Gender-specific modulation of neural mechanisms underlying social reward processing by Autism Quotient

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Abstract

Autism spectrum disorder refers to a neurodevelopmental condition primarily characterized by deficits in social cognition and behavior. Subclinically, autistic features are supposed to be present in healthy humans and can be quantified using the Autism Quotient (AQ). Here, we investigated a potential relationship between AQ and neural correlates of social and monetary reward processing, using functional magnetic resonance imaging in young, healthy participants. In an incentive delay task with either monetary or social reward, reward anticipation elicited increased ventral striatal activation, which was more pronounced during monetary reward anticipation. Anticipation of social reward elicited activation in the default mode network (DMN), a network previously implicated in social processing. Social reward feedback was associated with bilateral amygdala and fusiform face area activation. The relationship between AQ and neural correlates of social reward processing varied in a gender-dependent manner. In women and, to a lesser extent in men, higher AQ was associated with increased posterior DMN activation during social reward anticipation. During feedback, we observed a negative correlation of AQ and right amygdala activation in men only. Our results suggest that social reward processing might constitute an endophenotype for autism-related traits in healthy humans that manifests in a gender-specific way.

Key words: autism quotient; precuneus; default mode network; amygdala; fusiform face area; social reward; gender differences

Introduction

Typically developing children begin to attend to social stimuli in early infancy (Farroni et al., 2002). This naturally occurring behavior is markedly reduced in autism, a multifactorial neurodevelopmental syndrome with a strong genetic component (Klin et al., 2009). ICD-10 (World Health Organisation, 1992) and DSM-IV (American Psychiatric Association, 1994) describe autism spectrum disorder (ASD) as a pervasive developmental disorder characterized by deficits in communication, repetitive stereotyped behavior and impaired social interactions. ASD is also associated with decreased motivation to attend to social stimuli conveyed through the face (Dawson et al., 2005; Schultz,
2005). Dawson et al. (2004) demonstrated that autistic children were less likely to orient to acoustic social cues such as humming or calling the child’s name when compared with typically developing children. Several authors suggest that ASD reflects the extreme of a continuum, and that autism-related traits exist to some extent in healthy individuals (Frith, 1991; Baron-Cohen, 1995, 2001a). To quantify the presence of autistic features in adults with normal intelligence, Baron-Cohen et al. (2001b) introduced the autism spectrum quotient (AQ) and developed a self-report questionnaire. In line with the endophenotype concept of neuropsychiatric disorders (Gottesman and Gould, 2003), an association between the AQ and performance in adults with normal intelligence, Baron-Cohen et al. (2001b) introduced the autism spectrum quotient (AQ) and developed a self-report questionnaire. In line with the endophenotype concept of neuropsychiatric disorders (Gottesman and Gould, 2003), an association between the AQ and performance in adults with normal intelligence, Baron-Cohen and Wheelwright (2004) reported higher self-reported empathy scores in women relative to men, a finding in line with more pronounced orienting towards social stimuli in women (Cloninger et al., 1991; Proverbio et al., 2008). One previous functional magnetic resonance imaging (fMRI) study has explicitly assessed gender differences in social and monetary reward processing during performance of an incentive delay task. Women exhibited comparable ventral striatal responses to anticipation of both monetary and social reward, whereas men showed both faster reaction times (RTs) and more extensive brain responses during anticipation of monetary relative to social reward (Spreckelmeyer et al., 2009).

While both differential processing of social vs monetary reward in general (Izuma et al., 2008), and with respect to autism (Scott-Van Zeeland et al., 2010; Delmonte et al., 2012; Dichter et al., 2012b; Kohls et al., 2013), and gender differences (Spreckelmeyer et al. 2009) in particular have been reported before, this study was aimed at whether such a modulation of social vs monetary reward processing might also be present in individuals with subclinical autistic traits. Specifically, in this study, we aimed to investigate individual differences in social reward processing related to gender and autistic phenotype in young, healthy individuals. Guided by previous literature, we hypothesized striatal activation during anticipation of both monetary and social reward (Izuma et al., 2008; Spreckelmeyer et al., 2009; Rademacher et al., 2010). We further expected amygdala and fusiform face area (FFA) responses to social feedback (Rademacher et al., 2010; Richarz et al., 2013b). Given the previously reported role of the default mode network (DMN) in social cognition (Schilbach et al., 2008b; Whitfield-Gabrieli et al., 2011), we further hypothesized an increased activation of DMN structures like the posterior cingulate cortex (PCC), the medial prefrontal cortex (mPFC) and the temporoparietal junction (TPJ) during social reward processing. Regarding individual differences related to gender in ASD, we hypothesized that women would exhibit higher sensitivity to social reward than men and that AQ scores would correlate negatively with responses of the striatum, amygdala, FFA, and possibly also DMN structures to social reward.

Materials and methods

Note

The experimental paradigm, study cohort and data acquisition have been reported previously (Barman et al., 2014) and are described in detail as Supplementary information.

Participants

Sixty-three participants (31 women, mean age = 23.5 ± 2.19 years, age range 20.4–29.1 years; 32 men, mean age = 25.6 ± 2.90 years, age range 20.8–36.6 years) were recruited from a cohort of 709 participants (371 women, mean age = 23.4 ± 2.63 years, age range 18.8–34.6 years; 338 men, mean age = 24.2 ± 2.83 years, age range 18.6–35.6 years) who had filled out the AQ self-report questionnaire. All participants gave written informed consent in accordance with the Declaration of Helsinki and received financial compensation for participation. The work was approved by the Ethics Committee of the University of Magdeburg.

Experimental paradigm

Participants performed a categorical monetary incentive delay task (Wittmann et al., 2005) and a social incentive delay task (Barman et al., 2014). The order of the runs (monetary vs social) was counterbalanced across participants. Each trial started with a...
cue (1000 ms) signaling either a potential reward or a neutral feedback. Participants were asked to attend to the cues and to respond via button press (right index or middle finger) whether they expected a reward or not. After a variable delay (500–3500 ms), a number comparison task (target, 250 ms; Pappata et al., 2002; Wittmann et al., 2005) followed. Participants were instructed to give a speeded response whether a target number was larger or smaller than 5. During reward trials, participants could win 1€ (signaled by photographs of 1€ coins) or positive social feedback (photographs of smiling persons) upon a successful target response. In case of a wrong and/or slow response, a black/white pattern noise-image was presented. During neutral trials, a black/white pattern noise-image was shown irrespective of outcome. Feedback (750 ms) was given 500–2500 ms after target presentation and was followed by a variable fixation phase (1000–4000 ms). Figure 1 shows the timing of an example trial. Details of the experimental paradigm and stimulus material are described in the Supplementary information.

fMRI acquisition and analysis
fMRI was performed using a 3 Tesla Siemens Magnetom Trio MR tomograph (SIEMENS Medical Systems, Erlangen, Germany). We acquired a structural T1-weighted MR image, followed T2*-weighted gradient-echo echo-planar images, during which the task was performed (Supplementary information for detailed protocols). Data analysis was performed using Statistical Parametric Mapping (SPM8, Wellcome Trust Centre for Neuroimaging, London, UK). After image preprocessing (correction for acquisition delay and head motion, spatial transformation to the Montreal Neurological Institute (MNI) reference frame, spatial smoothing), a two-stage general linear model analysis was carried out. At the first stage, time courses of the experimental conditions were convolved with a canonical hemodynamic response function and submitted to a restricted maximum likelihood fit. At the second stage, conditions of interest (anticipation of both reward types and anticipation of their respective neutral baseline), separated by gender, were submitted to random effects analyses. Specifically, full-factorial 2 × 2 ANOVA models, for anticipation (presentation of the reward-predicting cue) and feedback phase (reward delivery after successful performance of the number comparison task) respectively, were generated with the conditions of interest (monetary reward > neutral baseline, social reward > neutral baseline) as within-subject factor and gender as between-subject factor. Because of our strong a priori anatomical hypotheses regarding neural correlates of reward processing, face perception and social cognition, we focused our analyses on the brain regions previously implicated in such tasks. We employed combined anatomical and probabilistic regions of interest (ROIs; Supplementary methods and Figures S1–S3) of the striatum and the DMN (mPFC, PCC/precuneus, TPJ) in the anticipation phase, and of the bilateral amygdala and FFA) in the feedback phase. The significance level was set to $P < 0.05$, family-wise error (FWE)-corrected for the volumes of the respective ROIs.

Correlational analyses
To assess a potential relationship between AQ and neural underpinnings of social vs monetary reward processing, robust Shepherd’s pi correlations (Schwarzkopf et al., 2012) were computed between individual AQ scores and blood-oxygen-level-dependent (BOLD) signal change values (contrasts of parameter estimates) at the peak voxels of a priori defined ROIs in which a significant difference ($P < 0.05$, small-volume FWE-corrected) between social and monetary reward was observed (striatum, precuneus, TPJ, amygdala and FFA). Correlations were computed separately for men and women. The significance level was set to $P < 0.05$, two-tailed and Bonferroni-corrected for the number of ROIs.

Results
Questionnaire data
A non-parametric Mann–Whitney-test in the entire cohort ($N = 709$) revealed significantly higher AQ values in males.
compared with females (women: $M = 14.3 \pm 5.0$, median = 14; men: $M = 16.5 \pm 5.4$, median = 16; Mann–Whitney’s $U = 47656.5$, $P < 0.001$). In the fMRI cohort ($N = 63$), participants were recruited according to their AQ scores, and thus, no significant gender-related differences in AQ were observed (women: $M = 14.0 \pm 6.7$, median = 13; men: $M = 16.4 \pm 7.1$, median = 16; Mann–Whitney’s $U = 386.5$, $P = 0.131$).

**Behavioral responses in the fMRI experiment**

RTs and rates of correct responses (i.e. hit rates) in the number comparison task are displayed in Table 1, separated by gender (Supplementary Figure S4).

The analyses of RTs revealed a significant main effect of reward ($F_{1,61} = 111.67$, $P < 0.001$; two-way ANOVA for repeated measures with reward and task as within-subject factors and gender as between-subject factor) and a significant reward (reward vs neutral baseline) by task (monetary vs social) interaction ($F_{1,61} = 39.04$, $P < 0.001$). There were no further significant effects ($P > 0.07$). Post hoc paired t-tests revealed faster RTs for correct responses in reward trials relative to neutral trials (monetary: $t_{62} = 11.39$, $P < 0.001$; social: $t_{62} = 7.06$, $P < 0.001$). Moreover, monetary reward elicited significantly shorter RTs than the social reward ($t_{62} = 3.95$, $P < 0.001$).

The analyses of hit rates showed a main effect of reward ($F_{1,61} = 32.62$, $P < 0.001$), but no further significant effects (all $P > 0.08$). Post hoc paired t-tests revealed higher hit rates in reward trials in both conditions (monetary: $t_{62} = 4.88$, $P < 0.001$; social: $t_{62} = 3.32$, $P = 0.002$). Hit rates did not differ between reward conditions ($t_{62} = 0.91$, $P = 0.368$).

ANOVA with AQ as covariate revealed no effect of either AQ or gender on RTs or hit rates (all $P > 0.080$).

**Functional MRI data**

We focused our analyses on neural correlates of reward anticipation, i.e. presentation of reward-predicting cues and outcome, i.e. reward delivery after successful performance of the number comparison task.

**Effects of reward anticipation**

Neural responses to reward anticipation were compared in a two-by-two mixed effects ANOVA model with the factors gender (men/women) and reward type (monetary reward/neutral baseline, social reward/neutral baseline). A positive effect of reward (reward cues vs neutral cues) was observed in the bilateral striatum (left: $[x y z] = [-12 -8 -5]$, $t_{120} = 11.75$, $P < 0.001$, FWE-corrected for ROI volume; right: $[x y z] = [12 -8 -2]$, $t_{120} = 11.64$, $P < 0.001$, FWE-corrected for ROI volume; Figure 2), replicating previous results (Knutson et al., 2001; Knutson and Cooper, 2005; Wittmann et al., 2005; Spreckelmeyer et al., 2009; Rademacher et al., 2010; Richter et al., 2013a). We further observed activation in the insula ($[x y z] = [33 23 -5]$, $t_{120} = 9.37$, $P < 0.001$, whole-brain FWE-corrected) during the presentation of reward cues, which is in line with previous studies (Kirsch et al., 2003; Izuma et al., 2008). Further neural whole-brain activation patterns ($P < 0.05$, FWE-corrected) related to reward anticipation included clusters within frontal lobe, and striatum (Table 2).

Anticipation of monetary vs social reward were directly compared in a two-by-two mixed effects ANOVA model across genders and the differential contrasts comparing the reward conditions to their respective neutral conditions (monetary reward > neutral baseline, social reward > neutral baseline; see Figure 3). Monetary relative to social reward elicited significantly higher bilateral striatal activation (right: $[x y z] = [9 11 5]$, $t_{120} = 4.05$, $P = 0.005$, FWE-corrected for ROI volume; left: $[x y z] = [-12 -8 -5]$, $t_{120} = 3.60$, $P = 0.021$, FWE-corrected for ROI volume). In line with the well-documented role of the DMN in social cognition (Schilbach et al., 2008b; Whitfield-Gabrieli et al., 2011), we observed increased activations to social vs monetary reward cues (social > monetary reward anticipation across genders) in the right PCC/precuneus ($[x y z] = [6 -61 43]$, $t_{120} = 4.08$, $P = 0.032$, FWE-corrected for ROI volume) and in the right TPJ ($[x y z] = [57 -55 31]$, $t_{120} = 3.83$, $P = 0.017$, FWE-corrected for ROI volume), Figure 4A. There were also trends for increased neural activation in the mPFC and left TPJ, but these did not survive FWE correction for the respective ROI volumes.

For completeness reasons, results of whole-brain analyses (thresholded at $P < 0.001$, uncorrected) are displayed in Table 3. Gender differences during reward anticipation were observed in the hippocampus and insula (supplementary information).

**Neural correlates of reward outcome**

The comparison of social vs monetary reward outcome was carried out as a two-by-two mixed-effects ANOVA model (between subjects factor = gender; within subjects factor = reward type). Irrespective of condition (monetary, social), positive relative to neutral feedback stimuli were associated with activation of bilateral secondary visual areas, fusiform gyrus, hippocampus and amygdala ($P < 0.05$, whole-brain FWE-corrected).

Positive social relative to monetary feedback was associated with increased bilateral activation of the FFA (right: $[x y z] = [42 -49 -20]$, $t_{120} = 14.90$, $P < 0.001$, FWE-corrected for ROI volume; left: $[x y z] = [-42 -52 -20]$, $t_{120} = 11.70$, $P < 0.001$, FWE-corrected for ROI volume) and amygdala (right: $[x y z] = [21 -7 -17]$, $t_{120} = 10.82$, $P < 0.001$, FWE-corrected for ROI volume; left: $[x y z] = [-18 -10 -17]$, $t_{120} = 10.66$, $P < 0.001$, FWE-corrected for ROI volume) (Figure 5A). Table 4 summarizes further significant whole-brain activations elicited by social compared with monetary feedback (contrast social > monetary, across genders; $P < 0.05$, FWE-corrected). The comparison monetary > social feedback revealed activations in a network of prefrontal, cingulate and parietal cortices, including DMN structures ($P < 0.05$, FWE-corrected; Table 4).

**Correlation of AQ and brain activations**

While there was no significant correlation of AQ and striatal activations during monetary or social reward anticipation

**Table 1. Descriptive statistics of the behavioral data**

|                          | Women       | Men        |
|--------------------------|-------------|------------|
| **RTs (ms)**             |             |            |
| Monetary condition       |             |            |
| Reward trials            | 446 ± 49    | 431 ± 57   |
| Neutral baseline         | 496 ± 53    | 489 ± 66   |
| Social condition         |             |            |
| Reward trials            | 474 ± 59    | 447 ± 56   |
| Neutral baseline         | 499 ± 57    | 479 ± 59   |
| Hit rate (%)             |             |            |
| Monetary condition       |             |            |
| Reward trials            | 76.3 ± 3.1  | 75.1 ± 3.4 |
| Neutral baseline         | 72.7 ± 4.3  | 73.0 ± 4.4 |
| Social condition         |             |            |
| Reward trials            | 74.3 ± 4.2  | 75.6 ± 4.2 |
| Neutral baseline         | 73.0 ± 5.6  | 73.1 ± 4.3 |

Means and standard deviations are reported. RTs, reaction times in reward number comparison task.
Reward types of reward led to ventral striatal activation that was significant after Bonferroni correction (Supplementary Table 5). AQ scores correlated significantly with the activation of the right prefrontal cortex (P = 0.0014; women: P = 0.005; Fisher’s Z = 2.41, P = 0.0160; Figure 5B).

To test how specific the correlations between AQ and DMN were to social reward, we computed correlations between AQ and the DMN activations during monetary vs social feedback. Only a negative correlation between AQ and mPFC activation in men was significant after Bonferroni correction (Supplementary Table S3).

**Discussion**

In this study, we aimed to investigate a potential modulation of monetary in comparison to social reward processing by gender and individual differences in subclinical autistic traits. To this end, we employed an incentive delay task (Knutson et al., 2000) with a social and a monetary condition. Anticipation of both types of reward led to ventral striatal activation that was accompanied by shorter RTs and higher hit rates. These effects were more pronounced for monetary relative to social reward. On the other hand, anticipation of social reward elicited relatively higher activation of DMN structures. At outcome, social reward was associated with bilateral activation of the amygdala and FFA. Correlations between AQ and neural correlates of social reward processing were, at least in part, gender-specific: During anticipation of social reward AQ correlated positively with right precentral activation in women and, to a lesser extent, also in men. However, only men showed a negative correlation between AQ and right amygdala activation during social reward feedback.

**Effects of motivation on task performance and neural correlates**

In both tasks, the motivation to obtain a reward was associated with shorter RTs and higher hit rates, which is in line with previous studies examining motivational effects on performance (Knutson et al., 2000, 2001; Richter et al., 2013a). In fMRI, anticipation of both reward types was associated with activation of the striatum, particularly the NAcc. This result is compatible with well-documented role of the NAcc in reward prediction (Knutson et al., 2000, 2001; Kirsch et al., 2003). Striatal reward anticipation responses were more pronounced to cues predicting monetary reward as compared with social reward, replicating previous results (Spreckelmeyer et al., 2009). Notably, Spreckelmeyer et al. (2009) reported such a striatal activation difference in men only, whereas we found this difference across both genders. Spreckelmeyer et al. (2009) used three levels of reward, while in the current study only one reward level was employed. Because in Spreckelmeyer’s study, the male-specific difference in striatal responses to monetary vs social reward cues was restricted to the high reward condition, we tentatively suggest that the application of multiple reward levels might be more suitable for detecting subtle gender-related differences in striatal responsivity to different reward types.

**Anticipation of social reward engages the DMN**

Contrasting anticipation of social vs monetary reward revealed relatively higher activation in the DMN (precuneus, TPJ). While
Fig. 3. Reward-dependent modulation of striatal activation. The anticipation of monetary reward elicited more pronounced striatal activation as compared with anticipation of social reward (monetary reward > social reward). This effect was significant at $P < 0.05$, FWE-corrected for ROI volume. Activations are superimposed on the MNI template brain provided by MRicron. Coordinates are in MNI space. Bar plots depict contrasts of parameter estimates at the peak coordinate separated by gender and reward condition. Error bars depict standard errors of the mean. Mon R: condition with monetary reward. Soc R: condition with social reward.

Fig. 4. Anticipation of social vs monetary reward. (A) The anticipation of social but not monetary reward (social reward > monetary reward) was associated with a relative activation difference in posterior DMN structures (PCC/precuneus and TPJ). This effect was significant at $P < 0.05$, FWE-corrected for ROI volume. Activations are superimposed on the MNI template brain provided by MRicron. Coordinates are in MNI space. Bar plots depict contrasts of parameter estimates at the peak coordinate separated by gender and reward condition. Error bars depict standard errors of the mean. Mon R: condition with monetary reward. Soc R: condition with social reward. (B) Relationship between Autism Quotient (AQ) and blood oxygen level-dependent signal in PCC/precuneus to anticipation of social vs monetary reward. Robust Shepherd’s $\pi$ correlations are shown. AQ was correlated positively with PCC/precuneus blood oxygen level-dependent signal to anticipation of social vs monetary reward in women, and a trend was observed in men.
prominently associated with resting conditions, the DMN has also been implicated in self-reference, theory of mind or, more generally, socio-emotional cognition (Corbetta et al., 2008; Schilbach et al., 2008b, 2012; Whitfield-Gabrieli et al., 2011; Mars et al., 2012). Schilbach et al. (2012) suggested that introspection might constitute a common feature of resting state and socio-emotional cognition. Introspection refers to the ability to examine one’s own feelings and thoughts, which is formed by previous social and emotional experiences (Gusnard et al., 2001; Schilbach et al., 2012). Schilbach et al. (2012) also investigated the underlying neural network of facial mimicry (spontaneous and involuntary response to facial expressions). They observed activation in the face motor area, but also in DMN structures (Schilbach et al., 2008a), which they attributed to social processing and self-other differentiation (Northoff and Bermpohl, 2004; Schilbach et al., 2008a). Our results extend these findings by showing that already the anticipation of a, broadly speaking, positive social experience may elicit DMN activation. One should note, however, that in our study, as in numerous previous studies of DMN function, ‘activation increases’ often reflected lower levels of deactivation relative to rest in one condition compared with another.

### Table 3. Neural correlates during anticipation of monetary reward and social reward (P < 0.001, uncorrected, minimal cluster size = 10)

| Region | BA | x | y | z | SPM T₁, 120 | P (uncor.) |
|--------|----|---|---|---|-------------|-----------|
| **Monetary reward > social reward** | | | | | | |
| Right caudate nucleus | 9 | 11 | -5 | 4.05 | <0.001 |
| Left putamen | -9 | 5 | -5 | 3.92 | <0.001 |
| **Social reward > monetary reward** | | | | | | |
| Right superior frontal gyrus | 10 | 24 | 59 | 19 | 3.89 | <0.001 |
| Left medial frontal gyrus | 10 | -12 | 56 | 19 | 3.76 | <0.001 |
| Right middle frontal gyrus | 8 | 36 | 17 | 40 | 3.93 | <0.001 |
| Right inferior parietal lobule | 40 | 48 | -61 | 49 | 4.74 | <0.001 |
| Right precuneus | 7 | 6 | -61 | 43 | 4.08 | <0.001 |

BA, Brodmann area.

### Fig. 5. Social vs monetary reward feedback

The present finding of pronounced bilateral FFA activation during social relative to monetary reward feedback is most likely attributable to the processing of face stimuli, as both the amygdala (Adolphs, 2010; Rademacher et al., 2010) and the FFA (Kanwisher et al., 1997; Richter et al., 2013b) have repeatedly been linked to human face perception and processing.

Notably, a fronto-parietal network, including DMN structures, showed relatively higher activation during monetary compared with social feedback (Table 4). A parsimonious explanation for this would be a rebound-like effect, namely relatively increased DMN activation after deactivation during the processing of monetary reward cues. In our view, however, it
seems more likely that, given the well-documented role of the, particularly anterior, DMN in self-related processing (Kelley et al., 2002), the activation of the mPFC in particular may reflect the higher self-relevance of actually receiving a monetary reward as compared with seeing a face that allows no further social interaction.

**Gender-specific manifestation of autism trait in social reward processing**

We had hypothesized that interindividual variability of autistic features among healthy participants might modulate brain activation patterns related to social reward anticipation and feedback processing in a gender-specific way. Contrary to our hypothesis, reward-related behavioral improvement and striatal activation were not modulated by AQ during reward anticipation. This is inconsistent with the previously reported activation patterns related to social reward anticipation and features among healthy participants might modulate brain reward processing (Sims et al., 2014). We suggest that the missing AQ-related modulation of striatal reward anticipation responses might be related to the observation that the same AQ scores in healthy participants vs clinically affected autistic individuals may not reflect the same degree of autistic traits (Murray et al., 2014). Therefore, one might require more powerful approaches to uncover AQ-related variability of striatal responsibility in neurotypical individuals. For example, Sims et al. (2014) recently reported a negative modulation of fronto-striatal functional connectivity by AQ in young, healthy individuals when face stimuli were paired with monetary rewards (Sims et al., 2014). Furthermore, functional connectivity approaches might be more suitable to detect a potential modulation of striatal reward responsivity by autism trait in non-clinical populations.

**Table 4.** Neural correlates during monetary feedback and social feedback (P < 0.05, FWE-corrected, minimal cluster size = 10)

| Region | BA | x  | y  | z  | SPM T1,120 P (FWE-cor) |
|--------|----|----|----|----|------------------------|
| Monetary reward > social reward | | | | | |
| Right superior frontal gyrus | 10 | 24 | 59 | 1 | 5.79 | 0.001 |
| Right middle frontal gyrus | 10 | 42 | 56 | 7 | 5.81 | 0.001 |
| Right anterior cingulate | 32 | 6  | 32 | 25 | 8.39 | <0.001 |
| Right/Left cingulate gyrus | 23 | 0  | -32 | 31 | 7.57 | <0.001 |
| Right inferior parietal lobule | 40 | 48 | -46 | 43 | 6.80 | <0.001 |
| Left lingual gyrus | 18  | -3 | -85 | -14 | 5.45 | 0.006 |
| Social reward > monetary reward | | | | | |
| Right orbital gyrus | 11 | 6  | 44 | -20 | 8.70 | <0.001 |
| Right inferior frontal gyrus | 47 | 33 | 32 | -14 | 7.67 | <0.001 |
| Left inferior frontal gyrus | 47 | -33 | 32 | -14 | 6.54 | <0.001 |
| Right middle temporal gyrus | 21 | 57 | -4 | -20 | 5.46 | 0.006 |
| Left amygdala | -18 | -10 | -17 | 10.66 | <0.001 |
| Right fusiform gyrus | 37 | 42 | -49 | -20 | 14.90 | <0.001 |
| Left fusiform gyrus | 37 | -42 | -52 | -20 | 11.70 | <0.001 |

BA, Brodmann area.

**Table 5.** Correlations of brain activation patterns and AQ

| Anticipation (monetary > neutral) | Women x (P) | Men x (P) | Fisher’s Z (P) |
|-----------------------------------|-------------|-----------|----------------|
| Right striatum                    | 0.112 (1.0000) | 0.087 (1.0000) | n/a |
| Left striatum                     | 0.123 (1.0000) | 0.087 (1.0000) | n/a |
| Anticipation (social > neutral)   |            |           |               |
| Right striatum                    | -0.021 (1.0000) | -0.092 (1.0000) | n/a |
| Left striatum                     | 0.059 (1.0000) | 0.022 (1.0000) | n/a |
| Anticipation (monetary > social)  |            |           |               |
| Right striatum                    | -0.247 (0.9342) | 0.292 (0.2359) | n/a |
| Left striatum                     | -0.180 (0.6818) | 0.084 (1.0000) | n/a |
| Anticipation (social > monetary)  |            |           |               |
| PCC/precuneus                     | 0.587 (0.0017") | 0.378 (0.0788) | 1.00 (0.1587) |
| Right TPJ                         | -0.495 (0.0127") | -0.156 (0.8224) | n/a |
| Feedback (social > monetary)      |            |           |               |
| Right amygdala                    | -0.005 (1.0000) | -0.583 (0.0014") | 2.41 (0.0160") |
| Left amygdala                     | -0.120 (1.0000) | -0.123 (1.0000) | n/a |
| Right FFA                         | 0.194 (0.6260) | 0.123 (1.0000) | n/a |
| Left FFA                          | -0.220 (0.5209) | 0.319 (0.1724) | n/a |

Shepherd’s pi correlations between AQ scores and BOLD signal change values (contrasts of parameter estimates) in a priori defined ROIs (striatum, precuneus, TPJ, amygdala, FFA) across women and men. All P-values are two-tailed. Significant at P < 0.05, uncorrected; **Significant at P < 0.05, Bonferroni-corrected for the number of ROIs (please note that Fisher’s Z tests were only performed when at least one correlation was significant after Bonferroni correction).
may be related to the task-specific dysfunction of posterior DMN structures, but an unspecific underrecruitment of anterior DMN regions in autism reported previously (Kennedy and Courchesne, 2008a). In another study, Kennedy et al. (2006) demonstrated impaired deactivation of the PCC/precuneus in ASD during an emotional Stroop task. Similarly, Murdough et al. (2012) reported a less pronounced DMN deactivation in individuals with ASD during a ToM task. While further research is clearly required, we suggest that the positive correlation between AQ and posterior DMN activation during anticipation of social reward and the, possibly less specific, negative correlation of anterior DMN activation during monetary reward feedback in healthy subjects point to altered DMN function as a potential endophenotype for autistic traits, as it qualitatively resembles some of the observations in individuals clinically affected with autism.

In addition to the positive relationship between AQ and DMN activation during anticipation of social reward, male participants also showed a negative correlation between AQ and the right amygdala during reward feedback. The existing literature on altered amygdala function in ASD is rather inconsistent. Studies have reported both increases (Monk et al., 2010; Weng et al., 2011) and decreases of amygdala responses to faces in ASD-affected individuals (Kleinhans et al., 2008; Finkham et al., 2008). Similarly, previous observations regarding FFA activation in ASD also yielded conflicting results (Schultz et al., 2000; Pierce et al., 2001, 2004 vs Hadjikhani et al., 2004; Kleinhans et al., 2008). One reason for these inconsistencies could be alterations within face processing networks in ASD at the level of functional connectivity (Kleinhans et al., 2008). In line with this notion, Dziobek et al. (2010) reported reduced anatomical covariance between amygdala volume and fusiform cortical thickness in individuals with ASD.

Despite these inconsistencies, the observation that the negative relationship between AQ and amygdala activation was only found in men, is noteworthy, given the higher prevalence of ASD in the male population (Kogan et al., 2009; Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008; Principal Investigators, 2012). Furthermore, neuroanatomical studies have suggested that individual differences in brain structure related to ASD resemble sex-related differences in brain anatomy (Baron-Cohen et al., 2005). Additionally, subtle sex differences in symptomatology of clinical autism have also been reported (Hartley and Sikora, 2009). While our present results may not be directly translatable to the clinic, they might yet to some extent reflect the suspected interactions between gender and autistic phenotypes.

Functional connectivity alterations in both the DMN and the face processing network in ASD have been repeatedly shown. Future studies should also employ functional connectivity approaches (Sims et al., 2014) to further elucidate the relationship between the neural processing of social vs monetary reward and gender and AQ.

Limitations

It must be noted that the social reward that could be obtained in this study, a photo of a smiling face, might have been a weak reinforcer relative to the actual monetary gain, as participants could not actually interact with the persons depicted. An alternative way to provide social reward would be an experimental manipulation of social status and recognition (Meshi et al., 2013).

Another limitation of this study is related to the correlations between AQ and neural activations in the feedback phase. As we did not implement a non-reward baseline, we cannot rule out that the reported correlations of AQ and social reward feedback might in fact not be reward-specific, but more generally linked to processing of the face stimuli per se.

Conclusions

In summary, our results suggest a gender-specific manifestation of autistic features in the healthy population during social reward processing. While increased DMN activation during anticipation of social cues might reflect a more general endophenotype of the DMN dysfunction observed in clinical autism, only male individuals exhibited an additional relationship between AQ and a lower amygdala response to faces, a finding that warrants further investigations in light of the higher prevalence of ASD in men.

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Supplementary data

Supplementary data are available at SCAN online.

Conflict of interest. None declared.

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