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Autistic traits modulate the activity of the ventromedial prefrontal cortex in response to female faces

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ABSTRACT

Previous findings have revealed abnormal visual attention or processing of faces among individuals with autism spectrum condition (ASC). However, little attention has been paid to the relationship between autistic traits and neural mechanisms associated with representing facial values. Using fMRI, we investigated the patterns of brain activity in the vmPFC and VS in response to faces of elderly males, elderly females, young males, and young females. During fMRI, subjects with a relatively high autism quotient (high group) and those with a relatively low autism quotient (low group) were presented with a face and asked to rate its pleasantness. After fMRI, the subjects were presented with pairs of faces and asked to select the face that they preferred. Our results indicate a dissociable modulatory effect of autistic traits on the vmPFC and VS: The vmPFC activity in the low group was more sensitive to age differences in female faces compared to that in the high group, whereas VS activity did not show differences between groups. These results suggest that, in the BVS, autistic traits selectively modulate the vmPFC activity associated with facial value representation.

1. Introduction

Autism spectrum condition (ASC) is characterized by difficulties in social communication and restricted interest and is more prevalent in males than females (Baron-Cohen et al., 2011; Fombonne, 2009). In daily social interactions, we more or less adapt our behavior by evaluating others' feelings and thoughts according to their facial expressions and behaviors. Thus, unveiling potential abnormalities in social cognition in ASC and finding evidence of these abnormalities is of great importance. In recent decades, the amount of research focusing on the characteristics of ASC has increased exponentially, and several aspects of the deficits seen in ASC have been highlighted (Baron-Cohen and Belmonte, 2005). To date, many theoretical models have been made to account for the social impairments in ASC (Baron-Cohen, 2002; Baron-Cohen and Belmonte, 2005; Dawson et al., 2005; Frith and Happe, 1994; Pelphrey et al., 2011). Among these models, the social motivation theory postulates that the deficits in social motivation during the early period of life prevent typical development of social cognition and can lead to diminished face processing (Dawson et al., 2005; Mundy and Neal, 2001).

Consistent with this view, an increasing number of behavioral and eye-tracking studies have shown abnormalities in visual attention or processing of faces, as revealed by a lower accuracy in facial emotion recognition tasks (Bal et al., 2010; Baron-Cohen et al., 2009; Evers et al., 2015; Fridenson-Hayo et al., 2016), shorter fixation time for faces (Dalton et al., 2005; Klin et al., 2002; Shi et al., 2015), and preference for objects rather than faces (Sasson and Touchstone, 2014) in ASC. Along with these findings, hypoactivation of regions responsible for visual (*e.g.*, the fusiform gyrus) and emotional (*e.g.*, the amygdala) processing of faces has been repeatedly shown in previous studies using fMRI (Corbett et al., 2009;

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Dalton et al., 2005; Grelotti et al., 2005; Hall et al., 2010; Humphreys et al., 2008; Pierce and Redcay, 2008).

More recently, several studies employed tasks requiring subjects to combine social and reward-related information with computational modeling (Sevgi et al., 2016), with event-related potentials (Stavropoulos and Carver, 2014), or with fMRI (Balsters et al., 2017; Dichter et al., 2012; Scott-Van Zeeland et al., 2010). Those studies have revealed a deterioration in performance in ASC individuals or individuals with relatively high autistic traits. For example, Sevgi et al. (2016) used a novel reward learning task combined with a social gaze cue and showed that individuals with high autistic traits specifically failed to efficiently utilize information from gaze shifting of a target face during learning. Moreover, Scott-Van Zeeland et al. (2010) revealed reduced activity in the frontostriatal network for smiling faces, and Kohls et al. (2013) revealed a dysfunction in the vmPFC and VS in reward processing (Kohls et al., 2013; Scott-Van Zeeland et al., 2010). Taking the above findings together with findings from psychological studies, there is a possibility that high autistic traits negatively affect facial value processing in the vmPFC and VS.

When we are presented with faces, subjective values are automatically assigned to each face, and these value signals guide subsequent preferential choices (Ito et al., 2015; Lebreton et al., 2009). Previous fMRI studies have repeatedly shown that the vmPFC and the VS underlie these processes (Bartra et al., 2013; Camille et al., 2011; Chib et al., 2009; Hare et al., 2008; Kim et al., 2011; Knutson et al., 2005; Lebreton et al., 2009; McNamee et al., 2013; Pessiglione et al., 2008; Wunderlich et al., 2012) and are called the "Brain Valuation System" (BVS) (Lebreton et al., 2009). To date, although prior ASC studies have delineated important features of ASC, such as abnormal visual attention, hypoactivation of visual areas, and abnormal reward processing, little attention has been paid to whether and how autistic traits affect BVS function for representing facial values.

Thus, the main purpose of the present study was to disentangle the relationship between the value representation of the BVS for faces and autistic traits. To address this issue, we used the faces of elderly males, elderly females, young males, and young females as experimental stimuli, which enabled us to systematically investigate whether the sensitivity of the BVS to the age and gender of facial stimuli was modulated by autistic traits. Because a previous fMRI meta-analysis (Di Martino et al., 2009) and MRI studies focusing on white matter structure (Barnea-Goraly et al., 2004; Samson et al., 2016) highlighted functional and structural abnormalities of the vmPFC in ASC, we hypothesized that modulation effects of autistic traits on the BVS would be stronger in the vmPFC than in the VS.

2. Experimental procedures

2.1. Subjects

Based on previous evidence indicating that autistic traits are distributed on a continuum across the general population and that a similar etiology has been found across the neurotypical and diagnostic population (Robinson et al., 2011), we employed neurotypical participants. This experimental approach of employing typically developing subjects enables us to make inferences about the etiology of autistic traits without potential confounding variables from various comorbid conditions often noted in patients with autistic spectrum disorders (Sevgi et al., 2016). Fifty-two neurotypical, young male volunteers (age range: 20–27 years; mean age: 21.8 years) with no history of neurological disease participated in this study. No pathological findings in the brains of the participants were identified using magnetic resonance imaging (MRI). All subjects had normal or corrected-to-normal vision and declared that they were heterosexual. After the subjects received a detailed description of the study, they provided written informed consent in accordance with the Declaration of Helsinki, and the guidelines were approved by the Ethical Committee of Hokkaido University. All subjects answered the Japanese version of the Autism-Spectrum Quotient (AQ) (Baron-Cohen et al., 2001). Based on the score, subjects were classified into the high group, in which individuals had a relatively high autism quotient (range, 18–31; mean score, 22.63), or the low group, in which individuals had a relatively low autism quotient (range, 4–16; mean score, 10.75), using a median split procedure (median score = 17). The data of four subjects whose AQ scores were 17 were used in whole brain analyses but were excluded from behavioral and region-of-interest (ROI) analyses. There was a significant difference in the AQ score between the high and low groups ($t(46) = 11.705$, $p < 0.001$). There was no significant difference in age ($t(46) = 0.33$, $p = 0.74$), education ($t(46) = 0.106$, $p = 0.92$), or IQ ($t(46) = 0.74$, $p = 0.47$) as measured by the Japanese version of the National Adult Reading Test (JART) (Matsuoka et al., 2006) between the two groups.

2.2. Stimuli

We employed the stimulus set used in the previous study (Ito et al., 2016). Sixty-four elderly males (age range, 61–79; mean age, 71.4 years), 64 elderly females (age range, 62–79; mean age, 69.1 years), 64 young males (age range, 20–28; mean age, 22.2 years), and 64 young females (age range, 20–28; mean age, 21.8 years) volunteers were recruited to pose for facial photographs. These volunteers were informed that the photographs would be used for research purposes only, and they provided written informed consent. The photographs were captured using a Panasonic DMC-LX2 digital camera with a flash and a resolution of 1920×1080 pixels. The photographed individuals were asked to present a neutral facial expression and to look directly into the camera. All images were subsequently downloaded onto a computer and edited in Adobe Photoshop CS5.1 and Adobe Illustrator CS5.1 (San Jose, CA, USA) to produce greater uniformity across the photographs. The photographs were also resized to 720×540 pixels. A separate group of 13 young volunteers (7 females and 6 males; age range, 18–25 years; mean age, 20.2 years) who did not participate in the fMRI study rated the 256 facial photographs using a 10-point scale for pleasantness. The mean pleasantness score was ranked within the four stimulus groups (*i.e.*, elderly males, elderly females, young males, and young females). Within each stimulus group, the photographs ranked "n" (n = 1–32) were paired with the photographs ranked "n + 32," which resulted in 32 pairs of photographs per group.

2.3. Experimental design

The experiment consisted of two tasks: the pleasantness rating task during the fMRI scan and the choice task after the fMRI scan. For the pleasantness rating task during the fMRI scan, 256 face photographs were presented in a random order. Each stimulus was presented for 2.5 s, and the inter-stimulus interval, during which a fixation cross was constantly presented, ranged between 3.5 and 11.5 s to maximize the efficiency of the event-related design (Dale, 1999). The pleasantness rating task was divided into four consecutive runs, each lasting approximately 10 min. The subjects were asked to rate each face based on how pleasant or unpleasant it was using an 8-point scale. The responses were counterbalanced with a Likert scale direction (1 = very unpleasant and 8 = very pleasant or vice versa). The choice task was performed outside the scanner immediately after the fMRI scan. The 128 pairs of photographs were displayed as two side-by-side photographs, and the subjects

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