| **Title**         | Sensory Processing Patterns and Fusiform Activity During Face Processing in Autism Spectrum Disorder |
|-------------------|----------------------------------------------------------------------------------------------------|
| **Author(s)**     | 藤田, 綾香                                                                                       |
| **Citation**      |                                                                                                   |
| **Issue Date**    |                                                                                                   |
| **Text Version**  | ETD                                                                                              |
| **URL**           | https://doi.org/10.18910/77527                                                                   |
| **DOI**           | 10.18910/77527                                                                                   |
| **Note**          |                                                                                                   |
Sensory Processing Patterns and Fusiform Activity During Face Processing in Autism Spectrum Disorder

大阪大学大学院
大阪大学・金沢大学・浜松医科大学・千葉大学・福井大学
連合小児発達学研究科
小児発達学専攻

藤田綾香

2020年8月博士学位論文
Sensory Processing Patterns and Fusiform Activity During Face Processing in Autism Spectrum Disorder

Ayaka Kuno-Fujita, Toshiki Iwabuchi, Keisuke Wakusawa, Hiroyuki Ito, Katsuaki Suzuki, Akira Shigetomi, Kosaka Hirotaka, Masatsugu Tsujii, and Kenji J. Tsuchiya

A growing body of evidence has indicated that individuals with autism spectrum disorder (ASD) exhibit abnormal reactions to sensory stimuli and impaired face processing. Although behavioral studies have reported that individual differences in sensory processing patterns are correlated with performance in face processing tasks, the neural substrates underlying the association between sensory processing patterns and face processing remain unknown. Using functional magnetic resonance imaging, the present study examined the relationships between sensory processing patterns assessed with the Adolescent/Adult Sensory Profile (AASP) and brain activity during a one-back task with two types of stimuli (face or house pictures). We enrolled 18 Japanese adults with ASD and 19 age- and IQ-matched controls. Sensation Avoiding scores, which were assessed using the AASP, were positively correlated with right fusiform activity during the presentation of pictures of faces in the ASD group, but not in the control group. This suggests that abnormal sensory processing patterns in ASD are associated with abnormal face-related brain activity, possibly resulting in impaired face processing.

**Introduction**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication deficits, restricted interests, and repetitive behaviors, according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders [DSM-5; American Psychiatric Association, 2013].

Growing behavioral evidence suggests that individuals with ASD often show difficulty in identifying others’ faces (see Weigelt, Koldewyn, and Kanwisher [2012] for review). When human faces were presented simultaneously with geometrical patterns, compared to typically developing (TD) individuals, individuals with ASD focused on human faces for a shorter period and instead fixed their gaze for longer on geometrical patterns [Fujioaka et al., 2016]. These findings suggest that individuals with ASD exhibit different visual processing patterns from those of their TD peers.

Functional magnetic resonance imaging (fMRI) studies have reported that the fusiform gyrus and amygdala exhibited lower activation during face processing in individuals with ASD than in TD individuals [Nomi & Uddin, 2015; Pierce, Muller, Ambrose, Allen, & Courchesne, 2001; Schultz et al., 2000]. An fMRI study reported that the activity in the fusiform face area increased with face-related working memory load [Druzel & D’Esposito, 2001]. Moreover, abnormal face processing in ASD is particularly prominent during tasks involving face memory [Weigelt et al., 2012]; therefore, using a memory task may be effective for investigating functional abnormalities related to face processing in individuals with ASD.

Individuals with ASD also have abnormal sensory experiences. The DSM-5 added sensory abnormalities, such as...
hypothesizing sensory hypersensitivity or hyposensitivity, to the diagnostic criteria of ASD [American Psychiatric Association, 2013]. Several studies have demonstrated that 90% or more of children with ASD exhibit some form of sensory abnormalities [Leekam, Nieto, Libby, Wing, & Gould, 2007; Tomchek & Dunn, 2007]. Sensory abnormalities, defined as atypical patterns of sensory processing, are assessed by measuring behavioral responses to sensory input in the field of occupational therapy [Brown, Tolleson, Dunn, Cromwell, & Filion, 2001]. The Adolescent/Adult Sensory Profile® (AASP) is a self-reported questionnaire used to evaluate such behavioral response patterns toward sensory stimuli in adults [Brown & Dunn, 2002; Hirashima et al., 2014]. It assesses sensory processing patterns according to four quadrants based on Dunn’s [1997] model: “Low Registration,” “Sensation Seeking,” “Sensory Sensitivity,” and “Sensation Avoiding.”

Methods

Participants

Eighteen Japanese adults with ASD (15 males, three females; mean age ± SD = 31.17 ± 3.29 years; age range 27–39 years) and 19 TD controls (15 males, four females; mean age ± SD = 31.37 ± 3.19 years; age range 29–39 years) participated in this study. All participants were right-handed as assessed by the Edinburgh Handedness Inventory [Oldfield, 1971].

Participants in the ASD group were recruited from the Asperger Society Japan and diagnosed with Autistic Disorder, Asperger Disorder, or Pervasive Developmental Disorder based on the DSM-IV TR [4th edition, text revision; American Psychiatric Association, 2000] by a local psychiatrist. An independent, certified psychologist (K.J.T.) and psychologist (K.M.), who were qualified to administer the Autism Diagnostic Interview-Revised [Lord, Rutter, & Le Couteur, 1994] and Autism Diagnostic Observational Schedule [Lord et al., 1989] confirmed that all participants in the ASD group fulfilled ASD diagnostic criteria.

Full-scale intelligence quotient (IQ) was measured with the Wechsler Adult Intelligence Scale, third edition [Wechsler, 1997]. Although age did not significantly differ between the two groups, there was a marginally significant difference in the full-scale IQ (Table 1). Participants also completed the AASP, Social Responsiveness Scales-Second Edition (SRS-2: Constantino & Gruber, 2012), SRS-2 Adult Self-Report Form [Constantino & Gruber, 2012], and Autism-spectrum Quotient [Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001]. Written, informed consent was provided by each participant. This study was conducted in accordance with the Declaration of Helsinki and approved by the Clinical Research Ethics Committee at the Hamamatsu University School of Medicine.

Stimuli and Experimental Design

A one-back task with a block-design paradigm was performed in the magnetic resonance scanner. The experiment comprised six stimulus blocks of 30 sec each. Forty gray-scale faces (half male and half female) or house pictures were presented in each stimulus block. Face blocks and house blocks were alternately repeated (Fig. 1). All face pictures were full-face and trimmed to remove apparent features such as the neck, ears, and hair. Similarly, house pictures were edited to eliminate the background and extraneous objects. Photoshop CS4 (Adobe Systems Inc.) was used to edit pictures. The duration of the presentation of each picture was 500 msec, followed by a 250-msec inter-stimulus interval. The presentation order within each block was pseudo-randomized. During stimulus blocks, no fixation cross was presented, but participants were instructed to observe presented pictures.
carefully and to memorize them temporarily. They were also required to press a button with their right index finger as quickly as possible when an identical picture was successively presented. Ten pictures served as target stimuli in each block. A fixation cross was presented for 20 sec before and after each stimulus block. In addition, a 25-sec fixation block was inserted at the beginning of the experiment, and a termination message was presented for 5 sec at the end of the experiment.

**fMRI Data Acquisition**

$T_2^*$-weighted images with blood oxygenation level-dependent contrast were collected with a 3-T MRI scanner (Signa HDxt, GE Healthcare) at the Kojin Hospital (Nagoya, Japan) using gradient-echo echo-planar imaging. The following parameters were used: repetition time (TR) = 2,500 msec, echo time (TE) = 30 msec, field of view = $210 \times 210$ mm$^2$, slice thickness = 3.0 mm with

![Figure 1. Schematic illustration of the stimuli and task.](image-url)

Table 1. Demographic Data and Behavioral Data in the One-Back Task

|                          | ASD ($n = 18$) | TD ($n = 19$) | Comparison |
|--------------------------|----------------|---------------|------------|
| Mean age (range)         | 31.17 (27–39)  | 31.37 (29–39) | $t = -0.17$ | $P = 0.87$ |
| Intelligence quotient (mean ± SD) | 87.12 ± 18.28 | 98.74 ± 8.83 | $t = -2.00$ | $P = 0.054$ |
| Autism spectrum quotient (mean ± SD) | 30.47 ± 8.00 | 15.42 ± 6.13 | $t = 6.51$ | $P < 0.001$ |
| Social Response Scale Second Edition (SRS-2) (mean ± SD) | 76.06 ± 23.01 | 30.05 ± 21.28 | $t = 6.35$ | $P < 0.001$ |
| SRS-2 Adult Self-Report Form | 88.41 ± 30.84 | 47.47 ± 21.46 | $t = 4.26$ | $P < 0.001$ |
| (mean ± SD)              |                |               |            |
| Adult/adult sensory profile (mean ± SD) | 32.06 ± 8.39 | 25.79 ± 8.67 | $t = 2.13$ | $P = 0.04$ |
| Low registration         | 36.88 ± 10.53  | 37.84 ± 5.52  | $t = -0.35$ | $P = 0.73$ |
| Sensation seeking        | 32.59 ± 9.43   | 32.53 ± 7.99  | $t = 0.01$  | $P = 0.99$ |
| Sensory sensitivity      | 37.41 ± 8.58   | 33.00 ± 7.30  | $t = 1.47$  | $P = 0.15$ |
| Sensation avoiding       | 13.94 ± 3.15   |               |            |
| Autism diagnostic observation schedule (mean ± SD) | 507.40 ± 85.41 | 512.24 ± 40.73 | $t = -0.22$ | $P = 0.83$ |
| Social reciprocity + communication | 485.09 ± 86.76 | 489.73 ± 41.00 | $t = -0.21$ | $P = 0.83$ |
| One-Back Task (mean ± SD) |                |               |            |
| Reaction time (msec)     | 0.86 ± 0.09    | 0.89 ± 0.12   | $t = -0.93$ | $P = 0.36$ |
| Face                     | 0.94 ± 0.10    | 0.91 ± 0.13   | $t = -0.92$ | $P = 0.36$ |
| House                    | 0.02 ± 0.08    | 0.00 ± 0.06   | $t = -0.73$ | $P = 0.47$ |
| Correct answer rate      | 0.06 ± 0.07    | 0.03 ± 0.08   | $t = 1.46$  | $P = 0.15$ |
| x (mm)                   | 0.07 ± 0.26    | 0.13 ± 0.18   | $t = -0.58$ | $P = 0.57$ |
| y (mm)                   | 0.00 ± 0.01    | 0.00 ± 0.01   | $t = 0.86$  | $P = 0.40$ |
| z (mm)                   | 0.00 ± 0.00    | 0.00 ± 0.00   | $t = -0.83$ | $P = 0.41$ |
| Pitch (radian)           | 0.00 ± 0.00    | 0.00 ± 0.00   | $t = -1.00$ | $P = 0.32$ |
| Roll (radian)            | 0.00 ± 0.00    | 0.00 ± 0.00   | $t = -1.00$ | $P = 0.32$ |
| Yaw (radian)             | 0.00 ± 0.00    | 0.00 ± 0.00   | $t = -1.00$ | $P = 0.32$ |

Abbreviations: ASD: individuals with autism spectrum disorder; TD: typically developing individuals.

For behavioral data in the one-back task, statistics on direct group comparisons in each picture type (face, house) are shown.

---

**Figure 1. Schematic illustration of the stimuli and task.**
formed into the Montreal Neurological Institute stereocerebrospinal of structural images into gray matter, white matter, and zation parameters were estimated during the segmentation to individuals was corrected; (c) the functional images were co-registered following: (a) the functional images were realigned to the mean image; (b) the difference of slice acquisition timing was corrected; and a by-subject random intercept. Moreover, we included full-scale IQ as a covariate because we observed marginally significant group differences in full-scale IQ. Data fitting was performed with Stata MP 15.1 (StataCorp, College Station, TX).

fMRI Data Analysis

SPM12 software (http://www.fil.ion.ucl.ac.uk/spm/) was used for preprocessing and statistical whole-brain analysis of fMRI data. The applied preprocessing steps included the following: (a) the functional images were realigned to the mean image; (b) the difference of slice acquisition timing was corrected; (c) the functional images were co-registered to individuals’ structural T1 images; (d) the spatial normalization parameters were estimated during the segmentation of structural images into gray matter, white matter, and cerebrospinal fluid; (e) all functional images were transformed into the Montreal Neurological Institute stereotaxic space using the estimated parameters, and resampled into $3 \times 3 \times 3 \text{ mm}^3$ voxels; and (f) the normalized functional images were smoothed with a 6-mm full width at half maximum Gaussian kernel.

The preprocessed data were analyzed using a general linear model approach. The functional images were high-pass filtered to remove low-frequency noise with a cut-off period of 128 sec. The serial correlations in the fMRI time series were considered using the autoregressive AR(1) model, as implemented in the standard pipeline of SPM12. The face and house conditions were modeled as separate box-car regressors that were convolved with a canonical hemodynamic response function. Additionally, six head-motion parameters were included as confounding covariates.

The beta maps yielded by the individual-level analysis were submitted to a $2 \times 2$ full factorial analysis of variance for group-level random-effects statistical inference, with a between-subjects factor (Group [ASD or TD]) and within-subjects factor (Picture Type [face or house]). To identify group-level local maxima within the fusiform gyrus and amygdala associated with face processing, the main effect of Picture Type was tested by comparing the face condition to the house condition. The statistical threshold was set at $P = 0.05$ with family-wise error (FWE) correction for multiple comparisons at voxel-level. We did not apply an additional cluster-level correction, taking into account small cluster sizes. Anatomical labels of the peaks were defined using the Neuromorphometrics function in SPM12.

Region of Interest Analysis

To create individual regions of interest (ROIs) in the bilateral fusiform gyrus and amygdala, we localized activation peaks for each participant within mask images of the four target regions (i.e., the right fusiform gyrus, left fusiform gyrus, right amygdala, and left amygdala), comparing the face and house conditions with a significance threshold of $P = 0.05$ uncorrected for multiple comparisons. Those mask images were generated using the SPM Anatomy toolbox [Eickhoff et al., 2005]. Activated clusters in these anatomical masks were regarded as individual functional ROIs. For those who did not show any significant activation within a masked region, we used the activated clusters in the group-level analysis ($P < 0.05$ with FWE correction for multiple comparisons at voxel-level) within the same anatomical mask images (i.e., bilateral fusiform gyrus and amygdala) as functional ROIs. We created these ROIs from the group-level activated clusters by the contrast between the face condition and the house condition. We used Marsbar software [Brett, Anton, Valabregue, & Poline, 2002] to build all ROIs and to extract the beta values for the face condition from these ROIs.

To test the hypothesis that behavioral characteristics of sensory processing were correlated with altered brain activity during face processing in ASD, we calculated the partial correlations between AASP scores and beta values for the face condition within the ROIs with full-scale IQ as a covariate. We used Bonferroni correction for multiple comparisons.

Correlation Analysis Between Sensory Profile Scores and Symptom Severity

There may be associations between symptom severity in ASD and sensory processing patterns assessed by the AASP. These possible associations may result in spurious correlations between sensory processing patterns and brain activity. We calculated correlations between sensory profile scores and symptom severity assessed by the ADOS and ADI-R, to exclude this possibility.

Results

Behavioral Data

We observed that Picture Type had a significant effect on reaction time ($\beta = 22.512$, 95% confidence interval [CI] 6.922 to 38.101, $P = 0.005$), suggesting that the
Table 2. MNI Coordinates for Individual Activation Peaks for the Contrast of Face > House

|      | Fusiform gyrus (L) | Fusiform gyrus (R) | Amygdala (L) | Amygdala (R) |
|------|-------------------|-------------------|--------------|--------------|
| ASD1 | [−50, −74, −8]    | [44, −72, −10]    |              | [16, −4, −16]|
| ASD2 | [−44, −48, −26]   | [40, −52, −20]    | −            | −            |
| ASD3 | [−44, −56, −22]   | [42, −68, −18]    | [−18, −2, −28]| −            |
| ASD4 | −                 | [46, −52, −18]    | −            | [26, 0, −30] |
| ASD5 | −                 | [44, −50, −24]    | −            | [22, −6, −12]| |
| ASD6 | [−40, −50, −20]   | [44, −52, −20]    | [−20, −4, −26]| [24, −6, −12]| |
| ASD7 | −                 | −                 | −            | [28, 4, −28] |
| ASD8 | −                 | [44, −56, −18]    | −            | −            |
| ASD9 | [−44, −48, −26]   | [46, −48, −22]    | [−28, −2, −22]| [22, −4, −18]|
| ASD10| [−42, −50, −16]   | [40, −58, −18]    | [−22, −4, −14]| [24, 0, −14] |
| ASD11| [−46, −46, −28]   | [46, −46, −26]    | [−22, −8, −24]| [24, −6, −18]|
| ASD12| [−48, −60, −22]   | [40, −54, −18]    | [−18, −8, −14]| [16, −4, −16]|
| ASD13| [−46, −50, −24]   | [44, −58, −14]    | [−24, −6, −18]| [30, −6, −16]|
| ASD14| [−20, −62, −8]    | [40, −72, −16]    | [−16, −6, −16]| [22, −8, −12]|
| ASD15| [−40, −50, −14]   | [42, −64, −12]    | −            | [16, −6, −20]|
| ASD16| [−44, −60, −14]   | [46, −64, −18]    | [−18, 2, −22] | [20, 0, −16] |
| ASD17| [−40, −42, −26]   | [46, −50, −18]    | −            | [20, −4, −16]|
| ASD18| [−46, −44, −18]   | −                 | [−18, 2, −22] | [34, −2, −24]|
| TD1  | [−38, −66, −10]   | [40, −52, −20]    | [−20, −10, −12]| −            |
| TD2  | [−48, −60, −18]   | [42, −56, −10]    | [−16, −4, −18]| [20, −4, −16]|
| TD3  | [−44, −52, −24]   | [40, −56, −10]    | [−16, −4, −16]| [22, −6, −12]|
| TD4  | [−36, −60, −8]    | [40, −48, −12]    | [−22, 0, −16] | [22, −2, −16]|
| TD5  | [−48, −64, −18]   | [40, −56, −20]    | [−22, −8, −14]| [26, −6, −22]|
| TD6  | [−50, −60, −16]   | [50, −46, −18]    | [−18, −6, −20]| [18, −6, −22]|
| TD7  | [−46, −58, −22]   | [48, −48, −24]    | −            | [30, 2, −26] |
| TD8  | −                 | −                 | −            | −            |
| TD9  | [−40, −80, −14]   | [38, −40, −18]    | [−26, −4, −14]| [20, 0, −16] |
| TD10 | [−46, −74, −14]   | [40, −74, −12]    | [−18, −8, −14]| [20, −6, −16]|
| TD11 | [−42, −54, −22]   | [44, −72, −18]    | [−26, 0, −24]| [20, −2, −26]|
| TD12 | [−42, −48, −16]   | −                 | [−18, −4, −16]| [24, −8, −12]|
| TD13 | [−40, −48, −16]   | [46, −46, −20]    | [−16, −2, −18]| [24, 4, −28] |
| TD14 | [−38, −44, −24]   | −                 | −            | [20, −4, −16]|
| TD15 | [−40, −60, −18]   | [46, −46, −20]    | [−18, −2, −18]| [26, 0, −18] |
| TD16 | [−44, −52, −20]   | [42, −50, −16]    | [−22, −12, −14]| [16, −4, −18]|
| TD17 | [−38, −54, −20]   | [46, −60, −16]    | [−20, −4, −14]| [24, −8, −14]|
| TD18 | [−42, −72, −6]    | [48, −56, −20]    | −            | −            |
| TD19 | [−48, −64, −20]   | [48, −58, −20]    | [−26, −4, −22]| [26, 0, −14] |

Horizontal lines indicate no significant activation at the individual level.
Abbreviations: MNI: Montreal Neurological Institute; L, left; R, right.

Figure 2. Group-level brain activation during the one-back task. The bilateral fusiform gyrus and amygdala showed increased activity for the face > house comparison when the two groups were combined. R: right, L: left.
Abbreviation: MNI: Montreal Neurological Institute.

reaction to face pictures was significantly delayed compared to that of house pictures (Table 1). The effect of Group and the interaction of Group × Picture Type were not significant ($\beta = -22.810$, 95% CI $-62.856$ to 17.237, $P = 0.26$, and $\beta = -0.201$, 95% CI $-22.552$ to 22.151, $P = 0.97$, respectively). The effect of Group ($\beta = 0.042$, 95% CI $-0.033$ to 0.116, $P = 0.27$) and that of Picture Type ($\beta = -0.016$, 95% CI $-0.052$ to 0.021, $P = 0.39$) on accuracy were not significant. However, we observed a significant interaction of Group × Picture Type ($\beta = -0.069$, 95% CI $-0.121$ to $-0.017$, $P = 0.009$). We conducted post hoc pairwise comparisons using the “pcompare” command in Stata, and found that the accuracy in the face condition was significantly lower than that in the house condition in the ASD group (contrast $= -0.085$, 95% CI $-0.135$ to $-0.034$, Bonferroni-corrected $q < 0.001$) but not in the TD group (contrast $= -0.016$, 95% CI $-0.065$ to 0.033, Bonferroni-corrected $q = 1$). Conversely, group differences were not significant for the face condition (contrast $= -0.016$, 95% CI $-0.065$ to 0.033, Bonferroni-corrected $q = 1$) or the house condition (contrast $= -0.023$, 95% CI $-0.128$ to 0.072, Bonferroni-corrected $q = 1$).

**fMRI Data**

Localizer analysis identified peak coordinates of each participant (Table 2). For participants whose peak was not identified in any ROI, we used local maxima revealed by the whole-brain group-level contrast of the face condition versus the house condition in the left fusiform gyrus, right fusiform gyrus, left amygdala, and right amygdala ($x = -42$, $y = -50$, $z = -20$ for the left fusiform gyrus; $x = 44$, $y = -52$, $z = -18$ for the right fusiform gyrus; $x = -20$, $y = -6$, $z = -14$ for the left amygdala; and $x = 24$, $y = -4$, $z = -14$ for the right amygdala) ($P < 0.05$, FWE corrected for multiple comparisons at voxel level; Fig. 2 and Table 3).

We calculated the partial correlations between scores in each quadrant of the AASP and beta value for the face condition in each ROI by controlling for full-scale IQ (Table 4). In the ASD group, right fusiform gyrus activity was positively correlated with Sensation Avoiding scores ($r = 0.78$, Bonferroni-corrected $q = P \times 48 = 0.009$; Fig. 3). Other correlations did not survive Bonferroni correction in the ASD group. In the TD group, no significant correlations were detected. For the bilateral amygdala, no significant correlation was observed in the ASD group, TD group, or a combination of the two groups.

We further tested the differences in correlation between right fusiform activity and Sensation Avoiding scores among groups. We observed that the correlation value was significantly higher in the ASD group than in the TD group ($z = 2.56$, $P = 0.01$). In addition, we divided each group into two subgroups on the basis of cut-off points for the Sensation Avoiding quadrant (42 for ages below 35 years, and 40 for ages 35 years and above), and compared right fusiform activity among these subgroups.

Table 3. Brain Activation for the Contrast of Face Versus House

| MNI coordinate | $x$ | $y$ | $z$ | $Z$-score | Cluster size |
|----------------|----|----|----|-----------|--------------|
| Right amygdala | 24 | -6 | -14 | 7.18 | 653 |
| Left amygdala | -20 | -6 | -14 | 5.77 | 664 |
| Right cerebellum exterior | 6 | -44 | -16 | 5.36 | 5731 |
| Right superior frontal gyrus | 28 | 44 | 40 | 5.08 | 1384 |
| Right thalamus proper | 26 | -24 | 12 | 4.57 | 107 |
| Right fusiform gyrus | 44 | -52 | -18 | 4.52 | 33 |
| Left supramarginal gyrus | -60 | -56 | 30 | 4.49 | 389 |
| Left fusiform gyrus | -42 | -50 | 20 | 4.47 | 16 |
| Left parietal operculum | -32 | -32 | 20 | 4.46 | 51 |

Table 4. Correlations Between AASP and Brain Activity

| Correlation coefficient ($r$) | Uncorrected $P$-value | Bonferroni corrected $q$-value |
|-------------------------------|------------------------|-------------------------------|
| Low registration | Sensation seeking | Sensory sensitivity | Sensation avoiding | Low registration | Sensation seeking | Sensory sensitivity | Sensation avoiding |
| Low registration | 0.03 | 0.17 | 0.26 | 0.52 | 0.08 | 0.09 | 0.17 | 0.21 | 0.29 | 0.30 | 0.25 | 0.15 |
| Sensation seeking | 0.18 | 0.32 | 0.27 | 0.48 | 0.01 | 0.11 | 0.16 | 0.10 | 0.16 | 0.21 | 0.24 | 0.19 | 0.13 |
| Sensory sensitivity | 0.06 | 0.11 | 0.33 | 0.55 | -0.23 | -0.20 | 0.10 | 0.06 | 0.21 | 0.21 | -0.04 | -0.05 |
| Sensation avoiding | 0.19 | 0.37 | 0.56 | 0.78 | 0.09 | 0.11 | 0.15 | 0.04 | 0.29 | 0.22 | 0.14 | 0.01 |
| Low registration | 0.87 | 0.31 | 0.31 | 0.03* | 0.75 | 0.72 | 0.32 | 0.21 | 0.27 | 0.24 | 0.31 | 0.54 |
| Sensation seeking | 0.30 | 0.06 | 0.29 | 0.05 | 0.98 | 0.67 | 0.35 | 0.58 | 0.70 | 0.35 | 0.45 | 0.60 |
| Sensory sensitivity | 0.74 | 0.51 | 0.19 | 0.02* | 0.36 | 0.43 | 0.55 | 0.71 | 0.41 | 0.41 | 0.89 | 0.85 |
| Sensation avoiding | 0.26 | 0.03* | 0.02* | 0.00** | 0.73 | 0.66 | 0.38 | 0.83 | 0.26 | 0.40 | 0.58 | 0.96 |

Abbreviation: AASP: Adolescent/Adult Sensory Profile.

*$P < 0.05$; **$P < 0.01$. 

746 Kuno-Fujita et al. / Sensory processing patterns in autism INSAR
No significant differences were observed between the high and low subgroups (4 for the high, 15 for the low) in the TD group. In the ASD group (5 for the high, 13 for the low), the high subgroup showed higher right fusiform activity than that in the low subgroup ($t = -5.68$, $P < 0.001$). We have to note, however, that there were very few participants in the high subgroups (five ASD, four TD), and these results should be interpreted cautiously. Moreover, we should also mention that there were marginally significant differences in age ($t = -1.71$, $P = 0.11$) and Sensory Sensitivity scores ($t = -1.94$, $P = 0.07$) when demographic, behavioral, and psychological measures were compared between the ASD subgroups. The results of the subgroup analysis could have been affected by some background factors.

**Correlation Analysis Between Sensory Profile Scores and Symptom Severity**

Sensation Avoiding scores, which were associated with right fusiform activity, showed no significant correlation with symptom severity (ADI-R social score, $r = 0.20$, $P = 0.4$; ADI-R communication score, $r = 0.37$, $P = 0.1$; ADI-R stereotype score, $r = 0.19$, $P = 0.45$; ADOS social reciprocity + communication score, $r = 0.05$, $P = 0.9$).

**Discussion**

In the present study, we examined the relationships between neural responses to pictures of faces and the sensory processing patterns in individuals with ASD. The results showed a positive correlation between Sensation Avoiding scores and right fusiform activity in the ASD group but not in the TD group. We also demonstrated that the correlation value was higher for the ASD group than for the TD group.

The magnitude of the Sensation Avoiding score, by definition, indicates a low threshold for sensory stimulation and engagement in behaviors to avoid sensory stimuli [Brown & Dunn, 2002; Dunn, 1997]. Therefore, the positive correlation between Sensation Avoiding scores and right fusiform activity implies that the greater the tendency to avoid sensory stimulation, the stronger the neural responses to face stimuli in ASD. Previous reports have indicated no significant differences between individuals with ASD and TD individuals in fusiform gyrus activity when both groups were subjected to a face recognition task and instructed to look into the eyes [Hadjikhani et al., 2004; Lassalle et al., 2017]. Although we did not provide explicit instructions to look into the eye region in pictures, we conjectured that individuals with ASD who had greater sensory abnormalities may have focused on the eyes more rigorously, given the positive correlations between fusiform gyrus activity and the Sensation Avoiding trait. Furthermore, in the present study, all participants were instructed to observe and memorize the presented faces carefully in the one-back task. For this reason, participants may have been unable to remove their gaze from face stimuli, although those with high “Sensation Avoiding” traits may have a tendency to look away from others’ faces. This experimental manipulation may have influenced greater activity in the fusiform face area in ASD individuals with a greater Sensation Avoiding tendency.

In both the ASD and TD groups, we did not observe a relationship between sensory processing patterns and amygdala activity. However, Green et al. [2013] reported a relationship between sensory processing patterns and amygdala activity using an unpleasant auditory stimulation task. These contrasting results may be due to differences in the task modality. To date, research on face perception has recognized the fusiform gyrus and amygdala as key brain areas underscoring face perception. However, while we observed a significant correlation between sensory profile scores and right fusiform activity, no significant correlation was found for the amygdala. Therefore, it is conceivable that these two sites, namely fusiform gyrus and amygdala, play distinct roles in face perception. Furthermore, we used neutral expressions as the face stimuli, which may have contributed to the lack of increased brain activity in both groups.

In the Introduction, we described how individuals with ASD often exhibit local precedence over holistic processing, and this may be associated with abnormal face processing in ASD. The association between the Sensation Avoiding trait and right fusiform activity may be mediated by weakened global processing, but caution should be exercised when proposing such a causal
relationship. It is noteworthy that the ASD population exhibits considerable heterogeneity. Indeed, impaired global processing is not common across the entire ASD population [Simmons et al., 2009; Van der Hallen, Vanmarcke, Noens, & Wagemans, 2017]. Further studies are needed to investigate links between sensory processing patterns, local/global precedence in visual processing, and face processing in ASD.

Studies have reported that individuals with ASD show higher Sensation Avoiding scores than those of their TD counterparts [Crane et al., 2009]. It is thus possible that the association between abnormal sensory processing patterns and face-related brain activity is explained by the severity of ASD symptoms. However, Sensation Avoiding scores, which were associated with the right fusiform activity, showed no significant correlation with symptom severity. Moreover, the correlations of right fusiform activity with both ADI-R and ADOS scores were not significant, except for a marginal correlation with ADI-R social score ($r = 0.45, p = 0.06$). These results suggest that the Sensation Avoiding trait, rather than the overall severity of ASD symptoms, is associated with activity in the right fusiform face area in ASD.

Several studies have implicated abnormal face processing in ASD with social communication deficits, which is a core symptom of ASD [Schultz, 2005; Schultz et al., 2003; Webb, Neuhau, & Faja, 2017]. The present study demonstrated that activity in the fusiform face area was increased as a function of the tendency to avoid sensory stimulation in ASD. This indicates that ASD individuals with high Sensation Avoiding trait display more “TD-like” brain activity during face processing, especially when instructed to look at other’s faces carefully. It may be useful to explore treatment approaches focused on the Sensation Avoiding trait for social communication deficits, such as atypical eye contact.

Limitations

This study had several limitations. First, sensory processing patterns were evaluated based solely on a single subjective self-reported questionnaire in the present study. However, since the AASP is standardized and its reliability and validity have been confirmed [Crane et al., 2009; Hirashima et al., 2014], biases in the measurements were unlikely.

Second, the ASD group included four individuals with IQ scores in the 60s. Full-scale IQ could influence task performance in general, but the task accuracy of these four participants ranged between 85% and 90%, suggesting that they adequately understood the task requirements. Moreover, the correlation between right fusiform activity and Sensation Avoiding scores remained significant, even after adjusting for full-scale IQ.

Third, participants were recruited without considering sensory processing patterns. Previous research has identified significant differences between individuals with ASD and TD individuals regarding all quadrants in the AASP, but we only identified score differences for the Low Registration trait. For this reason, there were variations in the sensory processing patterns of participants, which may have made it difficult to observe a link between ASD and a specific brain function. Future research should refine recruitment by increasing the number of participants to reduce bias.

Finally, since our sample size was small, further studies with larger samples are needed. Despite these limitations, the present study contributes to our understanding of the neurobiological basis of ASD, as we provide the first evidence of an association between atypical sensory processing patterns and atypical fusiform activity during face processing, which may partly underlie abnormal face processing in ASD.

Acknowledgments

We would like to thank Mr. Hideto Yogo, Mr. Yuuta Nishimiya, and Mr. Yuuki Nishigaki from the Department of Radiology, Kojin Hospital for their technical assistance in MRI data acquisition. We would also like to thank Dr. Kaori Matsumoto from Kanazawa Institute of Technology for her help in clinical assessment using ADOS, and Professor Nori Takei of Hamamatsu University School of Medicine for helpful comments. We would like to thank Editage (http://www.editage.com) for editing and reviewing this manuscript for English language. This study was partly supported by Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (15H04771), and by the Joint Usage/Research Center of United Graduate School of Child Development, Osaka University, Kanazawa University, Hamamatsu University School of Medicine, Chiba University and University of Fukui.

Conflict of Interest

The authors declare no conflict of interest.

References

American Psychiatric Association. (2000). Diagnostic and Statistical Manual of Mental Disorders (4th ed.). Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th ed.). Washington, DC: American Psychiatric Association.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): Evidence from Asperger syndrome/high-functioning autism,
Brett, M., Anton, J. L., Valabregue, R., & Poline, J. B. (2002). Region of interest analysis using an SPM toolbox. Paper presented at the the 8th International Conference on Functional Mapping of the Human Brain, Sendai, Japan.

Brown, C., & Dunn, W. (2002). Adolescent/adult sensory processing. The American Journal of Occupational Therapy, 55(1), 75–82. https://doi.org/10.5014/ajot.55.1.75

Constantino, J. N., & Gruber, C. P. (2012). Social responsiveness scale (2nd ed.). Los Angeles, CA: Western Psychological Services.

Crane, L., Goddard, L., & Pring, L. (2009). Sensory processing in adults with autism spectrum disorders. Autism, 13(3), 215–228. https://doi.org/10.1177/1362361309103794

Drugeó, T. J., & D’Esposito, M. (2001). Activity in fusiform face area modulated as a function of working memory load. Brain Research Cognitive Brain Research, 10(3), 355–364. https://doi.org/10.1016/S0926-6410(00)00056-2

Dunn, W. (1997). The impact of sensory processing abilities on daily lives of young children and their families: A conceptual model. Infants and Young Children, 9(4), 23–35. https://doi.org/10.1097/00011633-199704000-00005

Eickhoff, S. B., Stephan, K. E., Mohlberg, H., Grefkes, C., Fink, G. R., Amunts, K., & Zilles, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. NeuroImage, 25(4), 1325–1335. https://doi.org/10.1016/j.neuroimage.2004.12.034

Fujisawa, T., Inohara, K., Okamoto, Y., Masuya, Y., Ishii, T., Saito, D. N., ... Kosaka, H. (2016). Gazefinder as a clinical supplementary tool for discriminating between autism spectrum disorder and typical development in male adolescents and adults. Molecular Autism, 7, 19. https://doi.org/10.1186/s13229-016-0083-y

Green, S. A., Rudie, J. D., Colich, N. L., Wood, J. J., Shirinyan, D., Hernandez, L., ... Bookheimer, S. Y. (2013). Overreactive brain responses to sensory stimuli in youth with autism spectrum disorders. Journal of the American Academy of Child and Adolescent Psychiatry, 52(11), 1158–1172. https://doi.org/10.1016/j.jaac.2013.08.004

Gross, T. F. (2005). Global-local precedence in the perception of facial age and emotional expression by children with autism and other developmental disabilities. Journal of Autism and Developmental Disorders, 35(6), 773–785. https://doi.org/10.1007/s10803-005-0023-8

Hadjikhani, N., Joseph, R. M., Snyder, J., Chabris, C. F., Clark, J., Steele, S., ... Tager-Flusberg, H. (2004). Activation of the fusiform gyri when individuals with autism spectrum disorder view faces. NeuroImage, 22(3), 1141–1150. https://doi.org/10.1016/j.neuroimage.2004.03.025

Happé, F., & Frith, U. (2006). The weak coherence account: Detail-focused cognitive style in autism spectrum disorders. Journal of Autism and Developmental Disorders, 36(1), 5–25. https://doi.org/10.1007/s10803-005-0039-0

Hirashima, T., Ito, H., Iwanaga, R., Hagiiwara, T., Tani, I., Yukihiro, R., ... Tsujii, M. (2014). Construct validity of the Japanese version of the Adolescent/Adult Sensory Profile in the assessment of individuals with autism spectrum disorder [in Japanese]. Seishinigaku, 56(2), 123–132.

Jao Keehn, R. J., Sanchez, S. S., Stewart, C. R., Zhao, W., Grenesko-Stevens, E. L., Keehn, B., & Muller, R. A. (2017). Impaired downregulation of visual cortex during auditory processing is associated with autism symptomatology in children and adolescents with autism spectrum disorder. Autism Research, 10(1), 130–143. https://doi.org/10.1002/aur.1636

Lassalle, A., Asberg Johnels, J., Zurcher, N. R., Hippolyte, L., Billstedt, E., Ward, N., ... Hadjikhani, N. (2017). Hypersensitivity to low intensity fearful faces in autism when fixation is constrained to the eyes. Human Brain Mapping, 38(12), 5943–5957. https://doi.org/10.1002/hbm.23800

Leekam, S. R., Nieto, C., Libby, S. J., Wing, L., & Gould, J. (2007). Describing the sensory abnormalities of children and adults with autism. Journal of Autism and Developmental Disorders, 37(5), 894–910. https://doi.org/10.1007/s10803-006-0218-7

Lord, C., Rutter, M., Goode, S., Heemsbergen, J., Jordan, H., Mawhood, L., & Schopler, E. (1989). Autism diagnostic observation schedule: A standardized observation of communicative and social behavior. Journal of Autism and Developmental Disorders, 19(2), 185–212. https://doi.org/10.1007/BF02211841

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. Journal of Autism and Developmental Disorders, 24(5), 659–685. https://doi.org/10.1007/BF02172145

Nomi, J. S., & Uddin, L. Q. (2015). Face processing in autism spectrum disorders: From brain regions to brain networks. Neuropsychologia, 71, 201–216. https://doi.org/10.1016/j.neuropsychologia.2015.03.029

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. Neuropsychologia, 9(1), 73–113. https://doi.org/10.1016/0028-3932(71)90067-4

Pierce, K., Muller, R. A., Ambrose, J., Allen, G., & Couchesne, E. (2001). Face processing occurs outside the fusiform 'face area' in autism: Evidence from functional MRI. Brain, 124( Pt 10), 2059–2073. https://doi.org/10.1093/brain/124.10.2059

Schultz, R. T. (2005). Developmental deficits in social perception in autism: The role of the amygdala and fusiform face area. International Journal of Developmental Neuroscience, 23(2–3), 125–141. https://doi.org/10.1016/j.ijdevneu.2004.12.012

Schultz, R. T., Gauthier, I., Klin, A., Fulbright, R. K., Anderson, A. W., Volkmar, F., ... Gore, J. C. (2000). Abnormal ventral temporal cortical activity during face discrimination among individuals with autism and Asperger syndrome. Archives of General Psychiatry, 57(4), 331–340. https://doi.org/10.1001/archpsyc.57.4.331

Schultz, R. T., Grelotti, D. J., Klin, A., Kleinman, J., Van der Gaag, C., Marois, R., & Skudlarski, P. (2003). The role of the
fusiform face area in social cognition: implications for the pathobiology of autism. Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 358(1430), 415–427. https://doi.org/10.1098/rstb.2002.1208
Shah, A., & Frith, U. (1983). An islet of ability in autistic children: A research note. Journal of Child Psychology and Psychiatry, 24(4), 613–620. https://doi.org/10.1111/j.1469-7610.1983.tb00137.x
Shah, A., & Frith, U. (1993). Why do autistic individuals show superior performance on the block design task? Journal of Child Psychology and Psychiatry, 34(8), 1351–1364. https://doi.org/10.1111/j.1469-7610.1993.tb02095.x
Simmons, D. R., Robertson, A. E., McKay, L. S., Toal, E., McAleer, P., & Pollick, F. E. (2009). Vision in autism spectrum disorders. Vision Research, 49(22), 2705–2739. https://doi.org/10.1016/j.visres.2009.08.005
Stevenson, R. A., Sun, S. Z., Hazlett, N., Cant, J. S., Barense, M. D., & Ferber, S. (2018). Seeing the forest and the trees: Default local processing in individuals with high autistic traits does not come at the expense of global attention. Journal of Autism and Developmental Disorders, 48(4), 1382–1396. https://doi.org/10.1007/s10803-016-2711-y
Stewart, C. R., Sanchez, S. S., Grenesko, E. L., Brown, C. M., Chen, C. P., Keehn, B., ... Muller, R. A. (2016). Sensory symptoms and processing of nonverbal auditory and visual stimuli in children with autism spectrum disorder. Journal of Autism and Developmental Disorders, 46(5), 1590–1601. https://doi.org/10.1007/s10803-015-2367-z
Tomchek, S. D., & Dunn, W. (2007). Sensory processing in children with and without autism: A comparative study using the short sensory profile. The American Journal of Occupational Therapy, 61(2), 190–200. https://doi.org/10.5014/ajot.61.2.190
Van der Hallen, R., Vanmarcke, S., Noens, I., & Wagemans, J. (2017). Hierarchical letters in ASD: High stimulus variability under different attentional modes. Journal of Autism and Developmental Disorders, 47(6), 1854–1865. https://doi.org/10.1007/s10803-017-3108-2
Webb, S. J., Neuhaus, E., & Faja, S. (2017). Face perception and learning in autism spectrum disorders. Quarterly Journal of Experimental Psychology (Hove), 70(5), 970–986. https://doi.org/10.1080/17470218.2016.1151059
Wechsler, D. (1997). Wechsler Adult Intelligence Scale (3rd ed.). San Antonio: The Psychological Corporation.
Weigelt, S., Koldewyn, K., & Kanwisher, N. (2012). Face identity recognition in autism spectrum disorders: A review of behavioral studies. Neuroscience and Biobehavioral Reviews, 36(3), 1060–1084. https://doi.org/10.1016/j.neubiorev.2011.12.008