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Neural processing of social rejection: the role of schizotypal personality traits

Running head: fMRI of social rejection in schizotypy

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Abstract

A fear of being rejected can cause perceptions of more insecurity and stress in close relationships. Healthy individuals activate the dorsal anterior cingulate cortex (dACC) when experiencing social rejection, while those who are vulnerable to depression deactivate the dACC presumably in order to down-regulate salience of rejection cues and minimize distress. Schizotypal individuals, characterised by unusual perceptual experiences and/or odd beliefs, are more rejection sensitive than normal. We tested the hypothesis, for the first time, that individuals with high schizotypy also have an altered dACC response to rejection stimuli. Twenty-six healthy individuals, 14 with low schizotypy (LS) and 12 with high schizotypy (HS), viewed depictions of rejection and acceptance and neutral scenes while undergoing functional MRI. Activation maps in LS and HS groups during each image type were compared using SPM5 and their relation to participant mood and subjective ratings of the images was examined. During rejection relative to neutral scenes, LS activated and HS deactivated the bilateral dACC, right superior frontal gyrus and left ventral prefrontal cortex. Across both groups, a temporo-occipito-parieto-cerebellar network was active during rejection, and a left fronto-parietal network during acceptance, relative to neutral scenes, and the bilateral lingual gyrus during rejection relative to acceptance scenes. Our finding of dACC-dorso-ventral PFC activation in LS, but deactivation in HS individuals when perceiving social rejection scenes suggests that HS individuals attach less salience to and distance themselves from such stimuli. This may enable them to cope with their higher-than-normal sensitivity to rejection.

Key words: Schizotypal personality, rejection, acceptance, dorsal anterior cingulate cortex, lingual gyrus; fMRI

Introduction

Rejection sensitivity (RS) is the tendency to expect rejection by significant people in a person's life (Downey and Feldman, 1996). Rejection sensitive individuals perceive more insecurity and stressors in close relationships, express more vulnerability towards people around them and feel more anxious in social situations (Mehrabian and Ksionzky, 1974; Sokolowski et al., 2000; Vorauer et al., 2003; Langens and Schuler, 2005). Increased RS in the form of reflected appraisals of vulnerability in turn create 'authenticity doubts', that is where the person feels that the significant other expresses more positive regard than he/she truly feels (Lemay and Clark, 2008).

Across various psychiatric disorders, greater RS is associated with greater perceived social stress and fewer perceived coping resources (Rusch et al., 2009). Patients with a diagnosis of schizotypal personality disorder show greater RS than healthy individuals (Torgersen et al., 2002). In addition, a high level of criticism by a relative towards the patient aggravates communication disorder in schizophrenia patients (Rosenfarb et al., 1995; Rosenfarb et al., 2000), and such patients are more likely to endorse stronger beliefs about the consequences of being rejected (Grant and Beck, 2009). A high level of expressed emotion, the negative emotion expressed by a family member towards a patient in the form of criticism, hostility, rejection, emotional over-involvement or decreased warmth (Leff and Vaughn, 1985), is associated with a greater likelihood of relapse to psychosis (Rutter and Brown, 1966; Kreisman et al., 1988; Bailer et al., 1994; Kuipers et al., 2010) and a greater number of psychotic exacerbations (Heresco-Levy et al., 1992).

The neural basis of RS has been examined in healthy populations. In healthy individuals, greater RS activates the dorsal anterior cingulate cortex (dACC)

(Eisenberger et al., 2003; Somerville et al., 2006; Burklund et al., 2007; Kross et al., 2007; Masten et al., 2009). For instance, a higher level of RS was associated with greater activity in the dACC when watching video clips of people expressing disapproval compared to no emotion, anger or disgust (Burklund et al., 2007). A frontal lobe network that included the dACC was activated when healthy individuals viewed images of individuals experiencing social rejection than acceptance (Kross et al., 2007). The dACC is also known to be involved in conflict detection (Carter et al., 2001; Somerville et al., 2006) and emotional decision-making in healthy individuals (Walton et al., 2004; Walton et al., 2007); these additional cognitive-emotional processes may contribute towards perception of rejection. High RS individuals show greater activation in the dACC, VLPFC and SFG when viewing social rejection scenes compared to low RS individuals (Kross et al., 2007). The VLPFC and SFG are involved in empathising with others (Hooker et al., 2010b; Kramer et al., 2010; Sommer et al., 2010) and regulating emotion (Mak et al., 2009; Hooker et al., 2010a).

The neural basis of elevated RS has been explored in depression, but not in schizophrenia. Patients in remission from depression, but not healthy people, deactivate the dACC on hearing maternal criticisms (Hooley et al., 2005; Hooley et al., 2009). An explanation for this finding was that people who are vulnerable to depression down-regulate salience to criticism by deactivating the dACC (Hooley et al., 2005; Hooley et al., 2009).

The present study examined the neural basis of RS in individuals with a high level of schizotypal personality traits, precursory to a study of patients with a schizophrenia or schizoaffective diagnosis. The advantage of examining the response to social rejection in a group of healthy individuals with schizotypal traits over patients with a schizophrenia or schizoaffective diagnosis is that observed effects would not be confounded by illness chronicity and medication. Schizotypy is a personality trait within the normal range of the schizophrenia spectrum, but related to schizophrenia at the clinical (Mason et al., 2005; Cochrane et al., 2010), genetic (Fanous et al., 2001; Fanous et al., 2007), neuropsychological (Gooding et al., 2006) and neurophysiological levels (Ettinger et al., 2005; Bollini et al., 2007). Schizotypal traits include magical thinking, unusual perceptual experience, odd behaviour and speech (Mason et al., 1995) that are thought to correspond to positive symptoms of psychosis (Mason et al., 1995; Mason et al., 2005; Cochrane et al., 2010) and anhedonia that is thought to correspond to negative symptoms (Vollema and van den Bosch, 1995). Studying the neural basis of RS in schizotypal individuals may help to understand how RS interacts with other stress-provoking situations and interpretation of one's emotions at the neural level. Individuals with high levels of schizotypal personality traits may have altered ways of perceiving rejection cues (Torgersen et al., 2002) in order to minimize distress and may down-regulate salience to rejection cues, similar to what was observed in recovered depressed patients (Hooley et al., 2009).

Given the conflicting evidence for the level of neural response to rejection between high RS healthy individuals and formerly depressed clinical individuals, and following earlier reports of greater RS in schizotypal personality disorder patients (Torgersen et al., 2002), it was hypothesized that normal individuals with a high level of schizotypal traits (high schizotypy, HS group) compared with individuals with a low level of schizotypal traits (low schizotypy, LS group) would show deactivation in the dACC in the neural response to social rejection scenes.

Methods and Materials

Subjects

Participants were drawn from the general population with no known psychiatric diagnosis and selected only if they had very low or high levels of unusual experiences related to schizotypal personality (Mason et al., 2005). Of 26 selected participants, 12 had a high level of unusual experiences [HS group, i.e. scored ≥7 on the Unusual Experiences (UE) sub-scale of the short form of the Oxford and Liverpool Inventory of Feelings and Experiences, O-LIFE] (Mason et al., 2005) and 14 had a very low level of unusual experiences (LS group, i.e. scored ≤2 on the O-LIFE UE sub-scale). The UE subscale of the O-LIFE was chosen to identify HS and LS participants, as a high score on this subscale is associated with greater positive symptom severity in schizophrenia patients (Cochrane et al., 2010). A score of ≥7 out of a maximum score of 12 on the UE subscale on the O-LIFE short form was based on a score of >1 standard deviation above the UE scores found in the normal population (Mason et al., 2005).

The O-LIFE was also used to measure other facets of schizotypy, namely cognitive disorganisation which measures aspects of poor attention and concentration and is thought to relate to thought disorder and other disorganised aspects of psychosis, introvertive anhedonia which measures lack of enjoyment from social and physical sources of pleasure and is thought to relate to weakened forms of negative symptoms, and impulsive non-conformity which measures forms of behaviour suggesting a lack of self-control (Mason et al., 1995).

Potential participants were recruited from a database of healthy volunteers (MindSearch, Institute of Psychiatry; n≥500) and by circular emails sent to the staff and students of King's College London. Inclusion criteria were: (i) IQ>90, estimated

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as >5 correct responses on the National Adult Reading Test (Nelson and Wilson, 1991), (ii) right-handed, (iii) 18−45 years age range, (iv) normal-to-corrected vision, and (v) normal hearing. Exclusion criteria were: (i) Beck Depression Inventory (BDI) (Beck et al., 1996) score >30, (ii) a history of mental disorder, brain injury, neurological disorder, learning disabilities, or loss of consciousness for more than five minutes, and (iii) a history of alcohol or drug abuse within the last 12 months. Parental socio-economic status was classified as follows: 1–Professional (doctor/lawyer), 2–Intermediate (manager/ teacher/ nurse), 3–skilled (secretary/bus driver), 4–semi-skilled (shop assistant) and 5–manual (cleaner, labourer).

Study procedures were approved by the King's College London Research Ethics Committee (CREC/07/08-66). Participants provided written informed consent to their participation and were compensated for their time and travel.

fMRI paradigm and procedure

Rejection-acceptance task: stimulus selection

Images depicting social rejection, acceptance and neutral scenes were sourced from the International Affective Pictures System (Lang et al., 1999) or purchased from a web-based company (www.jupiterimages.co.uk) supplying stock photographic images for professional use. Images of different types of rejection and acceptance situations (parental, partner or peer) were sourced. One hundred and sixty-four images (35 rejection, 49 acceptance and 80 neutral) were obtained. Six doctoral or post-doctoral level psychology researchers were asked to rate the images blind to the emotional content of the image on two indices: rejection level (rejection-acceptance) and valence (negative-positive) on 11-point Likert scales from -5 to +5. Fifteen images from each category were chosen based on the means and S.D. of the six researchers' ratings of each image on rejection level (rejected-accepted) and valence (negative-positive). In the rejection category, 15 images with a mean score nearest to -5 on rejection level and valence and the lowest S.D. were chosen (summary statistics of the six raters' scores are provided in Appendix A). In the acceptance category, 15 images with a mean score nearest to +5 on rejection level and valence and lowest S.D. were chosen. In the neutral category, 15 images with a mean score nearest to 0 on rejection level and valence and lowest S.D. were chosen. Across the three categories, images were matched for the number of people in the scene, their gender and their ethnicity.

On-line task

Participants were presented with the rejection-acceptance task projected onto a screen at the end of the scanner bed. During this task, the three types of images (rejection, acceptance, neutral) were shown in 15 second blocks of three images each, with each image being presented for five seconds (Figure 1). Immediately after each block, the participant had to respond to the question, 'How do you feel right now?' within a five-second time period. The participant responded on an 11-point visual analogue scale (VAS) ranging from -5 (sad) to +5 (happy) by pressing left or right with their right hand on a button-box. The order of rejection, acceptance and neutral blocks was pseudo-randomised. Each 20 second block (15 seconds to view the images plus 5 seconds to make a response) was separated by a 10 second rest block (blue blank screen). Two stimulus playlists were used in a random manner (using a randomisation list) in order to counterbalance for whether the participant viewed images of rejection or acceptance in the first block.

Off-line task

After the scanning session, the participants once again viewed the rejection-acceptance task images on a laptop computer. Each image appeared for five seconds in the same sequence as during fMRI. Participants rated each image on 11-point VASs on the following three themes: rejection-acceptance [rejected (-5) to accepted (+5)], affect [sad (-5) to happy (+5)], and arousal [low (0) to high (10)] taking as long as they wished. Participants were not restricted in the time they took to respond to each question. The task usually took approximately 25 minutes to complete.

Participants completed the Positive and Negative Affect scale (PANAS, Watson et al., 1988) – moment subscale before the scanning session and the full scale after the scanning session, but before performing the off-line task. The PANAS contains 10 positive (e.g., interested, proud) and 10 negative (e.g., ashamed, irritable) mood descriptors and six time points, namely moment, today, past few days, past few weeks, year and general. Participants rated all subscales; only ratings of the moment subscale before scanning and general subscale were taken for statistical analyses in the present study.

Participants were also asked to complete the Beck Anxiety Inventory (BAI) (Beck and Steer, 1993) and the Adult Rejection Sensitivity Scale (RSS) (Downey and Feldman, 1996) before performing the off-line task in order to measure anxiety and rejection sensitivity traits. As mentioned earlier, participants completed the BDI at the time of their screening and were included only if they did not have depression scores at a clinically important level.

***** Figure 1 about here *****

Image acquisition

Echo-planar T2*-weighted MR images of the brain were acquired using a 1.5 Tesla GE Signa HDx scanner (General Electric, Milwaukee WI, USA) at the Centre for Neuroimaging Sciences, Institute of Psychiatry, King's College London. Head movements were minimised using foam padding. A localiser scan for placing the volume of interest and a high-resolution structural scan for image co-registration were first acquired. An eight channel radio frequency head coil working in parallel mode was used to acquire images from each of 36 near-axial non-contiguous planes parallel to the inter-commissural plane. These MR images depicting BOLD contrast were acquired with an echo time (TE)=40 ms, repetition time (TR)=2.5 s, field of view (FOV)=24 cm, flip angle=85°, in-plane resolution=3.75 mm, slice thickness=3 mm, interslice gap=0.3 mm. Four dummy scans followed by two hundred and ten volumes were acquired (total scan time 8 minutes and 55 seconds). An inversion recovery prepared fast 3D SPGR was acquired (TR=11.1 ms, TE=4.9 ms, TI=300 ms, acquisition matrix 256x160, 150 locations, slice thickness 1.1 mm in-plane resolution 1.094 mm flip angle = 18 degrees, scan time 6 minutes and 4 seconds).

Statistical analysis

Demographic, behavioural characteristics and ratings of the rejection-acceptance task in the HS and LS groups

A Chi-squared test for group differences in gender was performed. For continuous variables with no heterogeneity of variance, namely O-LIFE cognitive disorganisation, introvertive anhedonia and impulsive non-conformity subscales, BDI, RSS and PANAS moment positive and general positive and negative subscales, analysis of variance (ANOVA) was performed with group as the independent variable, and for variables with heterogeneity of variance (parental socio-economic status, O-LIFE UE subscale, BAI and PANAS moment negative), Mann-Whitney U test was performed. Effect size (Cohen's d) was also calculated to determine whether the size of the difference in continuous variables was small (Cohen's d<0.5), medium (≥0.5 and <0.8) or large (≥0.8).

Two (Group) x three (rejection, acceptance and neutral conditions) repeated-measures ANOVAs were performed on each off-line task rating scale (rejection-acceptance, sad-happy and high-low arousal).

Statistical significance was set a priori at p level <0.05; analyses of behavioural data were carried out using Statistical Package for the Social Sciences (SPSS, version 16).

fMRI analysis

fMRI pre-processing

For each participant, the 210 volume functional time series images were motion corrected, transformed into stereotactic space (Montreal Neurological Institute, MNI), smoothed with an 8 mm FWHM Gaussian filter and band pass filtered using statistical parametric mapping software (SPM, version 5-1782, 2008; http://www.fil.ion.ucl.ac.uk/spm).

Statistical inferences

Data were analysed using the general linear model within SPM. At the single-subject level, contrast maps of each of the three conditions (rejection, acceptance and neutral) were created, covarying for motion parameters, with the resting period as the implicit baseline. This analysis was carried out by modelling each condition at each voxel using a boxcar function which incorporates the delay inherent in the hemodynamic response. The resulting maps were entered into a random-effects procedure at the second level to investigate task condition-related activation differences (rejection vs. neutral, acceptance vs. neutral and rejection vs. acceptance) (i) across all participants using one sample t-tests (height threshold $p<0.001$ and cluster corrected $p<0.05$), and (ii) between HS and LS groups using SPM ANOVA (height threshold $p<0.005$, cluster corrected $p<0.05$).

Due to a slight difference in gender distribution and significant difference in PANAS moment negative scores between HS and LS groups, subject-specific average activation values from clusters showing significant differences between groups were extracted using the MarsBaR toolbox (http://marsbar.sourceforge.net/projects/marsbar), entered into SPSS and analysed using analyses of covariance with subject-specific average activation values as the dependent variable, group as the between-subjects variable and gender or PANAS moment negative scores as the covariate.

Correlation between neural response to rejection-acceptance task and ratings of the off-line task and mood

Subject-specific average activation values from clusters showing significant task condition differences (rejection vs. neutral, acceptance vs. neutral and rejection vs. acceptance) (total number of clusters=7) across all participants were extracted using MarsBar and entered into SPSS. Correlations between these subject-specific activation values and the three post-fMRI off-line task ratings and mood (PANAS moment and general subscales) were evaluated first using Pearson's correlations and then using partial correlations controlling for gender. For the correlation between the rejection vs. acceptance contrast activation values and off-line rejection-acceptance and sad-happy ratings, the off-line ratings of the rejection and acceptance images were combined by calculating the difference between the ratings for two image types, the assumption being that the difference in ratings between the two image types would give an estimate of the emotional range across image type. Due to the large number of correlations, correlations with $p \leq 0.01$ were considered significant.

Results

Demographic and behavioural characteristics of groups

In both groups, participants were mostly female (Table 1). The HS group scored higher than the LS group on the cognitive disorganisation and impulsive non-conformity subscales of the O-LIFE and reported more negative current mood than the LS group ($p<0.05$; large effect size) (Table 1). The HS group also had higher self-reported anxiety and rejection sensitivity ($p>0.05$ but medium effect sizes) (Table 1).

***** Table 1 about here *****

Group differences in ratings of the rejection-acceptance task

There was no significant difference between groups in the off-line ratings of the three types of images (Table 2).

***** Table 2 about here *****

fMRI results

All participants

Rejection versus neutral: Across both groups, greater activation in the left middle occipital/middle temporal gyri, left pre-/post-central gyri, right cerebellum and right superior/middle temporal gyri during rejection relative to neutral images was observed (Table 3 and Figure 2). No area showed greater activity during neutral, relative to rejection, images.

Acceptance versus neutral: Participants activated the left medial frontal gyrus and left postcentral gyrus during acceptance relative to neutral images. No area showed greater activity during neutral, relative to acceptance, images.

Rejection versus acceptance: Participants activated the lingual gyrus bilaterally during rejection compared to acceptance images. No area showed greater activity during acceptance, relative to rejection, images.

***** Table 3 about here *****

***** Figure 2 about here *****

High versus low schizotypy groups

Groups differed when viewing rejection, compared to neutral, images in the activation of the dACC bilaterally, right superior frontal gyrus (SFG) and left ventrolateral prefrontal cortex (VLPFC)/ventromedial prefrontal cortex (VMPFC) (Table 4 and Figure 3). A plot of the percentage fMRI signal change showed that the LS group activated, but the HS group deactivated these areas (Figure 3).

The effect of schizotypy on activity changes between task conditions remained significant with comparable significance values after co-varying for gender (Table 5). The effect of schizotypy also remained significant in all clusters after covarying for PANAS moment negative scores though the effect was slightly reduced (F value reduced from 16.09 to 11.46) in the dACC cluster (Table 5).

***** Table 4 and 5 about here *****

***** Figure 3 about here *****

Relation between neural response to rejection-acceptance task and ratings of the off-line task and mood

Greater bilateral activation of the lingual gyrus in the rejection>acceptance contrast across all participants was correlated with smaller emotional range between ratings (i.e. range of scores on the rejection-acceptance VAS) of acceptance and rejection images (r=-0.488, p=0.011; partial correlation controlling for gender, r=-0.497, p=0.012), lower arousal ratings of rejection images (r=-0.521, p=0.006; partial correlation controlling for gender, r=-0.492, p=0.012) and lower arousal ratings of acceptance images (r=-0.555, p=0.003; partial correlation controlling for gender, r=-0.551, p=0.004).

Greater activation of the right superior temporal gyrus in the rejection>neutral contrast across all participants was correlated with higher ratings of negative mood on the PANAS general subscale (r=0.493, p=0.011; partial correlation controlling for gender, r=0.507, p=0.010).

Discussion

The study aimed to determine whether activity in the dACC, which is normally activated during experiences of social rejection, differs between HS and LS individuals when viewing scenes of social rejection. It was hypothesized that HS individuals would show decreased activation of the dACC during social rejection scenes relative to LS individuals similar to patients in remission from depression when listening to maternal criticisms (Hooley et al., 2005; Hooley et al., 2009). We expected this pattern on the basis that HS individuals may have altered ways of perceiving rejection cues (Torgersen et al., 2002) in order to minimize distress and that HS individuals may down-regulate salience to rejection cues, similarly to what was observed in recovered depressed patients (Hooley et al., 2009). As hypothesized, the HS group deactivated, while the LS group activated the dACC bilaterally during social rejection compared to neutral conditions. In addition, the HS group deactivated, while the LS group activated the right SFG and left

VLPFC/VMPFC during social rejection compared to neutral conditions. The findings suggest that the mental processes that are involved in perceiving social rejection differ between HS and LS individuals. This might be due to different ways of coping with stress-provoking situations.

Activation differences between HS and LS groups in response to rejection compared to neutral conditions

The LS group activated the dACC bilaterally, right SFG and left VLPFC/VMPFC, whereas the HS group deactivated these areas during social rejection compared to neutral conditions. Studies of the neural response to rejection in healthy individuals have shown increased activation in the dACC (Eisenberger et al., 2003; Somerville et al., 2006; Burklund et al., 2007; Kross et al., 2007; Masten et al., 2009), as well as the VLPFC and SFG (Kross et al., 2007) during experiences of social rejection. Greater activation of a frontal lobe network comprising the dACC bilaterally, left VMPFC/VLPFC and right SFG in the LS group may reflect the LS individuals' ability to attend to and process rejection cues without being anxious about the consequences of social rejection. The LS group may effectively engage the dACC and VLPFC in conflict detection and emotional decision-making (Bechara et al., 2000; Carter et al., 2001; Walton et al., 2004; Somerville et al., 2006; Walton et al., 2007) and the SFG and VLPFC/VMPFC to empathise with others (Hooker et al., 2010b; Kramer et al., 2010; Sommer et al., 2010) and regulate emotion (Mak et al., 2009; Hooker et al., 2010a) in response to perceived rejection. A recent study (Hooker et al., 2010a) showed that healthy individuals activate the left VLPFC when viewing their partners' negative facial expressions and that left VLPFC activation is associated with the occurrence of interpersonal conflicts between participant and their partner in predicting weaker negative mood and stronger positive mood.

The neural response to rejection in our group of participants with elevated schizotypal personality traits, however, showed deactivation of this frontal lobe network. Our HS group tended to have a higher level of RS than the LS group (p=0.1, medium effect size), supporting an earlier study (Torgersen et al., 2002) where individuals with a schizotypal personality disorder had greater RS than healthy individuals. The HS group, selected on the basis of a high level of unusual experiences, also had a higher level of cognitive disorganisation, impulsive non-conformity, momentary negative affect and on average higher anxiety than the LS group. HS individuals with a greater-than-normal propensity for these schizotypal personality traits and low mood may adopt alternative ways of dealing with social rejection compared to LS individuals, for instance by down-regulating their responses to rejection cues by distancing themselves from the rejection scenes (Koenigsberg et al., 2010). This may explain why, in the present study, the HS group did not differ from the LS group in the off-line rejection-acceptance ratings of the images. When participants are expected to mentalize a given emotional state but also to see their own emotional state as distinct from the observed emotion, they may express a more neutral mood (Polivy and Doyle, 1980). Low RS individuals activated, while high RS individuals deactivated the VLPFC and SFG when perceiving social rejection (Kross et al., 2007), which suggested that these areas may be important for interpreting rejection-related events in ways that minimize personal distress. HS individuals, like high RS individuals (Kross et al., 2007), who deactivate these regions during social rejection may do so in order to distance themselves from the observed emotional state, i.e. social rejection, rather than engage themselves in meaningful interpretation of the event. HS individuals, who have greater anxiety and RS levels due to their greater propensity for unusual experiences, may find it more beneficial to distance themselves from, rather than engage in, stress-provoking situations.

Patients with a past history of major depression who had been symptom free for more than six months deactivated the dACC compared to healthy participants on hearing maternal criticisms (Hooley et al., 2009). Hooley et al. (2009) discussed that increased dACC activity in healthy individuals when listening to maternal criticisms may reflect increased attention to emotionally salient stimuli, while the previously depressed patients may be able to reduce attention to such stimuli as a protective strategy and consequently 'turn off' the dACC. In the present study, a difference in current negative mood between HS and LS groups seemed to contribute towards some – but not all – of the variation in dACC activation, suggesting that negative affect may play a similar role in individuals with a schizotypal personality to that observed in patients with depression. Individuals with a schizotypal personality and patients with depression may have similar ways of responding to negative expressed emotion in the form of rejection or criticism, as positive schizotypy is associated with depression (Lewandowski et al., 2006). A high level of relative's expressed emotion in the form of criticism is associated with a greater likelihood of relapse in patients with a major depressive disorder (see Wearden et al., 2000 for a review of the literature). Altered responses to perceived rejection in individuals with a schizotypal personality who are rejection sensitive may also be due to higher levels of relative's expressed emotion. Such an explanation needs to be tested in future studies on expressed emotion in schizotypy.

Greater lingual gyral activation during rejection compared to acceptance conditions across all participants

The lingual gyrus was activated bilaterally to a greater extent during rejection than acceptance conditions across all participants. The lingual gyrus is frequently associated with the identification of facial emotional expressions (Keightley et al., 2007; Scheuerecker et al., 2007; Kitada et al., 2010), but also when individuals simulate other people's facial expressions (Kim et al., 2007). The lingual gyrus is also activated when experiencing a form of rejection, i.e. when a person is immersed in a social interaction with his/her partner and learns that his/her partner has failed to reciprocate cooperation (Rilling et al., 2008). Our findings confirm that the lingual gyrus is involved in social cognition, but more specifically in discriminating between rejection and acceptance, and in this regard the HS group showed a normal neural response to social rejection. In addition, greater activation of the lingual gyrus was associated with a more restricted emotional range (as measured by the VAS ratings) between rejection and acceptance conditions, and with lower arousal ratings of rejection and acceptance images. These relationships may suggest an association between more effortful use of the lingual gyrus to discriminate between rejection and acceptance conditions and possibly cognitive control (top-down processing) of emotions. These relationships may also suggest an attenuated ability to interpret rejection and acceptance scenes as extremely rejecting and accepting, respectively, and an increased ability to regard these scenes in a more neutral way. Kross et al. (2007) found that a stronger neural response to rejection scenes was associated with lower subsequent distress ratings of rejection images.

Greater right superior temporal gyrus activation during rejection compared to neutral images is associated with more negative mood

Greater activation of the right superior temporal gyrus across all participants during rejection compared to neutral conditions was associated with greater negative mood in general. Recent research has shown that the superior temporal gyrus is associated with the regulation of negative emotions (Mak et al., 2009; Koenigsberg et al., 2010; Winecoff et al., 2010). In recent studies (Koenigsberg et al., 2010; Winecoff et al., 2010), healthy participants activated the superior temporal gyrus when reappraising negative images using a response style that involved detaching themselves from the image. Our results suggest that greater use of the right superior temporal gyrus when viewing rejection scenes may cause individuals to experience more negative mood. Conversely, individuals who do not show this neural response to rejection are able to feel less general negative mood.

Limitations and future research

Firstly, the groups did not differ in the behavioural response to the task stimuli. The demand characteristics of the situation, viz. favouring the prototypical expression of how a person should feel after exposure to such scenes, may have minimised differences in subjective ratings of LS and HS individuals. This does not necessarily preclude the presence of a group difference in the neural response to the stimuli (Wilkinson and Halligan, 2004); the neural response can be used to inform some of the cognitive processes engaged in behaviours that are less well understood or in need of further explanation (Wilkinson and Halligan, 2004). Secondly, our HS group had only a marginally higher level of RS than the LS group (p=0.1, medium effect size). The small sample sizes would have made it difficult for some of the group differences to have reached a statistically significant level. The study's findings therefore need to be replicated in a larger sample. Thirdly, given the association between positive schizotypy and depression (Lewandowski et al., 2006), it is possible that the observed neural response to rejection scenes in the HS group may be further moderated by depression. However, the HS and LS groups in our study did not differ in the level of depression as measured by the BDI because we excluded those with high levels of depression. The neural response to perceived rejection may be stronger in individuals with a high level of depression and schizotypal personality. Future studies may consider the role of depression in behavioural and neural response styles to rejection in individuals with a schizotypal personality. Fourthly, the RSS was administered after participants performed the RS on-line task, but before the RS off-line task, that may have temporarily altered their responses on the RSS. Fifthly, this study was not powered to investigate potential sex-specific effects of schizotypy in response to social rejection. Finally, the rejection scenes may not have had personal relevance to the participants and therefore not engaged the participants optimally. It is possible that schizotypal individuals are able to regulate their subjective and neural responses to social rejection only when the scenes are not personally relevant.

Conclusions

Schizotypal individuals deactivate a dorso-ventral frontal lobe network, consisting of the dACC, right SFG and left VLPFC/VMPFC. The neural and behavioural response to rejection stimuli suggests that schizotypal individuals may employ strategies that help them to distance themselves from and minimize the salience attached to rejection-provoking stimuli.

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Figure legends

Figure 1. A representation of a 20 second rejection block from the rejection-acceptance task.

Figure 2. Activation maps showing differences between rejection, acceptance and neutral conditions across all participants (maps thresholded at p=0.001; displayed clusters corrected for multiple comparisons, p=0.05).

Figure 3. Activation maps and boxplots of percentage fMRI signal showing differences between high versus low schizotypy groups in the rejection>neutral activation contrast (maps thresholded at p=0.005; displayed clusters corrected for multiple comparisons, p=0.05).

Table 1. Demographic and behavioural characteristics of high schizotypy (HS) and low schizotypy (LS) groups

Characteristic	**HS (n=12)**	**LS (n=14)**	**Test**	**χ^2 or z (df)**	**p**	**Effect size (Cohen's d)**
Gender: male/female (n)	3/9	2/12	χ^2	0.478 (1)	0.490	-
			M-W U	0.287 (1)	0.820	-
Parental socio-economic status						
Professional	6	6				
Intermediate	5	7				
Skilled	1	1				
	mean, s.d.	**mean, s.d.**		**F or z (df)**		
Age in years	30.00 (10.58)	28.64 (6.07)	ANOVA	0.167 (1,24)	0.686	0.157
Years in education	16.67 (3.05)	17.28 (1.68)	ANOVA	0.426 (1,24)	0.520	0.247
O-LIFE						
Unusual experiences	8.17 (2.33)	1.00 (0.96)	M-W U	4.381 (1)	<0.001	4.024
Cognitive disorganisation	3.07 (2.97)	4.35 (2.87)	ANOVA	5.782 (1,24)	0.024	0.438
Introverted anhedonia	1.00 (1.13)	1.28 (0.91)	ANOVA	0.509 (1,24)	0.482	0.273
Impulsive non-conformity	4.50 (2.47)	2.71 (1.94)	ANOVA	4.268 (1,24)	0.050	0.806
Total	18.92 (5.81)	8.07 (5.01)	ANOVA	26.138 (1,24)	<0.001	2.000
BDI	7.75 (6.70)	5.93 (5.93)	ANOVA	0.541 (1,24)	0.469	0.287
BAI	10.50 (9.93)	5.36 (5.21)	M-W U	0.878 (1)	0.380	0.648
RSS	11.44 (4.12)	8.88 (3.80)	ANOVA	2.721 (1,24)	0.112	0.646
PANAS moment						
Positive	30.50 (10.71)	29.43 (8.64)	ANOVA	0.080 (1,24)	0.780	0.110
Negative	14.50 (4.52)	11.36 (1.60)	M-W U	2.314 (1)	0.023	0.926
PANAS General						
Positive	35.17 (7.87)	32.57 (7.26)	ANOVA	0.764 (1,24)	0.939	0.343
Negative	16.17 (5.29)	16.00 (5.60)	ANOVA	0.006 (1,24)	0.391	0.031

BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; M-W U: Mann-Whitney U test; O-LIFE: Oxford and Liverpool Inventory of Feelings and Experiences; PANAS: Positive and Negative Affect Scale: RSS: Rejection Sensitivity Scale

Table 2. Participant ratings of the rejection-acceptance task

Image type	**HS (n=12)**	**LS (n=14)**	**Test**	**F (df)**	**p**	**Effect size (Cohen's d)**
Rejection level rating [-5 (rejected) to +5 (accepted)]						
Rejection images	-1.58 (1.20)	-1.45 (0.96)	ANOVA	0.001	0.972	0.119
Acceptance images	2.73 (1.59)	2.47 (1.28)				0.180
Neutral images	0.08 (0.32)	0.24 (0.80)				0.263
Affect level rating [-5 (sad) to +5 (happy)]						
Rejection images	-1.59 (1.23)	-1.58 (0.79)	ANOVA	0.149	0.703	0.009
Acceptance images	2.80 (1.39)	2.85 (1.07)				0.040
Neutral images	0.07 (0.29)	0.19 (0.70)				0.224
Arousal level rating [0 (low) to 10 (high)]						
Rejection images	1.14 (1.43)	1.90 (1.67)	ANOVA	1.517	0.230	0.489
Acceptance images	2.25 (2.36)	3.15 (2.30)				0.386
Neutral images	0.52 (0.58)	0.99 (1.33)				0.458

Table 3. Brain regions showing differences in activation between task conditions (rejection, acceptance and neutral images) across all participants (n=26) at height threshold p=0.001.

Region	BA	Cluster size	Cluster p corrected	Side	MNI coordinates x	y	z	Voxel T
Rejection>neutral								
Middle occipital gyrus	19	1,151	<0.001	Left	-44	-78	2	6.23
Middle temporal gyrus	39			Left	-50	-64	8	5.83
Middle occipital gyrus	19			Left	-52	-76	2	5.80
Postcentral gyrus	1	684	<0.001	Left	-52	-22	54	5.36
Postcentral gyrus	2			Left	-36	-36	60	5.09
Precentral gyrus	4			Left	-34	-20	48	4.31
Cerebellum		431	0.002	Right	12	-48	-22	5.13
Superior temporal gyrus	22	549	0.001	Right	58	-46	12	4.75
Middle temporal gyrus	37			Right	44	-64	0	4.73
Middle temporal gyrus	39			Right	50	-66	10	4.67
Acceptance>neutral								
Medial frontal gyrus	10	389	0.021	Left	-4	54	0	5.57
Postcentral gyrus	1	342	0.033	Left	-40	-28	58	5.37
Rejection>acceptance								
Lingual gyrus	18	988	<0.001	Left	-8	-82	2	5.68
Lingual gyrus	19			Right	18	-68	-2	4.51
Lingual gyrus	18			Right	4	-78	0	4.31

Table 4. Brain areas showing differences between low (LS) relative to high (HS) groups in the rejection>neutral activation contrast at height threshold p=0.005.

Region	BA	Cluster size	Cluster p corrected	Side	MNI coordinates x	y	z	Voxel T
Dorsal ACC	32	2,920	<0.001	Right	2	4	48	4.96
Dorsal ACC	24			Left	-4	-8	42	4.67
Dorsal ACC	32			Right	12	6	54	4.48
Superior frontal gyrus	10	696	0.014	Right	22	66	4	4.52
Superior frontal gyrus	10			Right	12	64	22	4.48
Superior frontal gyrus	10			Right	18	66	12	3.92
Ventrolateral PFC	47	517	0.052	Left	-48	24	-6	4.50
Ventromedial PFC	11			Left	-12	48	-12	3.79
Ventromedial PFC	10			Left	-8	54	0	3.64

ACC: Anterior cingulate cortex; BA: Brodmann area; PFC: Prefrontal cortex

Table 5. The main effect of Group in subject-specific activations (ANOVAs) with gender and PANAS moment negative as covariates (ANCOVAs)

Region	**ANOVA df = 1,24**	**ANCOVA with Gender as a covariate df= 1,23**	**ANCOVA with PANAS moment negative as a covariate df=1, 23**
Dorsal ACC	F=16.09, p=0.001	F=15.77, p=0.001	F=11.46, p=0.003
Right Superior frontal gyrus	F=14.36, p=0.001	F=13.16, p=0.001	F=13.15, p=0.001
Left Ventrolateral/ ventromedial PFC	F=29.00, p<0.001	F=29.30, p<0.001	F=24.04, p<0.001

In all analyses, F<1 (non-significant) for Gender effect.

Appendix A. Average of the ratings on rejection level and valence provided by six doctoral or post-doctoral researchers of the 15 rejection, 15 acceptance and 15 neutral images used in the rejection-acceptance task

Image type	**Rejection level**	**Valence**
Rejection images		
Mean	-2.83	-2.34
Minimum	-3.50	-3.33
Maximum	-2.50	-1.50
Acceptance images		
Mean	4.03	3.82
Minimum	3.67	3.50
Maximum	4.50	4.33
Neutral images		
Mean	0.00	0.66
Minimum	-0.50	0.26
Maximum	0.50	1.21

Rejection level rated from -5 rejected to +5 accepted; valence rated from -5 negative to +5 positive

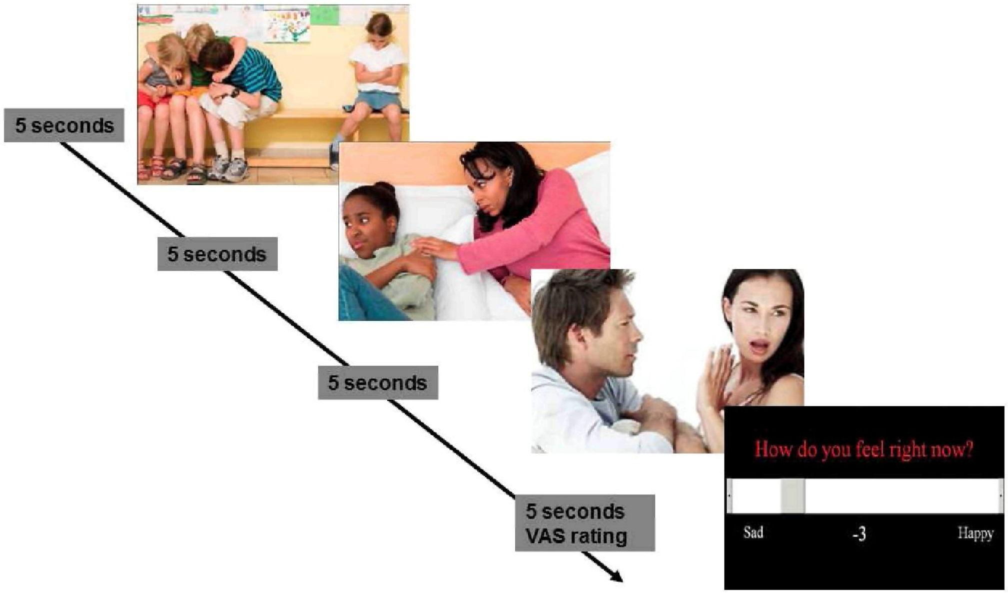

Figure 1
248x146mm (96 x 96 DPI)

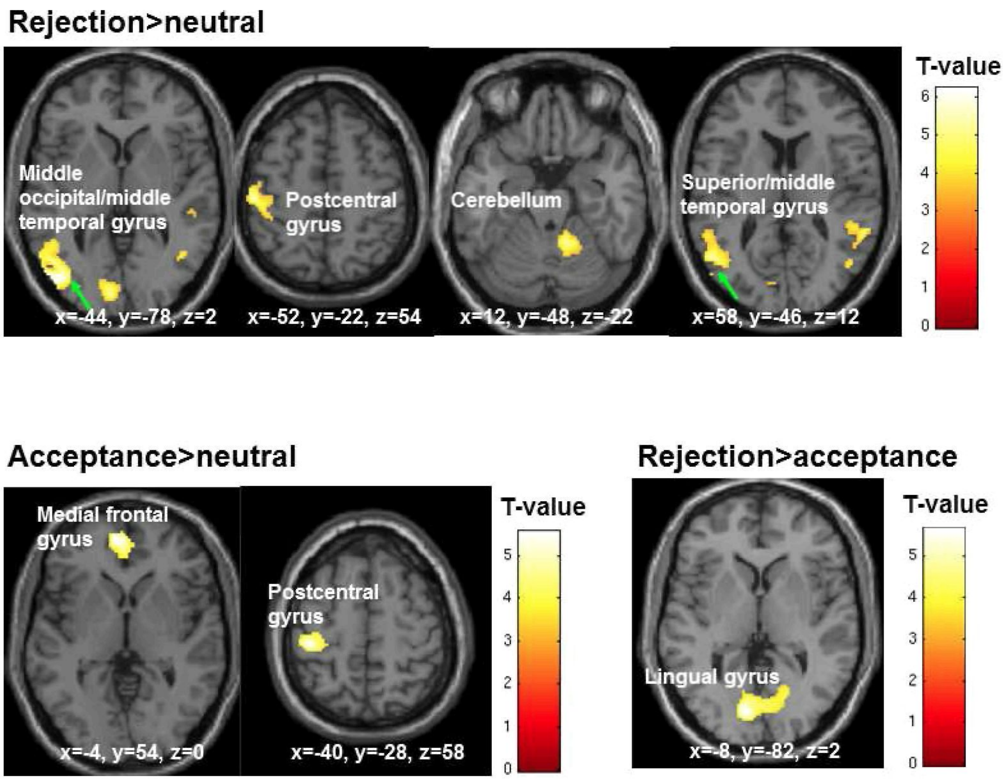

Figure 2
206x158mm (96 x 96 DPI)

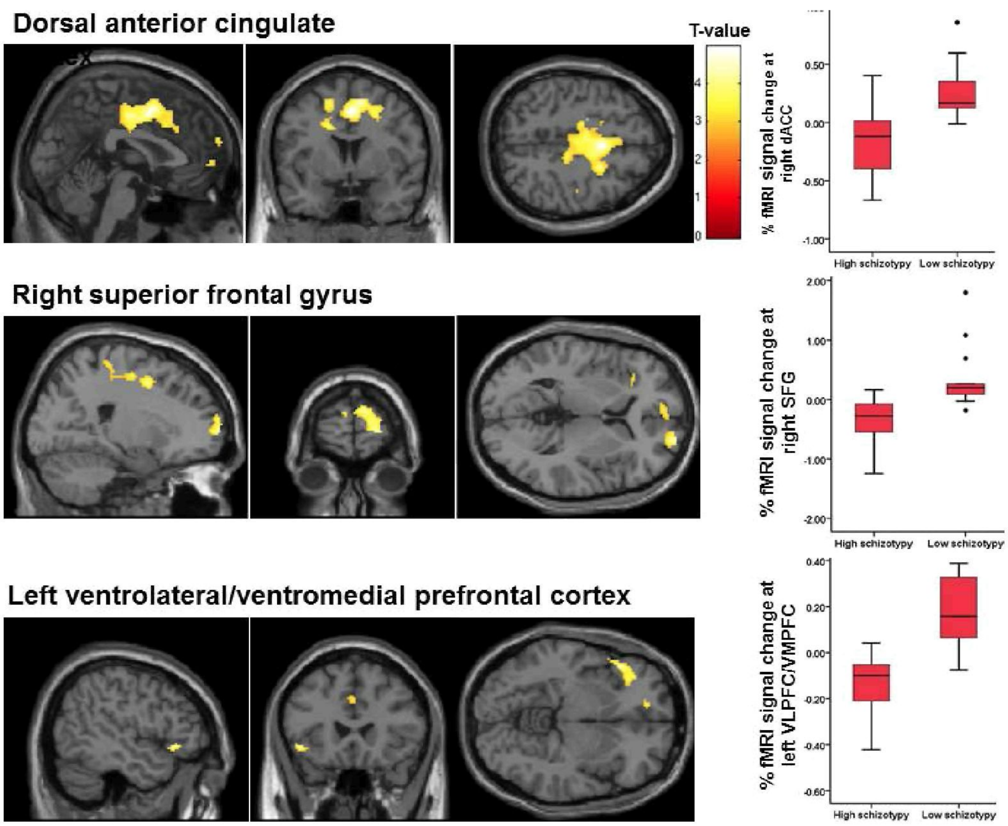

Figure 3
232x188mm (96 x 96 DPI)