19</sup> suggests that adolescents with ASDs have heightened neural responses to novel sounds in higher-level processing areas, including prefrontal and inferior parietal areas. Individuals with ASDs may also have overreactive brain responses to unpleasant touch but a diminished response to pleasant touch,<sup>20</sup> highlighting the importance of using aversive sensory stimuli when examining patients with SOR.

To our knowledge, other than the study by Green et al,<sup>10</sup> no studies have examined fMRI responses to multiple sensory stimuli simultaneously, which more closely resembles real-world environments. We aimed to follow up on whether SOR is related to reduced habituation rather than to a higher initial response to sensory stimuli. In a tactile discrimination study,<sup>21</sup> adaptation stimuli were found to have a reduced effect on youth with ASDs, suggesting deficits in habituation and inhibition. Youth with ASDs have also shown decreased amygdala habituation to other arousing stimuli (eg, faces).<sup>12,22</sup> Accordingly, we hypothesized that SOR would be related to reduced habituation to sensory stimuli, particularly in the amygdala and primary sensory cortices.

Finally, Green et al<sup>10</sup> found that SOR symptoms correlated with hyperactivity in the amygdala and OFC. The OFC receives inputs from all sensory modalities, has strong connectivity with the amygdala,<sup>23</sup> and is associated with top-down emotion regulation.<sup>24</sup> Amygdala and prefrontal (including the OFC) activity is typically negatively coupled such that increased prefrontal activation is associated with decreased amygdala activation in response to threat-relevant stimuli.<sup>25-27</sup> Simultaneous overactivity in the amygdala and OFC could indicate an ineffective regulatory system, whereby the OFC activates but fails to sufficiently downregulate the amygdala, such as in social anxiety disorder.<sup>28,29</sup> Alternatively, this pattern could indicate an immature emotion regulation system. Neurotypical youth display positive connectivity between the amygdala and prefrontal cortex,<sup>30</sup> and there is evidence of reduced structural connectivity between the amygdala and OFC in ASDs.<sup>31</sup> Herein, we examined functional amygdala-OFC connectivity during exposure to sensory stimuli to determine how it might relate to SOR in youth with ASDs.

## Methods

### Participants

Participants were 19 youths with ASDs and 19 TD matched controls 9 to 17 years old (mean [SD] age, 13.66 [2.11] years). The groups did not differ significantly in age, IQ, or motion during fMRI (**Table 1** and eMethods in the Supplement). Participants with ASDs had a prior

diagnosis of ASDs, confirmed using the Autism Diagnostic Interview–Revised<sup>32</sup> and the Autism Diagnostic Observation Schedule, Second Edition.<sup>33</sup> All study procedures were approved by the University of California, Los Angeles, Institutional Review Board. Written informed consent was obtained from parents and participants 13 years or older. Written assent was obtained from participants younger than 13 years. The study was conducted between March 2012 and February 2014.

### fMRI Sensory Paradigm

Participants were exposed to 3 stimulus conditions in a counterbalanced block design paradigm (eFigure 1 in the Supplement). These stimuli included an auditory condition, a tactile condition, and a joint condition in which the auditory and tactile stimuli were presented simultaneously. Auditory stimuli consisted of traffic noises. The tactile stimulus was a scratchy wool fabric rubbed on participants' inner arms at the rate of one stroke per second. Stimuli were chosen that best differentiated the ASDs vs TD groups based on pilot testing with the Sensory Over-Responsivity Scales.<sup>34</sup> Participants were instructed to focus on a central fixation cross throughout the task. Each condition was presented 4 times, lasting 15 seconds (each defined as one block), with 12.5 seconds of fixation between trials. Total scan length was 5 minutes and 42.5 seconds, including 12.5-second initial and final fixations. The eMethods in the Supplement contains information on functional magnetic resonance imaging data acquisition.

### Behavioral Measures

Diagnostic and cognitive measures were administered at a clinical assessment visit. Child anxiety and sensory responsivity questionnaires were completed by parents (Table 1 and eMethods in the Supplement). An SOR composite score was created by standardizing and averaging relevant subscales of the SOR measures (Short Sensory Profile<sup>17</sup> auditory and visual sensitivity, tactile sensitivity, and auditory filtering scales and Sensory Over-Responsivity Scales<sup>34</sup> auditory and tactile scores) across all participants. Children in the top 25th percentile of this composite (9 with ASDs and 1 TD) were categorized as having elevated SOR. For analyses comparing SOR subgroups, participants were divided into the following 3 groups: ASDs with SOR, ASDs without SOR, and TD without SOR. For analyses comparing diagnostic groups (TD vs ASDs), subgroups were collapsed so that all TD participants were compared with all participants with ASDs.

### fMRI Data Analysis

Within-group activation maps for each condition (vs fixation) were thresholded at  $z > 2.30$  ( $P < .01$ ) and whole-brain cluster corrected at  $P < .05$  using the FMRIB Software Library (<http://www.fmrib.ox.ac.uk/fsl>). Between-group comparisons were thresholded at  $z > 1.70$  ( $P < .05$ ) and whole-brain cluster corrected at  $P < .05$ , and only clusters with peaks of  $z > 2.30$  are reported as significant. For all analyses except habituation analyses, activation was averaged across the 4 blocks in each condition. For habituation analyses, activation parameter estimates (PEs) were extracted separately from each block in the joint condition. Age was covaried in group-level analyses. Because of a priori interest in the amygdala (defined by the Harvard-Oxford Probabilistic Atlas [<http://fsl.fmrib.ox.ac.uk/fsl/fsl4.0/fslview/atlas-descriptions.html#ho>], thresholded at 75%), small-volume correction was used

to correct for multiple comparisons within this region of interest using AlphaSim ([http://afni.nimh.nih.gov/pub/dist/doc/program\\_help/AlphaSim.html](http://afni.nimh.nih.gov/pub/dist/doc/program_help/AlphaSim.html)).

**Correlation With SOR Scores**—To determine whether SOR predicted blood oxygen level–dependent response over and above anxiety, regression analyses were performed with the SOR composite score as the independent variable and the Screen for Child Anxiety Related Emotional Disorders<sup>35</sup> total anxiety scores as covariates. Parameter estimates for significant clusters in functionally defined regions of interest (primary somatosensory and auditory cortices and the amygdala) were extracted from each participant and plotted.

**Neural Habituation**—Habituation was assessed by examining the pattern of activation across time in the amygdala and somatosensory and auditory cortices. Region-of-interest masks were created by drawing a sphere around the peak coordinate in each region of interest for each group and then adding the spheres together. Sphere sizes (before adding) were 4 mm for the amygdala, 6 mm for the somatosensory cortex, and 10 mm for the auditory cortex (**Table 2** gives the coordinates). For each participant, PEs from the 4 blocks of the joint condition (vs rest) were extracted from the masks. Repeated-measures analyses of variance were used to examine group differences in PEs between diagnostic groups (ASDs vs TD) and across SOR subgroups (ASDs without SOR vs ASDs with SOR vs TD). We report results for the joint condition because this condition elicited the greatest between-group differences.

**Functional Connectivity**—A psychophysiological interaction analysis was used to examine functional connectivity between the amygdala and OFC during the joint condition. This analysis examines interaction between a task and the time series of seed region (here the amygdala) to identify brain areas (here the OFC as the a priori region of interest) where activity is more correlated with the seed region during the task vs baseline. Both positive connectivity and negative connectivity (areas showing increased and decreased activity as a function of increased activity in the amygdala) were examined.

## Results

### Behavioral Findings

Independent-sample *t* tests showed that the ASDs group was rated as having significantly more severe anxiety and SOR symptoms than the TD group on all measures except the Sensory Over-Responsivity Scales tactile count (Table 1). Correlation between the Screen for Child Anxiety Related Emotional Disorders anxiety total score and the SOR composite score was significant in both groups ( $r = 0.56$ ,  $P < .05$  for the TD group and  $r = 0.69$ ,  $P < .01$  for the ASDs group). The eResults in the Supplement contains additional group comparisons.

### fMRI Findings

**Within-Group and Between-Group Findings**—Within-group and additional between-group results are summarized in Table 2 and **Figure 1** and eTables 1, 2, and 3 and eFigures 2 and 3 in the Supplement. There were no significant TD vs ASDs group differences in the

auditory condition. During the tactile condition, the ASDs group had greater activation in the bilateral somatosensory cortex. In the joint condition, the ASDs group had greater activation in the bilateral somatosensory cortex, left superior temporal gyrus, right OFC, and left amygdala as well as additional subcortical areas. There were no clusters with significantly greater activation in the TD group compared to the ASDs group.

**Correlation With SOR Severity**—In youth with ASDs, SOR scores were positively correlated with signal increases in bilateral somatosensory cortices and the right amygdala as well as additional parietal and temporal areas. These results are summarized in Table 2 and eTable 3 and eFigure 4 in the Supplement.

**Neural Habituation During the Joint Condition**—In primary auditory cortex, there were significant linear and quadratic decreases in activation across the scan, indicating that auditory neural responses decreased quickly but then leveled off. No significant differences were observed among diagnostic groups or SOR subgroups (Figure 2 and eTable 4 in the Supplement).

Activation in the somatosensory cortex decreased linearly across the scan, and no main effect of diagnostic group was observed. There was a trend-level ( $P = .06$ ) diagnosis  $\times$  time interaction for the quadratic slope term, indicating that somatosensory cortex activation decreased more slowly across the scan in the ASDs group than in the TD group. There was no significant main effect of SOR subgroup  $\times$  time interaction. However, a post hoc least significant difference test indicated that activation in the ASDs with SOR subgroup was marginally higher than activation in the ASDs without SOR subgroup ( $P = .07$ ) and the TD subgroup ( $P = .05$ ).

In the amygdala, there was a main effect of time such that activation decreased significantly, and the rate of decrease slowed across the 4 joint condition blocks. No main effect of diagnostic group was observed, but there was a significant diagnosis  $\times$  time interaction for the cubic slope parameter, reflecting that, for the ASDs group, amygdala activation began to rise again toward the second half of the scan, whereas it continued to decrease for the TD group. There was a trend-level main effect of SOR subgroup ( $P = .08$ ) and a significant SOR subgroup  $\times$  time interaction for the cubic slope parameter. A post hoc least significant difference test showed a significant difference between the ASDs with SOR subgroup and the ASDs without SOR subgroup ( $P = .04$ ) and the TD subgroup ( $P = .047$ ). There was no significant difference between the ASDs without SOR subgroup and the TD subgroup.

Taken together, these results show SOR subgroup differences in habituation in the amygdala and somatosensory cortices but not in the auditory cortex. All groups had similar initial activity, but it quickly decreased in the TD subgroup and the ASDs without SOR subgroup, whereas it decreased more slowly or inconsistently in the ASDs with SOR subgroup.

**Functional Connectivity**—Within the TD group only, the right amygdala had positive functional connectivity with the bilateral OFC during the joint condition. Between-group analyses showed significant group differences in connectivity between the right amygdala and left OFC (peak coordinates,  $-42, 36, -6$ ). Extraction of PEs from the left OFC showed

that the ASDs group had negative connectivity with the left OFC, whereas the TD group had positive connectivity.

To further examine differences in amygdala-prefrontal connectivity among the 3 SOR subgroups, we conducted a 1-way analysis of variance using PEs of connectivity between the amygdala and OFC (Figure 3). There were significant differences between all 3 subgroups ( $F_2 = 16.96$ ,  $P < .001$ ). A post hoc least significant difference test indicated that the ASDs without SOR subgroup (mean [SD],  $-0.32$  [0.29]) showed significantly greater negative connectivity than the ASDs with SOR subgroup (mean [SD],  $-0.13$  [0.07];  $P = .03$ ) and the TD sub-group group (mean [SD],  $0.09$  [0.14];  $P < .001$ ). The TD subgroup was also significantly different from the ASDs with SOR subgroup ( $P = .006$ ). In summary, the ASDs without SOR subgroup showed the most strongly negative connectivity, the ASDs with SOR subgroup showed less negative connectivity, and the TD subgroup showed slightly positive connectivity between the right amygdala and OFC.

## Discussion

This study investigated the neurobiological basis of SOR by comparing brain responses to aversive sensory stimuli in TD youth and youth with ASDs with and without SOR. In addition, we explored whether SOR is related to abnormalities in initial sensory processing or to regulation of emotional response to sensory information by examining neural habituation in sensory cortices and the amygdala as well as amygdala-OFC functional connectivity during exposure to mildly aversive stimuli.

Results indicated that youth with ASDs have greater neural responses to mildly aversive sensory stimuli compared with TD youth. There were no group differences in response to auditory stimuli alone. Lack of aversiveness or familiarity with these traffic sounds might have reduced differential group responses in this condition. Conversely, the tactile condition elicited group differences in the primary somatosensory cortex, and the extent of activation in this area correlated with parent-reported SOR symptoms. There were no overall ASDs vs TD group differences in emotional processing regions in response to the tactile stimulus, but SOR symptoms within the ASDs group were correlated with increased response in the insula and amygdala. The insula is involved in interoception and emotional processing of sensory stimuli and receives inputs from the amygdala based on the perceived saliency of touch.<sup>36,37</sup> Furthermore, overreactive insula response during emotional processing is associated with anxiety,<sup>38,39</sup> consistent with the common co-occurrence of SOR and anxiety.

The greatest differences between youth with and without ASDs occurred in response to simultaneous auditory and tactile stimuli. Here, the ASDs group showed stronger neural responses in sensory processing regions, including auditory and tactile sensory cortices and the thalamus, and in emotional processing regions, including the amygdala and OFC. Consistent with previous findings,<sup>11</sup> the extent of activation in sensory cortices, the amygdala, and the insula was correlated with SOR severity within the ASDs group.

Habituation analyses in the amygdala and somatosensory cortex showed that both diagnostic groups began with similar activation, which decreased over time, but that the TD group

habituated more quickly. When the ASDs group was divided into 2 subgroups with and without SOR, it became clear that the ASDs with SOR subgroup not only habituated more slowly but also ended the scan with higher activity levels than the other subgroups, whereas the ASDs without SOR subgroup had habituation more similar to that of the TD subgroup.

To further understand how emotion regulation might relate to SOR, we examined functional connectivity between the amygdala and OFC during the joint condition. The ASDs without SOR subgroup had the most significant negative amygdala-OFC connectivity, the ASDs with SOR subgroup had slightly negative connectivity, and the TD subgroup had slightly positive connectivity. This finding is in contrast to the study by Green et al,<sup>10</sup> who found that higher SOR was related to higher OFC activation. However, medial OFC in their study was related to SOR as opposed to the more lateral areas seen in the present study. Medial OFC has more connectivity with the hippocampus,<sup>40</sup> which showed more activation in the study by Green et al,<sup>10</sup> perhaps due to the participants' associating sounds with the visual context.<sup>40</sup> Lateral OFC has greater connectivity with the amygdala and insula and is involved in inhibiting instinctive responses.<sup>40</sup> Such inhibition could help youth with ASDs without SOR avoid the behavioral responses to sensory stimuli seen in youth with ASDs with SOR, which is consistent with the more typical habituation pattern found in the ASDs without SOR subgroup. Conversely, the TD subgroup may not perceive the stimuli as aversive, thus not having an overreactive amygdala response and not requiring prefrontal downregulation.

Taken together, these results confirm previous evidence of overreactive brain responses to sensory stimuli in youth with ASDs.<sup>10</sup> Our findings further show that these overresponses are specific to youth with ASDs and elevated SOR, who show decreased habituation in the amygdala and sensory cortex and absence of amygdala-prefrontal negative connectivity. These results are consistent with previous studies<sup>22,41</sup> of amygdala overreactivity and reduced habituation in ASDs in response to faces but also suggest that amygdala abnormalities in ASDs are not limited to social contexts. Rather, youth with ASDs may have overall difficulty determining the saliency and threat relevance of stimuli. Reduced top-down regulation in youth with ASDs and SOR could contribute to deficits in using context to assess the saliency of stimuli<sup>31</sup> as well as to failures of selective inhibition and attention, which is consistent with sensory gating hypotheses.<sup>7,8</sup>

Strengths of this study include examining multiple modalities of sensory stimuli, accounting for within-group heterogeneity in SOR, and investigating brain overreactivity from multiple perspectives. We had limited power to examine within-group differences, but the pattern of results was consistent in showing greater overreactivity and reduced habituation in the ASDs with SOR subgroup. Additional research should examine this subgroup with larger samples. Future studies should also examine youth with ASDs without SOR in more detail because this subgroup may have developed unique coping strategies to inhibit sensory responses. In addition, we were limited to parental reports of SOR, and future studies might benefit from including examiner-administered physiological measures to help identify the role of state anxiety in SOR.



## Conclusions

These findings have implications for intervention. First, the greatest overresponsiveness occurred in response to multiple simultaneous stimuli, suggesting that minimizing exposure to multiple sensory modalities could help youth with ASDs cope with SOR (eg, a child might be more tolerant of being touched in a quiet house than in a noisy movie theater). Second, youth with ASDs without SOR appear to have more ability to downregulate their response to sensory stimuli. This finding may indicate that intervention for SOR should focus on building coping strategies rather than on normalizing sensory processing. Successful interventions for teaching coping strategies to reduce anxiety in ASDs already exist.<sup>42,43</sup> Given the high co-occurrence of anxiety and SOR in ASDs,<sup>11</sup> it may be possible to adapt these interventions to target SOR.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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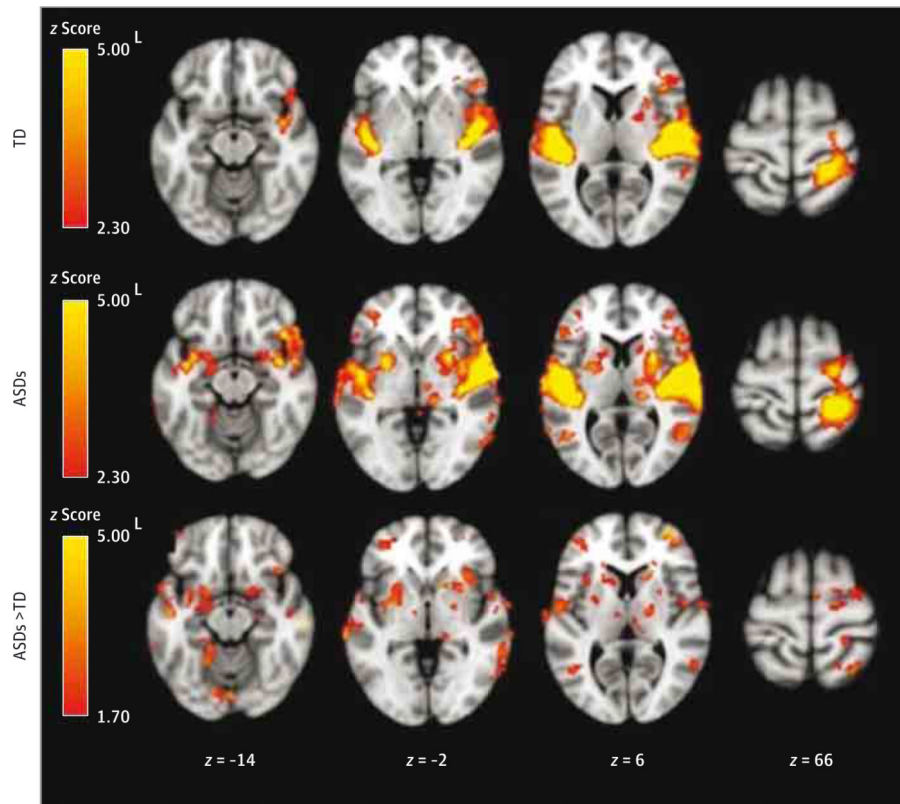
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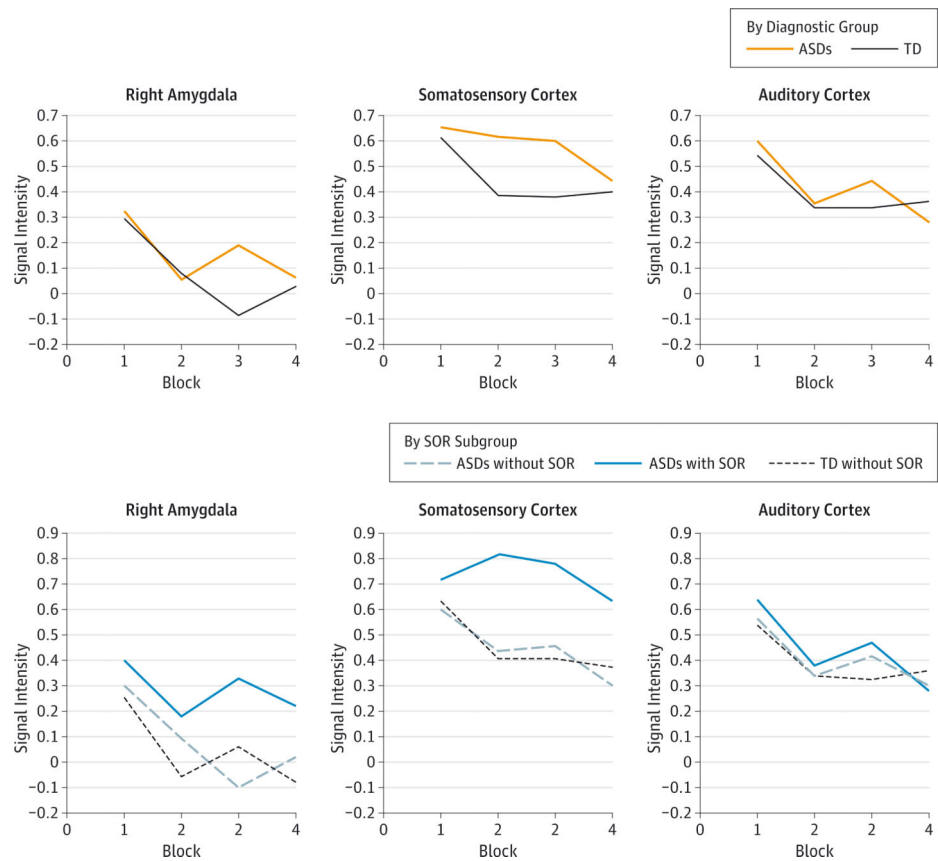
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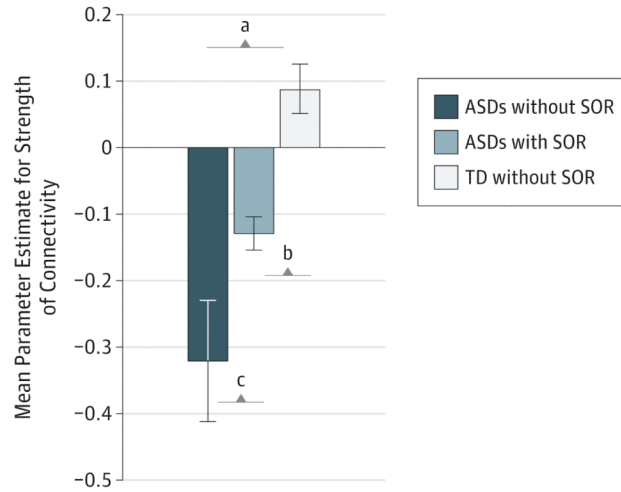
**Figure 1.** Within-Group and Between-Group Results for the Joint Auditory and Tactile Condition. Within-group contrasts are thresholded at  $z > 2.30$  (corrected at  $P < .05$ ). Between-group contrasts are thresholded at  $z > 1.70$  (corrected). Between-group maps are masked by regions active in either within-group condition at  $z > 1.70$  (uncorrected). ASDs indicates autism spectrum disorders; L, left; and TD, typically developing.



**Figure 2.**

**Amygdala and Sensory Cortex Habituation by Diagnostic Group and by Sensory Overresponsivity (SOR) Subgroup**

The vertical axis represents region-of-interest parameter estimates during the tactile or joint condition compared with baseline. The horizontal axis represents each block of the condition. ASDs indicates autism spectrum disorders; TD, typically developing.



ASDs indicates autism spectrum disorders; TD, typically developing.

<sup>a</sup>  $P < .001$ .

<sup>b</sup>  $P < .01$ .

<sup>c</sup>  $P < .05$ .

**Figure 3.** Amygdala–Orbitofrontal Cortex Connectivity by Sensory Overresponsivity (SOR) Subgroup

**Table 1**

## Descriptive Statistics

Variable	ASDs (n = 19)	TD (n = 19)	t Statistic or $\chi^2$ Statistic
Age, mean (SD), y	13.71 (1.60)	13.61 (2.57)	0.13
Male sex, No. (%)	16 (84)	16 (84)	0.00
Right-handedness, No. (%)	18 (95)	19 (100)	0.31
IQ, mean (SD)			
Full-scale	104.63 (13.22)	107.37 (15.06)	-0.59
Verbal	103.74 (13.49)	107.63 (13.17)	-0.90
Performance	103.70 (14.47)	105.76 (16.00)	-0.42
Absolute motion, mean (SD), mm			
Mean	0.33 (0.17)	0.31 (0.23)	0.21
Maximum	0.94 (0.64)	0.87 (0.97)	0.29
Relative motion, mean (SD), mm			
Mean	0.09 (0.04)	0.13 (0.20)	-0.90
Maximum	0.80 (0.63)	0.61 (1.15)	0.62
Sensory Over-Responsivity Scales score, mean (SD)			
		(n = 17)	
Tactile count	4.79 (5.57)	2.76 (4.12)	1.22
Auditory count	6.89 (7.06)	1.56 (3.90)	2.87 <sup>a</sup>
Short Sensory Profile score, mean (SD) <sup>b</sup>			
		(n = 18)	
Auditory and visual	19.32 (5.10)	24.28 (2.11)	-3.90 <sup>a</sup>
Auditory filtering	17.42 (6.00)	26.11 (4.01)	-5.20 <sup>c</sup>
Tactile sensitivity	27.32 (6.19)	32.89 (3.64)	-3.31 <sup>a</sup>
Sensory overresponsivity composite score, mean (SD)	0.45 (0.93)	-0.45 (0.51)	3.71 <sup>a</sup>
Screen for Child Anxiety Related Emotional Disorders anxiety total score, mean (SD)	13.84 (9.44)	5.47 (5.88)	3.28 <sup>a</sup>

Abbreviations: ASDs, autism spectrum disorders; TD, typically developing.

<sup>a</sup> $P < .01$ .

<sup>b</sup>Lower scores indicate higher symptom severity.

<sup>c</sup> $P < .001$ .

**Table 2**

Montreal Neurologic Institute (MNI) Coordinates for the Joint Auditory and Tactile Condition Compared With Baseline<sup>a</sup>

Variable	TD		ASDs		ASDs > TD		Regress With Sensory Overresponsivity	
	<u>MNI Peak, mm</u> x, y, z	<u>Maximum</u> z Score	<u>MNI Peak, mm</u> x, y, z	<u>Maximum</u> z Score	<u>MNI Peak, mm</u> x, y, z	<u>Maximum</u> z Score	<u>MNI Peak, mm</u> x, y, z	<u>Maximum</u> z Score
Postcentral gyrus								
Right	26, -38, 66	4.98	24, -38, 68	6.58	50, -16, 36	4.63	30, -38, 58	3.64
Left	-52, -22, 24	3.64	-22, -42, 68	4.49	-60, -10, 40	3.47	-62, -26, 30	2.47
Precentral gyrus								
Right	28, -16, 66	3.30	26, -14, 64	4.01	58, 8, 36	3.42	34, -10, 70	4.30
Left	NA	NA	-62, 6, 26	4.41	NA	NA	-56, 4, 24	3.70
Right supplementary motor cortex	NA	NA	6, -10, 56	2.82	6, 6, 50	3.31	6, -12, 58	2.74
Inferior frontal gyrus								
Right	NA	NA	58, 16, -4	4.79	NA	NA	NA	NA
Left	NA	NA	-48, 10, 16	3.50	-48, 12, 16	2.50	NA	NA
Frontal gyrus								
Right superior	NA	NA	NA	NA	4, 22, 46	2.45	NA	NA
Right middle	NA	NA	NA	NA	54, 20, 38	3.58	NA	NA
Right frontal pole	NA	NA	12, 50, 46	4.11	38, 50, 16	4.43	NA	NA
Frontal orbital cortex								
Right	NA	NA	42, 22, -14	4.29	42, 22, -14	2.72	NA	NA
Left	NA	NA	48, 14, 46	3.15	NA	NA	NA	NA
Heschl gyrus								
Right	52, -20, 10	6.62	48, -20, 12	7.10	NA	NA	NA	NA
Left	-46, -14, 4	5.79	-42, -22, 0	5.34	NA	NA	NA	NA
Superior temporal gyrus								
Right	62, -34, 18	6.15	62, -20, 12	6.61	NA	NA	NA	NA
Left	-40, -32, 14	5.90	-54, -8, 4	5.99	-52, 10, -16	3.45	-66, -32, 18	4.92



Variable	TD		ASDs		ASDs > TD		Regress With Sensory Overresponsivity	
	MNI Peak, mm x, y, z	Maximum z Score	MNI Peak, mm x, y, z	Maximum z Score	MNI Peak, mm x, y, z	Maximum z Score	MNI Peak, mm x, y, z	Maximum z Score
Left temporal pole	NA	NA	NA	NA	NA	NA	-48, 10, -8	3.31
Middle temporal gyrus								
Right	NA	NA	54, 14, -16	3.15	62, -20, -14	3.90	NA	NA
Left	NA	NA	NA	NA	NA	NA	-52, -56, 8	2.36
Operculum								
Right	48, 10, 0	3.45	40, -26, 22	6.18	-54, -6, 4	3.07	58, -28, 26	4.31
Left	NA	NA	-40, -32, 18	7.15	NA	NA	-40, -4, 16	3.46
Insula								
Right	38, -20, 0	4.91	38, -20, 0	5.43	NA	NA	NA	NA
Left	NA	NA	-38, -4, -12	4.60	NA	NA	-34, -16, 8	2.80
Left supramarginal gyrus	NA	NA	-64, -30, 20	5.53	-64, -36, 32	3.12	-62, -52, 18	3.27
Posterior cingulate	NA	NA	NA	NA	-2, -36, 24	4.91	0, -26, 26	3.44
Superior parietal lobule								
Right	NA	NA	18, -50, 74	5.28	18, -52, 74	3.36	20, -50, 70	2.65
Left	NA	NA	-34, -46, 64	4.04	NA	NA	NA	NA
Left fusiform	NA	NA	NA	NA	-28, -74, -18	3.81	NA	NA
Caudate								
Right	NA	NA	14, -2, 18	3.19	16, 18, 10	3.15	NA	NA
Left	NA	NA	-12, 12, 12	3.22	-18, 26, 4	2.69	NA	NA
Putamen								
Right	NA	NA	28, 10, 2	4.87	28, 10, 0	3.06	NA	NA
Left	NA	NA	-26, 6, -6	3.97	-24, 12, 2	3.17	NA	NA
Right pallidum	NA	NA	NA	NA	20, -8, 0	3.00	NA	NA
Right thalamus								
Ventral nucleus	NA	NA	14, -16, 12	3.78	-10, -12, 4	2.31	NA	NA
Pulvinar	NA	NA	16, -26, 2	3.64	14, -28, 14	3.13	NA	NA

Variable	TD		ASDs		ASDs > TD		Regress With Sensory Overresponsivity	
	MNI Peak, mm	Maximum	MNI Peak, mm	Maximum	MNI Peak, mm	Maximum	MNI Peak, mm	Maximum
	x, y, z	z Score	x, y, z	z Score	x, y, z	z Score	x, y, z	z Score
Left hippocampus and parahippocampal gyrus	NA	NA	NA	NA	-28, -12, -22	3.84	NA	NA
Cerebellum	NA	NA	34, -78, -42	3.63	-42, -60, -46	4.29	-10, -70, -38	3.47

Abbreviations: ASD, autism spectrum disorder group; NA, not applicable; TD, typically developing.

<sup>a</sup>The x, y, and z refer to left-right, anterior-posterior, and inferior-superior dimensions, respectively, and the z score refers to the score at those coordinates (local maximum or submaximum). Within-group analyses are cluster corrected for multiple comparisons at  $z > 2.30$  ( $P < .05$ ), and between-group and regression analyses are thresholded at  $z > 1.70$  (corrected). Between-group analyses are masked by regions of significant activation in either within-group analysis at the liberal threshold of  $z > 1.70$  (uncorrected). Regression results show clusters with activation significantly correlated with the sensory overresponsivity composite score within the ASDs group over and above age and anxiety symptoms.