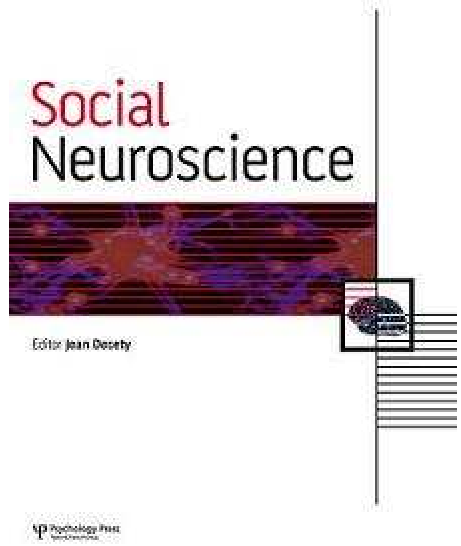

Emotional responses associated with self-face processing in individuals with autism spectrum disorders: An fMRI study

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Keywords:	Autism spectrum disorders, fMRI, Insular cortex, Posterior cingulate cortex, Self-face evaluation

Emotional responses associated with self-face processing in individuals with autism spectrum disorders: An fMRI study

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ABSTRACT

Individuals with autism spectrum disorders (ASD) show impaired emotional responses to self-face processing, but the underlying neural bases are unclear. Using functional magnetic resonance imaging, we investigated brain activity when 15 individuals with high-functioning ASD and 15 controls rated the photogenicity of self-face images and photographs of others' faces. Controls showed a strong correlation between photogenicity ratings and extent of embarrassment evoked by self-face images; this correlation was weaker among ASD individuals, indicating a decoupling between the cognitive evaluation of self-face images and emotional responses. Individuals with ASD demonstrated relatively low self-related activity in the posterior cingulate cortex (PCC), which was related to specific autistic traits. There were significant group differences in the modulation of activity by embarrassment ratings in the right insular (IC) and lateral orbitofrontal cortices. Task-related activity in the right IC was lower in the ASD group. The reduced activity in the right IC for self-face images was associated with weak coupling between cognitive evaluation and emotional responses to self-face images. The PCC is responsible for self-referential processing, and the IC plays a role in emotional experience. Dysfunction in these areas could contribute to the lack of self-conscious behaviors in response to self-reflection in ASD individuals.

INTRODUCTION

Patients with autistic spectrum disorders (ASD) have core impairments in social reciprocal interaction, abnormal development and use of language, repetitive and ritualized behaviors, and a narrow range of interests (Asperger, 1944; Kanner, 1943). These social and communication impairments are related to their difficulties in interpreting and inferring others' feelings, intentions, and beliefs (i.e., mentalizing). To date, behavioral and neural impairments in the understanding of others have been extensively studied in individuals with ASD. Noninvasive neuroimaging studies have found that individuals with ASD show hypoactivation of crucial components of the brain system involved in mentalizing — such as the medial prefrontal cortex (MPFC) and superior temporal sulcus (STS) — when they perform "theory of mind" tasks, which require the inference of others' emotions and beliefs (Happé et al., 1996; Nieminen-von Wendt et al., 2003; Wang, Lee, Sigman, & Dapretto, 2006, 2007).

In addition, recent studies have begun to explore the neural substrates for self-related processing in individuals with ASD. The self is a complex construct, which comprises multiple aspects rather than being unitary (Cacioppo & Decety, 2011; Northoff et al., 2006; Uddin, 2011). More than a century ago, William James distinguished between a physical self, a mental self, and a spiritual self. This early conceptual distinction set the stage for later work examining multiple dimensions of the self (Damasio, 1999; Gallagher, 2000; Gillihan & Farah, 2005; Neisser, 1995). Gillihan and Farah (2005) proposed a distinction between the physical and psychological aspects of the self. The physical self refers to the domain of the body, which could correspond to William James's description of the physical self. In contrast, the psychological self encompasses knowledge of the self, including that based on episodic and semantic memory, as well as first-person perspective of the self. This proposed distinction has been demonstrated in recent neuroimaging studies, which suggest that physical or embodied self-related processes and psychological or internal self-related processes rely on distinct brain networks (Lieberman, 2007; Uddin, Iacoboni, Lange, & Keenan, 2007). The majority of neuroimaging research on ASD has focused on introspection and internal aspects of the self. These studies have reported that individuals with ASD show reduced activation in cortical midline structures including the MPFC and CC (Chiu et al., 2008; Kennedy & Courchesne, 2008; Kennedy, Redcay, & Courchesne, 2006; Lombardo et al., 2010; Silani et al., 2008). Yet, to our knowledge, only one study has focused on the processing of physical aspects of the self in ASD (Uddin et al., 2008). Uddin and colleagues investigated brain activity while making self/other judgments about images of faces, and demonstrated that the right prefrontal areas involved in processing self-information in the sensory domain exhibited typical patterns of activation in children with ASD. In line with these findings, previous behavioral studies revealed that autistic children showed no deficits in self-recognition (Akagi, 2003; Dawson & McKissick, 1984; Spiker & Ricks, 1984). However, the authors also noted that the autistic children showed differences in responses to self-reflection compared with controls. Some of the control children demonstrated self-conscious or coy behavior, such as expressions of embarrassment, upon seeing their own reflections. These behaviors can arise in response to self-reflection when individuals experience self-conscious emotions. By contrast, autistic children showed relatively neutral responses to self-reflection. Despite several previous studies suggesting a lack of self-conscious behaviors in response to self-reflection in ASD, little is known about the specific brain mechanisms underlying these phenomena.

Here, we investigated the behavioral and neural responses associated with self-face processing in individuals with ASD, specifically focusing on the psychological aspects of self-face processing. We adopted a functional magnetic resonance imaging (fMRI) experimental design used in a previous study, in which healthy adults evaluated the attractiveness of photographs of their own faces and those of others (Morita et al., 2008). Emotional perturbation was introduced using facial feedback images chosen from video recordings, some of which deviated significantly from standard expressions. When human adults are exposed to self-feedback images, they automatically experience negative emotions (i.e., embarrassment), especially if the images deviate substantially from their mental representations of ideals or standards (Carver & Scheier, 1981, 1998; Duval & Wicklund, 1972). This type of embarrassment is therefore closely associated with self-evaluative processing. We predicted that the cognitive evaluation of self-face images would be tightly coupled with the extent of the embarrassment that they evoked. Correspondingly, our previous study showed that healthy individuals reported greater embarrassment in response to self-face images than those of others, the extent of which strongly correlated with the results of self-evaluation (Morita et al., 2008).

Here we investigated whether individuals with ASD showed typical emotional responses during self-face evaluation. We also looked for abnormalities in the brain system subserving self-face evaluation in individuals with ASD. We separately specified brain regions showing group differences in self-related processing and group differences specific to emotional processing. In order to identify group differences in self-related processing, we assessed the averaged activity (mean response) elicited by self-face images and those of others. By contrast, in order to identify group differences specific to emotional processing, we assessed the neural modulation based on the extent of embarrassment (parametric modulation). In brain areas showing these group differences, we then tested whether the activation patterns were related to behavioral patterns or individual autistic traits that represent the core features of ASD using a region-of-interest (ROI) approach. As an index of individual autistic traits, we used the Autism Spectrum Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), which can also be applied to assess milder variants of autistic-like traits in individuals.

MATERIALS AND METHODS

Participants

Fifteen individuals with high-functioning ASD (14 males and 1 female; mean age ± standard deviation [SD] = 23.7 ± 4.3 years; age range = 18–33 years) were recruited at the Department of Neuropsychiatry of the University of Fukui Hospital, Japan, and the Department of Psychiatry and Neurobiology of the Kanazawa University Hospital, Japan (Table 1).

The authors (H.K. and T.M.) diagnosed the participants based on the classifications described in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychological Association, 2000) and on standardized criteria taken from the Diagnostic Interview for Social and Communication Disorders (DISCO; Wing, Leekam, Libby, Gould, & Larcombe, 2002). The DISCO is reported to have good psychometric properties (Nygren et al., 2009; Posserud, Lundervold, & Gillberg, 2009). It also contains items on early development, and a section on activities of daily life, thereby giving the interviewer an idea of the level of functioning in several different areas, not only social functioning and communication (Posserud et al., 2009). The ASD group consisted of 5 participants with autistic disorder and 10 with Asperger syndrome. Fifteen age-matched and intelligence quotient (IQ)-matched control participants (13 males and 2 females; mean age ± SD = 23.3 ± 3.6 years; age range = 18–33 years) were recruited from the local community (Table 1). Participants were excluded if they had a history of major medical or neurological illness including epilepsy, significant head trauma, or a lifetime history of alcohol or drug dependence. They were screened to exclude individuals who had a first-degree relative with an axis I disorder, based on the DSM-IV criteria. IQ assessments were carried out using the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997). All of the participants had full-scale IQ scores > 85 (Table 1). To quantify autistic traits, we used the AQ (Baron-Cohen et al., 2001), which consists of the following five subscales: social skills, attention switching, attention to detail (AD), communication, and imagination (Table 2). Although the AQ score (mean ± SD = 33.2 ± 4.5 for the ASD group and 15.4 ± 6.2 for the control group) is not diagnostic, this measure is a useful support for diagnosis because it has been validated in a clinical sample

(Woodbury-Smith, Robinson, Wheelwright, & Baron-Cohen, 2005). All of the participants with ASD, but none in the control group, scored above the cut-off point of 26 for Asperger syndrome or high-functioning autism (Woodbury-Smith et al., 2005). The participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971), with the exception of two participants with ASD (one of whom was left-handed and the other ambidextrous). The protocol used for this study was approved by the Ethics Committee of the University of Fukui. After a complete explanation of the study, all of the participants gave written informed consent prior to participation.

Materials

The experiment took place over 2 days. On the first day, the participants made short speeches in front of a video camera. The subjects were informed that the purpose of the recording was to investigate the eye movements that occur when a person speaks, rather than being told the true aim of the study. Each participant wore a plain black T-shirt, and sat in a chair positioned opposite the camera and the experimenter. Participants wearing glasses were required to remove them. Initially, the participants were asked to answer mathematical quiz questions, and to say some familiar Japanese tongue twisters as quickly as possible for the video camera. After that, the participants were asked to answer interview-style questions about one of their hobbies for 1–2 min. Recordings of each participant's face were made throughout these speeches. Twenty-one black-and-white pictures of each participant's face, with ratings ranging from "good" ("attractive") to "bad" ("unattractive"), were selected from the recorded video images by the experimenter. The face images were rated as to whether each of the following items was attractive or unattractive: eyes, mouth, chin, and overall. Each item was scored on a five-point scale, and a total score was calculated for each image. The averages of the 21 scores were matched between the groups (control group, mean ± SD = 13.1 ± 0.25; ASD group, mean ± SD = 13.0 ± 0.25). An image in which the participant had an awkward facial expression (e.g., eyes rolled back or mouth wide open) was considered "bad"; by contrast, an image in which it appeared as if the participant had posed for a photograph, rather than it having been taken from a video recording, was considered "good". Twenty-one images per participant were used as the stimuli for the SELF condition. By contrast, in the OTHERS condition, we used 21 face images that were selected from three gender-matched unfamiliar individuals (seven images per person).

fMRI experimental procedure and design

A few weeks after the video-recording session, the participants underwent fMRI scanning. The fMRI experimental procedure was similar to that used in our previous fMRI study (Morita et al., 2008), except for the response method. During the fMRI scanning, the participants were asked to evaluate images of either their own face or faces of others. The participants lay in the fMRI scanner with their heads immobilized using an elastic band and sponge cushions, and with their ears plugged. Stimulus presentation was performed using Presentation 9.9 (Neurobehavioral Systems, Albany, CA). Visual stimuli were presented on a projection screen and viewed by the participants through a mirror mounted on the head coil. Participants completed four runs, each lasting 285 s. In each run, 21 images of the participant's own face (SELF condition), 21 images of others' faces (OTHERS condition), and seven "null events" in which no stimulus was shown, were presented in a pseudorandom order. Each face stimulus appeared in the center of the screen for 3 s. The participants were instructed to keep still during the presentation of the stimulus. Once the stimulus had disappeared, Japanese text prompting the participants to respond appeared in the center of the screen for 2 s, and was followed by a blank screen for 1 s. During the response period, the participants were required to evaluate how photogenic each face was on a scale ranging from 1 ("very bad") to 5 ("very good"). We used a five-point scale, instead of the seven-point scale reported in our previous study, in order to allow the individuals with ASD to accomplish the task without difficulty.

Additionally, the participants indicated their responses by holding up the relevant number of fingers, instead of using the five-button key-press device described in our previous study. Before the scanning session, all participants performed a practice task to familiarize themselves with the response method. The behavioral responses were recorded by a digital video camera set up in the fMRI room, and manually recorded by an experimenter positioned out of sight of the participants in the MRI room. We used the same rapid event-related design as that employed in our previous study (Morita et al., 2008).

Psychological measurements

Immediately following scanning, the participants performed a self-paced rating task, in which the same stimuli were used as those in the fMRI session. Participants sat on a chair in front of a 19-inch liquid crystal display (LCD) monitor (with their eyes ~60 cm from the monitor). In the rating task, each face stimulus subtended a visual angle of 14.3° and was arranged at the top of the screen, and seven buttons were located at the bottom of the screen. In the first trial, participants were asked to rate the images as to "how photogenic they appeared" on a scale ranging from 1 ("very bad") to 7 ("very good"). The photogenicity scores of the images were rated outside the MRI scanner, in order to ensure the reliability of the data measured inside the scanner. In the second trial, participants were asked to provide embarrassment scores (i.e., “How embarrassed do you feel when viewing each face?”) on a scale ranging from 1 (“not at all embarrassed”) to 7 (“very embarrassed”). We used the embarrassment scores as parametric covariates in our fMRI analysis (Büchel et al., 2002; Phan et al., 2003). In both trials, the participants rated each face stimulus by clicking on the relevant score using a computer mouse.

Following the rating task, the participants were asked to complete self-report questionnaires, including the Japanese version of the self-consciousness scale (Fenigstein, Scheier, & Buss, 1975; Sugawara, 1984), and the other-consciousness scale (Tsuji, 1993). The self-consciousness scale measures the tendency to be aware of both the publicly-displayed and the covert and hidden aspects of the self. The other-consciousness scale measures the tendency to care about others, and includes the following three subscales: the internal aspect, the external aspect, and the fantastic aspect.

MRI scanning procedure

Functional images were acquired using T2*-weighted gradient-echo echo-planar imaging (EPI) sequences with a 3-T MR imager (Signa Horizon; General Electric Medical Systems, Milwaukee, WI, USA) and a standard birdcage head coil. There were four fMRI runs, during each of which 95 volumes were acquired. Each volume consisted of 42 slices, with a thickness of 3 mm and a 0.5-mm gap, in order to cover the entire brain. The time interval between each two successive acquisitions of the same slice (TR) was 3,000 ms, with an echo time (TE) of 30 ms and a flip angle (FA) of 85°. The field of view (FOV) was 192 × 192 mm and the matrix size was 64 × 64, giving voxel dimensions of 3 × 3 mm. For anatomical reference, three-dimensional (3D) inversion-prepared spoiled gradient-echo (IR-SPGR) images (TR = 11.284 ms; TE = 5.252 ms; FA = 10°; matrix size = 256 × 256; slice thickness = 1.6 mm; a total of 244 transaxial images) were obtained as a high-resolution anatomical reference for each subject.

Behavioral data analysis

Behavioral data analysis was carried out using SPSS version 16.0J software (SPSS Japan, Tokyo, Japan). To compare the photogenicity ratings or embarrassment ratings for each condition and within each group, a two-way analysis of variance (ANOVA) with face type (SELF, OTHERS) × group (Control, ASD) was performed on the average ratings. To investigate the relationship between the photogenicity ratings and the embarrassment ratings, we calculated the correlation coefficient (r) between the two scores and transformed it into a Fisher's z coefficient. Questionnaire data were analyzed with *t*-tests to compare the control and ASD groups. The results were considered statistically significant at $p < .05$.

MRI data analysis

The first three volumes of each fMRI session were discarded because of unsteady magnetization, and the remaining 92 volumes per session were used for analysis. Image and statistical analyses were performed using Statistical Parametric Mapping (SPM5; The Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab 7.7 (Mathworks, Sherborn, MA). Initially, we used slice-timing correction to adjust for differences in slice-acquisition times. We interpolated and re-sampled the data so that, for each time series, the slices were acquired at the same time as the reference slice, which was the middle slice. These images were then realigned to correct for dislocations caused by head motion. The realigned images were normalized to the Montreal Neurological Institute (MNI) atlas (Evans, Kamber, Collins, & MacDonald, 1994). Finally, the anatomically normalized fMRI images were filtered using a Gaussian kernel with a full width at half maximum of 8 mm in the x, y, and z axes.

After preprocessing, the task-related activation was evaluated using the general linear model (GLM; Friston et al., 1995; Worsley & Friston, 1995). In the single-subject analyses, the design matrix contained two task-related regressors (the SELF and OTHERS conditions), two regressors for parametric modulation (the embarrassment scores for each condition), one regressor for motor responses, and one constant term (for a more detailed explanation of the regressors see Morita et al., 2008). We used a high-pass filter, which was composed of the discrete cosine basis function with a cut-off period of 128 s, in order to eliminate the artifactual low-frequency trend. Serial autocorrelation assuming a first-order autoregressive model was estimated from the pooled active voxels using the restricted maximum likelihood (ReML) procedure, and was used to whiten the data and the design matrix (Friston et al., 2002). The estimated parameters were calculated by performing least-squares estimation on the high-pass filtered and pre-whitened data and design matrix. The weighted sum of the parameter estimates in the individual analyses constituted contrast images that were used for the second-level analysis. We constructed appropriate contrast images for the mean response in order to examine the brain areas showing the main effects of condition in each group. Similarly, we produced contrast images for parametric modulation, which identified the brain areas in which activity covaried with the subjective embarrassment ratings for self-face images or those of others within each group.

In the second-level analysis, a two-way ANOVA, with group (Control, ASD) as a between-subject factor and face type (SELF, OTHERS) as a within-subject factor, was performed separately for the mean response and the parametric modulation according to embarrassment ratings, using the contrast images specified above. Both analyses searched for brain regions showing a significant interaction between group and face type. For these whole-brain analyses, we applied a statistical height threshold of $p < .005$ ($T > 2.67$) and an extent threshold of $p < .05$, corrected for multiple comparisons. Finally, using an ROI approach, a correlation analysis was performed with the individual psychological measurements. We identified ROIs as spheres with 8-mm radii centered on the maximal foci of activation using an interaction contrast between group and face type for the whole-brain analyses, and extracted the individual parameter estimates for the mean response in each condition for each ROI. Initially, as for the brain regions showing group differences in self-related processing, we tested whether the differences in activities between the conditions (SELF–OTHERS) were related to the strength of the relationship (coupling strength) in individual subjects between the photogenicity scores and the embarrassment ratings or autistic traits using the AQ scores in each ROI. Next, as for the brain regions showing group differences specific to emotional processing, we tested whether the activities in response to self-face images were related to the coupling strength between the photogenicity and the embarrassment ratings or autistic traits using the AQ scores in each ROI.

RESULTS

Behavioral performance

The photogenicity ratings for the self-face images and those of others were measured both during and after the fMRI session, in order to ensure the reliability of the data recorded in the scanner. Despite differences in the point-scale scores, the two measurements were strongly correlated for both the control group (SELF, r = .863 and OTHERS, r = .811) and the ASD group (SELF, r = .769 and OTHERS, r = .781). Figure 1 shows the range of photogenicity ratings measured during the fMRI session. A two-way ANOVA with face type (SELF, OTHERS) × group (Control, ASD) revealed no significant main effect of either factor, and no significant interaction between the two factors. The average embarrassment ratings measured outside the scanner are shown in Fig. 2. A two-way ANOVA with face type (SELF, OTHERS) × group (Control, ASD) revealed a significant main effect of face type [$F(1, 82) = 9.31$, $p < .01$], indicating that, on average, participants reported greater embarrassment in response to self-face images than those of others. By contrast, as with the photogenicity ratings, there was no significant group difference in the embarrassment ratings.

(Figures 1, 2 about here)

We then investigated the relationship between the photogenicity ratings measured inside the scanner and the embarrassment ratings measured outside the scanner, by calculating the Fisher's z-transformed correlation coefficients between the two ratings for each individual (Fig. 3). There was a significantly weaker correlation between these two ratings for self-face images in the ASD group compared with the control group ($p < .01$). In the OTHERS condition, the group difference did not reach statistical significance ($p = .08$). These results indicate that, compared with the control group, the ASD group showed weaker coupling between the two psychological ratings for faces, especially self-face images. Despite this group difference, the correlation coefficients for the SELF condition and the OTHERS condition were not significantly related to the individual total AQ scores (r = .349 and .263, respectively, $p > .05$ for both). We used the score of the normalized correlation coefficient as an indicator of the coupling strength between the two ratings in the imaging data analysis.

Table 2 shows the group mean scores from the questionnaires. There was no significant difference between the two groups for the self-consciousness scale or the other-consciousness scale.

(Figure 3 about here)

Imaging data

We initially identified the differences in mean response between the conditions in each group (Table 3 and Fig. 4). In the control group, the SELF versus OTHERS contrast revealed activations in the following areas: the bilateral inferior occipital cortex (IOC), inferior temporal gyrus (ITG), occipito-temporo-parietal junction (OTPJ), superior temporal gyrus (STG), insular cortex (IC), mid-inferior frontal gyrus (mid-IFG), and thalamus; the right ventral premotor cortex (PMv) and postcentral gyrus (PoCG); and the CC extending from anterior to posterior regions. The majority of these activation peaks were consistent with our previous results (Morita et al., 2008). By contrast, in the ASD group, the SELF versus OTHERS contrast revealed activation only in the bilateral mid-IFG and thalamus, the left STG, the right IC, and the anterior cingulate cortex (ACC). The reverse contrast (OTHERS versus SELF) revealed no significant activation in either group. An interaction contrast of group × face type (($SELF_{Control} – OTHERS_{Control}$) – ($SELF_{ASD} – OTHERS_{ASD}$)) revealed significant activation in the PCC (Table 3 and Fig. 5A). The reverse interaction contrast showed no group difference. We found that the PCC was activated more strongly during the evaluation of self-face images than those of others in the control group, whereas enhanced activity for self-face images was not observed in the ASD group. The PCC activity was not modulated by the embarrassment ratings in either group (Fig. 5A).

We then searched for differences in the modulation of neural activity by the embarrassment ratings between the conditions. No significant difference between the SELF and OTHERS conditions was found in either group. An interaction contrast of group × face type (($SELF_{Control}$ – $OTHERS_{Control}$) – ($SELF_{ASD}$ – $OTHERS_{ASD}$)) revealed significant activation in the right prefrontal region, with two peaks located in the IC and the lateral orbitofrontal cortex (LOFC) (Table 4 and Fig. 5B). The reverse interaction contrast showed no group difference. The right IC was more strongly activated during the evaluation of self-face images than when evaluating others' faces irrespective of the group, whereas the ASD group showed weaker activation of the right IC for both types of face compared with the control group. Regarding parametric modulation, the activity of the right IC evoked by self-face images was negatively modulated by the embarrassment ratings in the ASD group. By contrast, the activity of the right LOFC evoked by self-face images was positively modulated by the embarrassment ratings (Fig. 5B).

(Figure 5 about here)

Analyses were then performed with three ROIs defined by the interaction contrasts between the effects of group and face type in the preceding whole-brain analyses: the PCC, the right LOFC, and the right IC. We initially examined whether the self-related activity (SELF–OTHERS) in the PCC ROI was related to the strength of the relationship (coupling strength) between the two psychological ratings or autistic traits measured by the AQ in individual subjects (Fig. 6). The difference in the PCC activity between the SELF and OTHERS conditions was negatively correlated with the total AQ score ($r = -.394$, $p < .05$) (Fig. 6B), but was not correlated with the coupling strength (Fig. 6A). To identify which aspects of the autistic traits were most closely related to the reduction in self-related activity in the PCC, we calculated the correlation coefficients for the different subscales of the AQ. A significant negative correlation was found only with the subscale for AD ($r = -.715$, $p < .001$) (Table 5). The difference in the PCC activity between the SELF and OTHERS conditions was entered into an analysis of covariance (ANCOVA) with group (Control, ASD) as a between-subjects factor and each subscale as a covariate. This showed a significant effect of the subscale for AD [$F(1, 26) = 15.7$, $p < .001$], whereas the group effect and interaction were not significant (Fig. 6C). Next, we investigated whether the neural responses to self-face images in the right LOFC ROI and the right IC ROI were correlated with the coupling strength between the two psychological ratings or autistic traits measured by the AQ (Fig. 7). The brain activities in response to self-face images in the right IC were significantly negatively correlated with the individual coupling strength between the two ratings for self-face images in all participants ($r = -.562$, $p < .01$). The activities in response to self-face images in the right IC were entered into an ANCOVA with group (Control, ASD) as a between-subjects factor and coupling strength as a covariate. The right IC showed a significant effect of coupling strength [F(1, 26) = 6.27, $p < .05$], whereas the group effect and interaction were not significant. There was no significant correlation between the brain response to self-face images and each individual's full AQ score in either ROI.

(Figures 6, 7 about here)

DISCUSSION

The present study investigated the emotional responses to self-face images and the neural activities associated with self-face processing in individuals with ASD. Behaviorally, there was no significant difference between the groups in the embarrassment ratings for self-face images. However, there was a significant group difference in the relationship between the photogenicity ratings and the embarrassment ratings. In the control group, the embarrassment ratings for self-face images strongly correlated with the photogenicity ratings for the faces. This suggested that the control individuals experienced self-conscious emotions based on the results of evaluating self-face images. By contrast, the ASD group showed a relatively weak relationship between the two ratings compared with the control group. This weaker relationship suggests a decoupling between the cognitive evaluation of self-face images and emotional responses in ASD. Indeed, during the debriefing following the fMRI experiment, verbal feedback suggested atypical emotional responses to self-face recognition in the individuals with ASD. The control participants made statements such as “I was shocked to see my own face” or “I was surprised when my face was unexpectedly shown” during the experiment. By contrast, the participants with ASD had less emotional responses to the self-face images, making statements such as “A person who looked similar to me was shown in the photographs”.

These participants seemed to have an emotionally neutral response to the self-face images, and talked about themselves as if they were speaking of others. This phenomenon is similar to the lack of self-conscious behaviors in response to self-reflection reported in autistic children (Akagi, 2003; Dawson & McKissick, 1984; Spiker & Ricks, 1984). We therefore speculate that individuals with ASD might evaluate self-face images without experiencing self-conscious emotions, even though they are thought to be tightly coupled with self-evaluation.

The imaging data revealed a significant group difference in self-related processing in the PCC. The control group showed strong activation in this region when evaluating self-face images compared with others' faces, whereas the ASD group showed no difference between these conditions. A growing body of research suggests that a network composed of cortical midline structures — including the PCC, MPFC, and ACC — is related to internal or psychological aspects of the self, rather than the physical or embodied self (Lieberman, 2007; Uddin et al., 2007). In particular, the observed peak in the PCC was close to the peak of activation associated with a variety of self-referential tasks, including reflecting on one's own personality traits (D'Argembeau et al., 2008; Fossati et al., 2003; Johnson et al., 2002), episodic memory retrieval (Andreasen et al., 1995; Fink et al., 1996; Maddock, Garrett, & Buonocore, 2001), and emotional or moral judgment (Greene, Sommerville, Nystrom, Darley, & Cohen, 2001; Maddock, Garrett, & Buonocore, 2003; Ochsner et al., 2004). So far, several neuroimaging studies on ASD have reported reduced activity in the PCC during self-referential processing (Chiu et al., 2008; Kennedy et al., 2006; Silani et al., 2008). Based on this evidence, the reduced self-related activity of the PCC in the ASD group could be interpreted as reflecting a lack of self-referential processing. Moreover, the reduced self-related activity was correlated with the AQ scores indicating individual autistic traits, particularly with the subscale for AD. Individuals with or without ASD who had a strong tendency to pay excessive attention to local details showed a small increase in PCC activity when evaluating self-face images compared to images of others' faces. We speculate that focusing excessive attention on incoming external stimuli might lead to an absence of self-referential processing. A recent study demonstrated that familiarity might influence PCC activity during processing of self-related stimuli (Qin et al., in press). This finding fits well with previous studies on the familiarity of non-self-specific stimuli (Gobbini & Haxby, 2006; Kim et al., 1999; Kosaka et al., 2003; Leveroni, Seidenberg, Mayer, Mead, Binder, & Rao, 2000; Shah et al., 2001; Sugiura, Shah, Zilles, & Fink, 2005). In addition, the PCC is involved in the perception of emotionally salient stimuli (Maddock, 1999) and episodic or autobiographical retrieval (Maddock et al., 2001; Wagner, Shannon, Kahn, &

Buckner, 2005), suggesting that the stronger response to familiar stimuli in this region might be related to higher emotional content or memory function. From our data, we were unable to specify which factors in self-referential processing directly affected the PCC activity. However, our results suggest that individuals with ASD did not engage in non-physical self-referential processing when evaluating images of their own faces, and that the absence of this processing could be partly related to the lack of self-conscious behavior accompanying self-face processing in ASD.

We found a group difference in neural modulation according to embarrassment ratings in the right IC and the right LOFC. Although these peaks were included within a larger cluster, the activation patterns differed. In the right LOFC, the control group demonstrated activities in response to self-face images that positively covaried with the extent of embarrassment, but the mean activity in this region was not self-related (Fig. 5); this suggests that the LOFC was tuned to the more general negative emotions associated with the appraisal of affective value, rather than to specific negative emotions associated with the discrepancy between the presented self-face images and internal standards. In fact, the lateral area of the OFC was previously shown to be activated by angry expressions (Kesler-West et al., 2001; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998), and by stimuli related to actions likely to cause others to become angry, such as violations of social norms (Berthoz, Armony, Blair, & Dolan, 2002). By contrast, in the right IC, the control group showed greater activation during self-face evaluation compared with the evaluation of others' faces, but the self-related activity was independent of the extent of embarrassment. The peak area within the right IC demonstrating a group difference was located in the anterior portion of the IC, which is involved in various types of self-related processing (Fink et al., 1996; Fossati et al., 2003; Johnson et al., 2005; Kircher et al., 2000, 2001; Modinos, Ormel, & Aleman, 2009; Phan, Wager, Taylor, & Liberzon, 2004; Platek et al., 2006). This region is also active during a wide variety of tasks including the experience of subjective feelings, attention, cognitive choice, time perception, and awareness of sensation and movements (Craig, 2002, 2009). To explain this wide range of insular functions within a unitary account, Craig proposed a meta-representational model of integration across the IC, in which bodily, affective, sensory, and cognitive information are integrated to create emotional awareness (Craig, 2009). According to this model, the anterior IC is a critical relay between the cognitive, motivational, and social conditions represented in other brain regions (e.g., the ACC, ventromedial PFC, and dorsolateral PFC) and emotional awareness. Therefore, the constant self-related activity in the anterior insula appears mainly to reflect the integration of relevant information resulting from the evaluation of self-face images. In the right IC, a notable finding in individuals with ASD was the reduced activation compared with the control group, regardless of the face type. Furthermore, the reduced activity in response to self-face images was closely related to weak coupling between cognitive evaluation and emotional responses to self-face images, rather than to autistic traits. Several recent studies have reported ASD-related structural and functional abnormalities of the anterior insula (Di Martino et al., 2009; Kosaka et al., 2010; Uddin & Menon, 2009). A meta-analysis of neuroimaging studies on social processing in ASD revealed that the right anterior insula was less likely to be activated in individuals with ASD than in neurotypical controls (Di Martino et al., 2009; Uddin & Menon, 2009). These reviews suggest that ASD-related hypoactivation in the IC might be due to a disconnection between the anterior insula and other structures that project to it. Correspondingly, in individuals with ASD, the cognitive information that results from the evaluation of self-face images might not be fully transmitted to the IC, which in turn might lead to reduced activation in the right IC. Because of right IC dysfunction, individuals with ASD might not experience emotional awareness, or might experience abnormal self-conscious emotion that is not tightly linked to the cognitive evaluation of images of their own faces. Such abnormal awareness or self-conscious emotion might be related to the ASD-specific modulation of neural responses in the right IC in relation to the extent of embarrassment. We therefore propose that, in addition to the absence of self-referential processing, abnormal integrative processing in the IC could contribute to the lack of self-conscious behavior in response to self-reflection in individuals with ASD.

Limitations

Although most of the results for the healthy controls replicated our previous findings (Morita et al., 2008), there were some minor differences between the findings of the two studies.

The first difference was in the embarrassment ratings for the faces of others. On average, the participants in the present study reported stronger embarrassment in response to others' faces compared with that observed in the previous study. Embarrassment caused by images of others is categorized as empathic embarrassment, which occurs when an individual feels embarrassed as a consequence of someone else's predicament (Miller, 1987). We speculate that the degree of empathic embarrassment is influenced by an individual's empathic ability. If this is true, one possible cause of the inconsistent results could be a group difference in the participants' levels of empathy between the two studies. This issue requires further consideration and research.

The second difference was in the self-related activity. In the present study, the SELF versus OTHERS contrast revealed widespread activation in the CC. However, we did not discuss the cingulate activation in the previous study, because we focused on the functions of the right prefrontal regions, which play important roles in self-face processing (Keenan, Wheeler, Gallup, & Pascual-Leone, 2000; Platek, Keenan, Gallup, & Mohamed, 2004; Sugiura et al., 2006, 2008; Uddin, Kaplan, Molnar-Szakacs, Zaidel, & Iacoboni, 2005).

The third difference was in the neural modulation according to the embarrassment ratings. In the previous study, we found that the activity of the right mid-IFG was negatively correlated with the extent of embarrassment evoked by self-face images. However, in the present study, the activity of the right LOFC was positively correlated with the extent of embarrassment, albeit more weakly. The reason for this discrepancy was unclear, and requires further investigation.

Conclusion

The current study provides evidence for a lack of self-conscious behaviors in response to self-reflection in individuals with ASD. Behaviorally, individuals with ASD showed a weaker correlation between the photogenicity ratings and the extent of embarrassment evoked by self-face images, suggesting a decoupling between cognitive evaluation and emotional responses. At the neural level, individuals with ASD showed a reduction of self-related activity in the PCC, which was associated with specific autistic traits. They also showed abnormal neural modulation of activity according to the extent of embarrassment in the right IC and LOFC. In particular, the reduced activity in the right IC in response to self-face images was related to the weak coupling between cognitive evaluation and emotional responses. These findings suggest that dysfunction of the PCC, which is responsible for self-referential processing, and of the IC, which plays a key role in emotional experience, contributes to the lack of self-conscious behavior in response to self-reflection observed in individuals with ASD.

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FIGURE LEGENDS

Figure 1. Photogenicity ratings for individuals' self-face images and those of others measured during the fMRI session. Data represent the mean ± standard error (SE).

Figure 2. Mean embarrassment ratings for each condition and each group. Dots represent each individual's mean of the 21 ratings.

Figure 3. Correlation coefficients between the photogenicity ratings measured during the fMRI session and the embarrassment ratings measured after the fMRI session for self-face images and those of others' faces in each group. Data were normalized using Fisher's z transformation.

Figure 4. Brain areas showing significant activation caused by the SELF versus OTHERS contrast in each group (control group, red; ASD group, blue). Each activation was superimposed on a high-resolution anatomical MR image in nine contiguous transaxial slices with an 8-mm interval, extending from MNI coordinates $z = -8$ (left) to $z = +56$ (right). The height threshold was set at T > 2.67 ($p < .005$), and $p < .05$ corrected for multiple comparisons at the cluster level.

Figure 5. Brain areas showing a significant interaction between group and face type. (A) Brain areas in which the mean response showed a significant interaction between group and face type. The random-effects statistical parametric activation map (SPM{T}) was overlaid on a high-resolution anatomical MR image showing activation in the PCC (4, −38, 32). (B) Brain areas in which the parametric modulation according to the embarrassment ratings showed a significant interaction between group and face type. The SPM{T} was overlaid on a high-resolution anatomical MR image showing activation in the right LOFC (44, 40, −10) and the right IC (36, 18, −8). The height threshold was set at $p < .005$ uncorrected, with an extent threshold of $p < .05$ corrected for multiple comparisons. Averaged parameter estimates for the mean response (left graphs) and the extent to which the height of the modeled HRF was modulated by the embarrassment ratings for faces (parametric modulation) (right graphs) in the PCC, the right LOFC, and the right IC are plotted for each condition and each group. The asterisks indicate statistical significance (*, $p < .05$; **, $p < .01$; ***, $p < .001$).

Figure 6. Correlation between brain activity in the PCC ROI and individual psychological measures. Differences between the parameter estimates for the mean response during the

SELF and OTHERS conditions extracted from the PCC ROI are plotted against each individual subject's coupling strength between the photogenicity ratings and the embarrassment ratings (A), each individual's full AQ score (B), and the scores for the AD subscale of the AQ in each group (C). The asterisks indicate statistical significance (*, $p < .05$; ***, $p < .001$).

Figure 7. Correlation between brain activities in the LOFC and IC ROIs and individual psychological measures. Data for the right LOFC ROI (top) and right IC ROI (bottom) were analyzed. The parameter estimates for the mean response of the SELF condition in the right LOFC and the right IC are plotted against each individual's coupling strength between the photogenicity ratings and the embarrassment ratings (A, C) and the full AQ score (B, D) in each group. The asterisks indicate statistical significance (**, $p < .01$).

TABLES

TABLE 1

Participant characteristics

	ASD group (n = 15)	Control group (n = 15)	*p* value
Male / female	14 / 1	13 / 2	
Age (years)	23.7 ± 4.3	23.3 ± 3.6	n.s.
WAIS-III			
Full scale IQ	105.4 ± 11.7	110.1 ± 4.3	n.s.
Verbal IQ	111.1 ± 11.1	113.8 ± 6.6	n.s.
Performance IQ	96.3 ± 14.7	103.0 ± 5.9	n.s.

Note: Scores represent mean ± SD. WAIS-III, Wechsler Adult Intelligence Scale, 3rd edition.

TABLE 2

Questionnaire scores

	ASD group (n = 15)	Control group (n = 15)	*p* value
Self-consciousness scale:			
Public	39.3 ± 5.9	41.4 ± 7.9	n.s.
Private	33.7 ± 8.3	37.1 ± 5.6	n.s.
Other-consciousness scale:			
Inner	22.3 ± 6.8	24.1 ± 4.8	n.s.
Outer	13.4 ± 4.0	14.5 ± 2.8	n.s.
Fantasy	12.7 ± 5.1	13.3 ± 3.0	n.s.
Autism spectrum quotient (AQ):			
Total scores	33.2 ± 4.5	15.4 ± 6.2	< .001
Social skill	7.2 ± 1.8	2.6 ± 2.2	< .001
Attention switching	7.6 ± 1.1	4.1 ± 2.4	< .001
Attention to detail	6.1 ± 2.6	3.9 ± 1.9	< .05
Communication	7.2 ± 2.1	2.2 ± 2.1	< .001
Imagination	5.1 ± 2.2	2.5 ± 1.1	< .001

Note: Scores represent mean ± SD.

TABLE 3

Significantly activated voxels in the mean response for the SELF versus OTHERS contrast

Cluster level		Side	Area	MNI Coordinates			T value
p value	Cluster size			*x*	*y*	*z*	
Control group							
< .001	38,893	Rt	IC	38	8	−8	7.43
		Rt	PMv	48	6	26	6.96
		Rt	Mid-IFG	48	34	4	6.87
		Lt	IC	−40	20	−8	6.55
		–	ACC	−4	24	28	6.47
		Rt	PoCG	60	−22	28	6.31
		Rt	STG	52	14	−8	6.31
		Rt	NAcc	10	8	−8	6.30
		Rt	OTPJ	28	−78	32	6.21
		Lt	IC	−36	14	−6	6.16
		Lt	STG	−44	16	−12	6.09
		–	MCC	−6	8	32	6.03
		–	Extra-nuclear	4	−28	26	5.94
		Lt	OTPJ	−24	−78	22	5.92
		Rt	ITG	46	−62	−4	5.90
		–	MCC	8	20	32	5.82

			Lt	IOC	−44	−62	−12	5.77
			Lt	OTPJ	−26	−84	34	5.73
			Rt	PoCG	54	−22	42	5.73
			Rt	Thalamus	6	−12	6	5.69
			Lt	Thalamus	−4	−10	6	5.67
			Rt	PMv	46	4	42	5.62
			–	MCC	2	6	38	5.53
			Rt	IOC	38	−84	−6	5.49
			Lt	ITG	−46	−68	−4	5.48
			Rt	IC	32	16	4	5.41
			–	MCC	−4	−12	40	5.39
			Lt	Mid-IFG	−34	26	0	5.35
			Lt	SFG	−14	48	32	5.35
ASD group								
	< .001	3,412	Lt	Mid-IFG	−46	36	12	5.12
			Lt	STG	−46	18	−16	4.31
			–	ACC	2	28	20	4.28
	< .001	1,942	Rt	IC	32	20	2	4.02
			Rt	IC	46	16	−10	3.99
			Rt	Mid-IFG	48	32	12	3.89
	.003	954	Lt	PHG	−20	−26	−14	3.77

		Lt	Thalamus	–10	–28	4	3.74
		Rt	Thalamus	6	–12	10	3.67
Interaction (control group – ASD group)							
.03	601	Lt	Parietal lobe	–24	–42	34	4.60
		–	PCC	4	–38	32	3.53
		Lt	Parietal lobe	–28	–34	28	3.39

Note: Height threshold, $p < .005$; extent threshold, $p < .05$ corrected. The activity at every peak in the control group exceeded a height threshold of $p < .05$ (family-wise error [FWE]-corrected for multiple comparisons). Lt, left; Rt, right. IC, insular cortex; PMv, ventral premotor cortex; Mid-IFG, mid-inferior frontal gyrus; ACC, anterior cingulate cortex; PoCG, postcentral gyrus; STG, superior temporal gyrus; NAcc, nucleus accumbens; OTPJ, occipito-temporo-parietal junction; MCC; middle cingulate cortex; ITG, inferior temporal gyrus; IOC, inferior occipital cortex; SFG, superior frontal gyrus; PHG, parahippocampal gyrus; PCC, posterior cingulate cortex.

TABLE 4

Brain regions showing significant group-by-condition interaction for parametric modulation according to the embarrassment ratings

Cluster level		Side	Area	MNI Coordinates			T value
p value	Cluster size			*X*	*y*	*z*	
.02	591	Rt	LOFC	44	40	−10	3.73
		Rt	White matter	36	46	0	3.72
		Rt	IC	36	18	−8	3.22

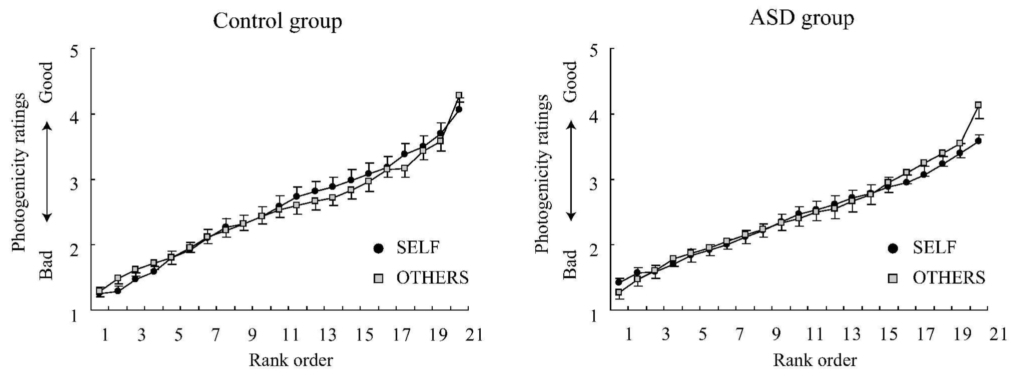
Note: Height threshold, $p < .005$; extent threshold, $p < .05$ corrected). Lt, left; Rt, right. LOFC, lateral orbitofrontal cortex; IC, insular cortex.

TABLE 5

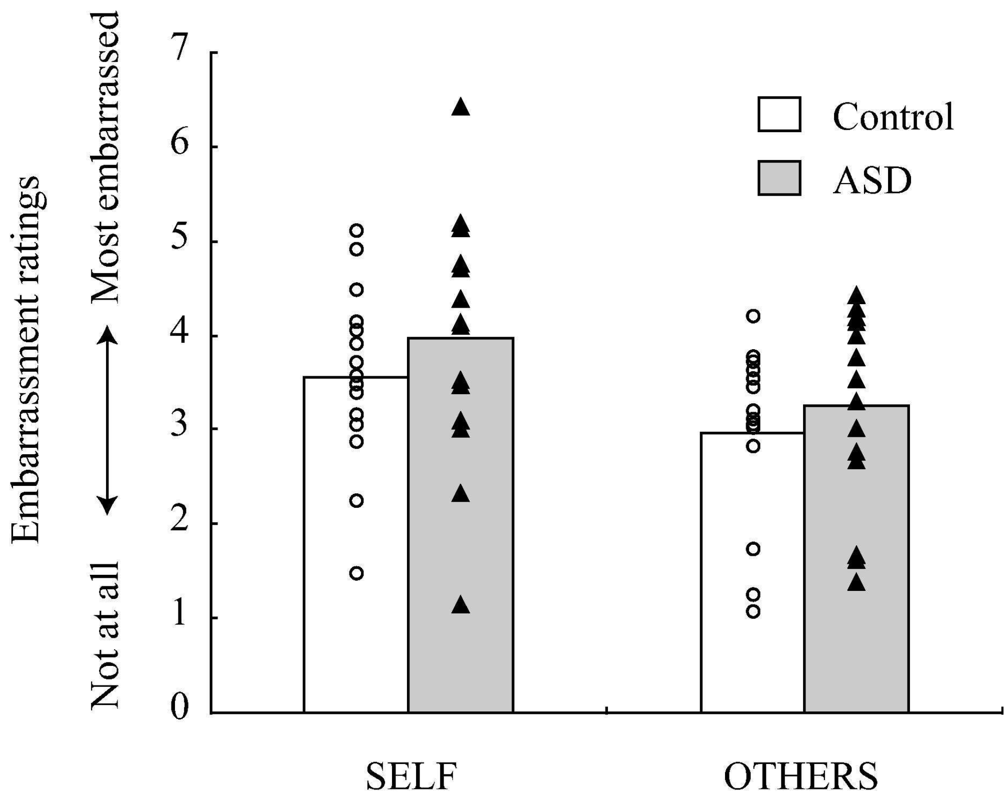
Correlation coefficients (*r*) between the self-related activity (SELF−OTHERS) in the PCC and the individual AQ scores for all participants

	Total AQ	S	AS	AD	C	I
r	− .394*	− .266	− .236	− .715***	− .189	− .143

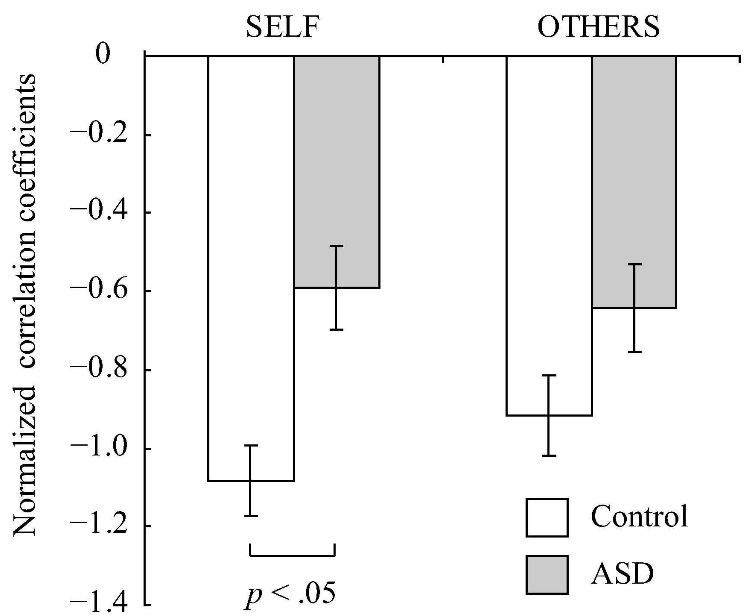
Note: * $p < .05$, *** $p < .001$. S, social skill; AS, attention switching; AD, attention to detail; C, communication; I, imagination.



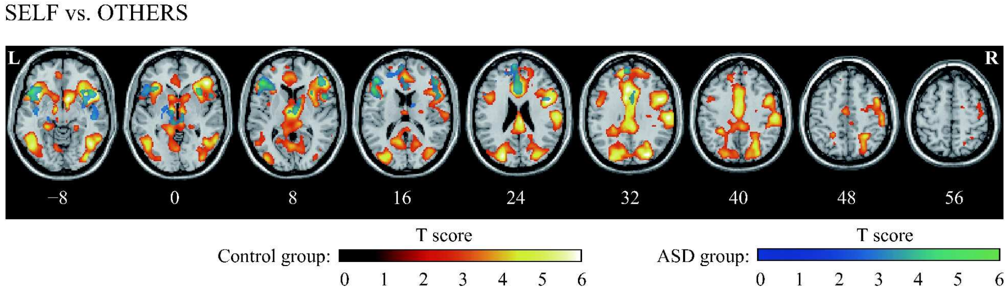
Photogenicity ratings for individuals' self-face images and those of others measured during the fMRI session. Data represent the mean ± standard error (SE).
169x62mm (600 x 600 DPI)



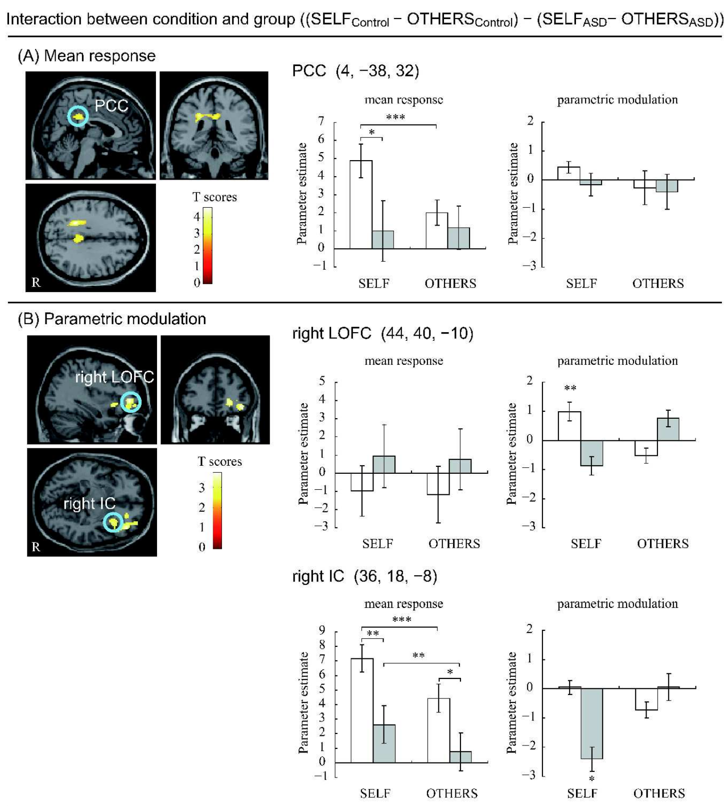
Mean embarrassment ratings for each condition and each group. Each dot represents the individual mean of 21 ratings.
79x62mm (600 x 600 DPI)



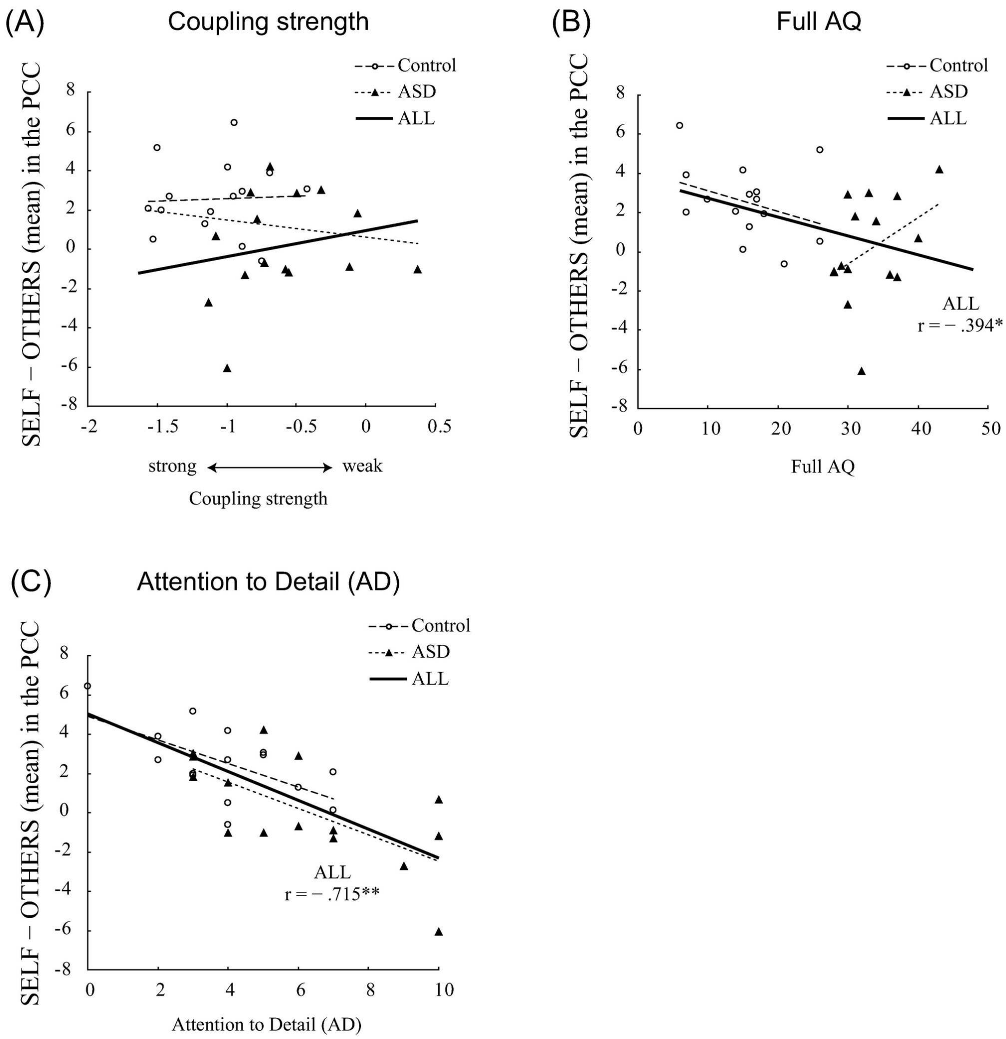
Correlation coefficients between the photogenicity ratings measured during the fMRI session and the embarrassment ratings measured after the fMRI session for self-face images and those of others' faces in each group. Data were normalized using Fisher's z transformation.
72x118mm (600 x 600 DPI)



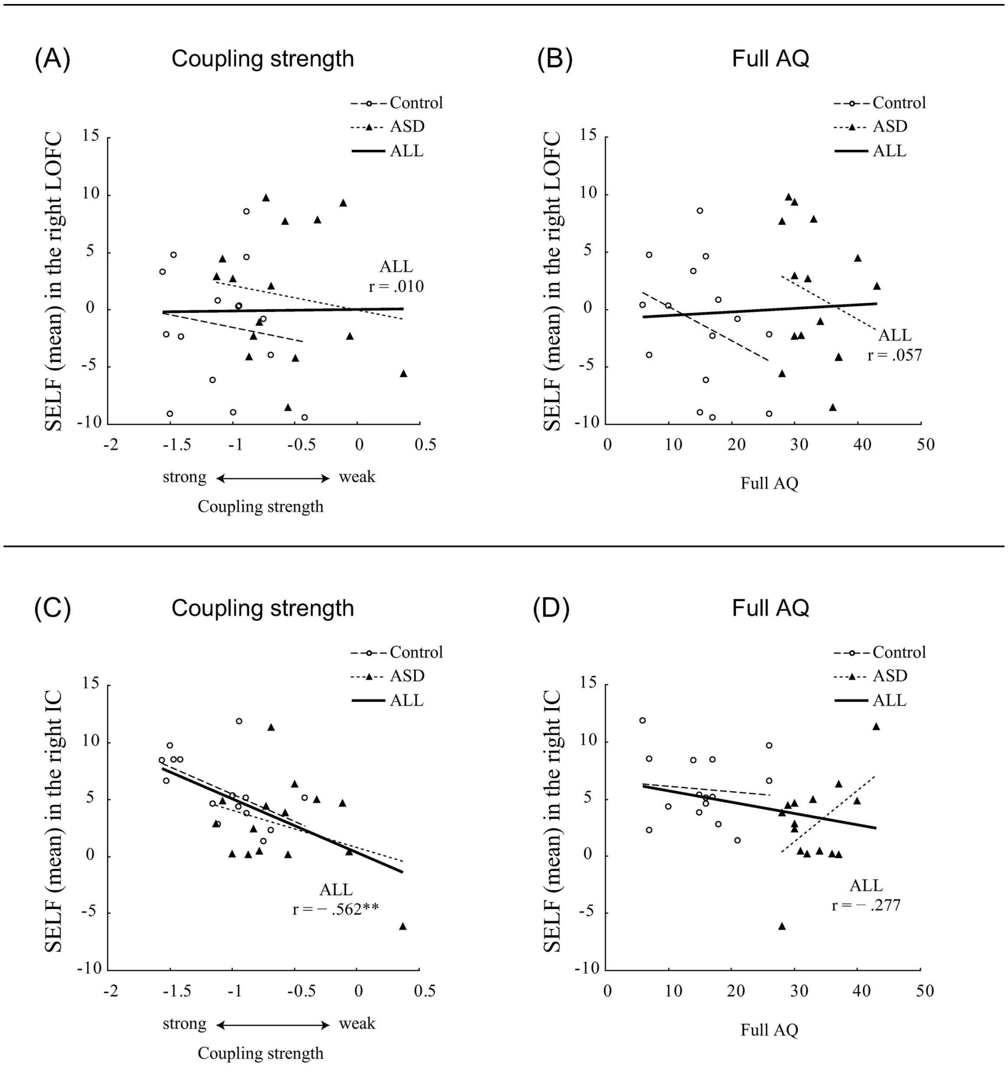
Brain areas showing significant activation caused by the SELF versus OTHERS contrast in each group (control group, red; ASD group, blue). Each activation was superimposed on a high-resolution anatomical MR image in nine contiguous transaxial slices with an 8-mm interval, extending from MNI coordinates z = −8 (left) to z = +56 (right). The height threshold was set at T > 2.67 (p < .005), and p < .05 corrected for multiple comparisons at the cluster level.
165x48mm (600 x 600 DPI)



Brain areas showing a significant interaction between group and face type. (A) Brain areas in which the mean response showed a significant interaction between group and face type. The random-effects statistical parametric activation map (SPM{T}) was overlaid on a high-resolution anatomical MR image showing activation in the PCC (4, −38, 32). (B) Brain areas in which parametric modulation according to embarrassment ratings showed a significant interaction between group and face type. The SPM{T} was overlaid on a high-resolution anatomical MR image showing activation in the right LOFC (44, 40, −10) and the right IC (36, 18, −8). The height threshold was set at $p < .005$ uncorrected, with an extent threshold of $p < .05$ corrected for multiple comparisons. Averaged parameter estimates for the mean response (left graphs) and the extent to which the height of the modeled HRF was modulated by the embarrassment ratings for faces (parametric modulation) (right graphs) in the PCC, the right LOFC, and the right IC are plotted for each condition and each group. The asterisks indicate statistical significance (*, $p < .05$; **, $p < .01$; ***, $p < .001$).
176x285mm (600 x 600 DPI)



Correlation between brain activity in the PCC ROI and individual psychological measures. Differences between the parameter estimates for the mean response during the SELF and OTHERS conditions extracted from the PCC ROI are plotted against each individual subject's coupling strength between the photogenicity ratings and the embarrassment ratings (A), each individual's full AQ score (B), and the scores for the AD subscale of the AQ in each group (C). The asterisks indicate statistical significance (*, p < .05; **, p < .001).
169x175mm (300 x 300 DPI)



Correlation between brain activities in the LOFC and IC ROIs and individual psychological measures. Data for the right LOFC ROI (top) and right IC ROI (bottom) were analyzed. The parameter estimates for the mean response of the SELF condition in the right LOFC and the right IC are plotted against each individual's coupling strength between the photogenicity ratings and the embarrassment ratings (A, C) and the full AQ score (B, D) in each group. The asterisks indicate statistical significance (**, $p < .01$).
195x211mm (300 x 300 DPI)