Negative Schizotypy and Altered Functional Connectivity during Facial Emotion Processing

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Abstract

Background: Impairment in facial emotion perception is an important domain of social cognition deficits in schizophrenia. Although individuals with negative schizotypy (NS) have been found to have impaired ability in identifying facial emotions, little is known about the corresponding change in brain functional connectivity.

Methods: Sixty-four participants were classified into a high NSgroup (n=34) and a low NS group (n=30) based on their total scores on the Chapman scales for physical and social anhedonia. All participants undertook a facial emotion discrimination functional imaging task that consisted of four emotional valences (angry, fear, happy and neutral). For univariate analysis, the signal change at the bilateral amygdala was extracted and compared for each emotional contrast using SPSS ($p < 0.05$). For the functional connectivity analysis, we calculated the beta-series functional connectivity of the bilateral amygdala with the medial prefrontal cortex (mPFC) and compared the group differences in SPM12 ($p < 0.05$, small volume FWE correction).

Results: No significant differences were found between the high and low NS groups in accuracy and reaction time in the facial emotion discrimination task. The high NS group showed reduced brain activations at the amygdala under fearful and neutral conditions. Reduced functional connectivity between the amygdala and the mPFC/dACC under the happy and fearful condition in the high NS group was also found.

Conclusions: Our findings suggest that the individuals with high NS showed altered brain activity and functional connectivity at the amygdala during facial emotion processing and provide new evidence for understanding social cognition deficits in at-risk individuals.

Keywords: facial emotion discrimination; functional connectivity; negative schizotypy; amygdala; mPFC

Introduction

Impairments in emotion perception have been considered one of the core social cognition deficits in patients with schizophrenia and it has been included as a social cognition measure within the Research Domain of Criteria (RDoC) framework.[1,2] Previous meta-analyses have found moderate to severe deficits ($d = 0.8$~1.0) in facial emotion perception in patients with schizophrenia.[3,4] Deficits in facial emotion processing has also been reported in first-episode psychosis patients[5] and clinical and genetic high-risk individuals.[6–8] Moreover, facial emotion recognition performance has been found to correlate with the severity of negative symptoms in schizophrenia patients[9–11] and subclinical negative symptoms in non-psychotic siblings of patients with schizophrenia.[10]

In terms of neural correlates, imaging studies have shown that brain activity changes across widespread brain regions, including the amygdala, the superior and medial frontal cortices, the fusiform gyrus and various subcortical regions are associated with facial emotion perception deficits in schizophrenia patients.[12,13] Li et al. [12] reported reduced activity in the bilateral amygdala and that this pattern persists regardless of task design and duration of illness. Taylor et al. [13] also found robust deficits in anterior cingulate cortex (ACC) activity in different contrasts of tasks. Recently, a functional magnetic resonance imaging (fMRI) study using a passive viewing task reported hypoactivation in face processing areas of the brain in both schizophrenia patients and their unaffected relatives compared with controls, while

hyperactivation at the frontal regions was found in unaffected relatives compared with both patients and controls.[14]

Although a number of fMRI studies have examined brain activation during facial emotion perception (see meta-analyses mentioned above), few studies have examined the functional connectivity correlate of this process. Functional connectivity measures statistical correlations among time-series of spatially separated brain regions.[15] Instead of looking at isolated regions, the connectivity between brain regions may be more informative in delineating the pattern of disconnection underlying facial emotion perception deficits.[16,17] Altered functional connectivity has been observed in patients with schizophrenia during facial emotion processing, including reduced connectivity between the amygdala and frontal and parietal regions[18,19] and between the visual and limbic sub-networks in first-degree relatives of schizophrenia patients.[20] Specifically, the ACC and the medial prefrontal cortex (mPFC) have been found to be involved in emotion appraisal and regulation,[21] and their decoupling with the amygdala has also been found to be related to the genetic risk of schizophrenia.[22,23]

Schizotypy, defined as a set of personality traits resembling the symptoms of schizophrenia in the general population, has been considered a phenotype of schizophrenia[24] and has been proposed as an approach to understand the development of psychosis.[25,26] The multidimensional structure of schizotypy with a positive or psychotic-like dimension (e.g., magical ideation, perceptual aberration), a negative

dimension (e.g., anhedonia) and a disorganized dimension has been commonly suggested.[27,28]

The findings on facial emotion perception in schizotypy are mixed because of the various tasks and measures used.[29,30] For example, some studies showed deficits of high schizotypy group on total performance of facial emotion perception,[31,32] while further analysis also indicated the group differences were mainly on neutral faces but not on other emotional faces.[32,33] For the associations with dimensions of schizotypy, some studies also found significant negative correlations between performance on facial emotion perception and negative schizotypy (NS)[31,34], while others reported no such significant correlation.[33]

Using task-based fMRI, a few studies have reported altered brain activations in regions involved in emotion processing in individuals with high schizotypy, especially in midline regions including mPFC/ACC.[35,36] A recent study found hyperactivation at the caudate and the ACC/mPFC regions while viewing emotion-laden pictures (including both positive and negative emotional stimuli) in individuals with high positive schizotypy compared with those with low positive schizotypy.[36] Using dynamic facial expression stimuli, Huang et al. found less deactivation at the ACC in the "happiness appearing minus disappearing" contrast, while more deactivation at the posterior cingulate cortex (PCC) and the superior temporal gyrus in the "praise minus blame" contrast in individuals with high schizotypy compared with controls.[35] Premkumar and colleagues found deactivation in individuals with high positive schizotypy at the dorsal ACC, the superior frontal

and ventral prefrontal cortex while viewing negative social interaction scenes.[37] In terms of amygdala activation during emotion processing, one study has reported increased activation of the amygdala in individuals with high positive schizotypy during an emotional Stroop task.[38] Another study examined both negative and positive schizotypy individuals found that only individuals with NS showed reduced activation at the amygdala during a reward task.[39] Taken together, these findings suggest the changes of brain activations in the mPFC/ACC and amygdala in schizotypy. NS may be associated with different patterns of brain activations compared with positive schizotypy. Since the negative dimension of schizotypy such as anhedonia is closely related to dysfunction in affective and social processing[31,40], and longitudinal studies have indicated the unique role of NS in predicting the development of psychosis,[41,42] it is important to examine the relationship between NS and altered functional connectivity during social cognition processing.

In the present study, we examined the changes in 1) brain activity during a facial emotion valence discrimination fMRI task in individuals with high levels of negative schizotypal traits; and 2) functional connectivity during the task, especially the amygdala-mPFC/ACC connectivity. Based on results from previous studies, we hypothesized that activation of the amygdala and some regions in the frontal lobe (mPFC/ACC in particular) may show reduced activity, and the functional connectivity of the amygdala would be altered in individuals with NS.

Methods

Participants

Sixty-four first-year college students (31 males and 33 females) between 17 to 21 years old (mean age = 19.3, SD = 0.9) were selected from a large sample pool from a Medical University in China. All participants completed the whole set of measurements and had good image quality with small head motion during the scan (the original sample was 76, 12 of them were excluded because of excessive head motion). All participants were right-handed as assessed by the Annett Handedness Scale.[43] None of them had a history of psychiatric disorder, substance abuse or neurological disorders. The IQ of the participants were estimated using the common sense, arithmetic, similarity and digit span subtests of the Chinese Version Wechsler Adult Intelligence Scale-Revised (WAIS-R).[44] The estimated IQ ranged from 98 to 139 (mean = 117.02, SD = 9.97).

We classified the participants into two groups based on the level of the NS. The level of NS was measured as the sum of scores on the Physical Anhedonia Scale and Social Anhedonia Scale of the Chapman Psychosis Proneness Scales,[45,46] with a mean score of 23 in a large sample from our previous study in mainland China.[47] The two groups in the present study, namely individuals with high level of NS (high NS, n=34, NS scores > 23) and individuals with low level of NS (low NS, n=30, NS scores < 23) were matched on age, gender and IQ estimates. This study was approved by the Ethics

Committee of the Institute of Psychology, the Chinese Academy of Sciences. Written informed consents were obtained from all participants.

Measures

All participants completed self-report scales capturing schizotypy. The Chinese version of the Chapman Psychosis-Proneness Scales,[48–50] including the Revised Social Anhedonia Scale, the Physical Anhedonia scale, the Magical Ideation Scale and the Perceptual Aberration Scale (166 items in total) were used to measure the positive and negative dimensions of schizotypy. The former two scales were used to capture negative schizotypal traits, whereas the latter two scales were used to capture positive schizotypal traits. The Schizotypal Personality Questionnaire (SPQ)[51,52] was also administered to all the participants to validate the two groups. It is a 74-item checklist that was developed based on the Diagnostic and Statistical Manual of Mental Disorders (3rd edition revised, DSM-III-R)[53] criteria for schizotypal personality disorder. The Chinese version of the SPQ has been shown to possess satisfactory psychometric properties. There were no significant differences in levels of positive schizotypy between the two groups (see Table 1 for more details).

Functional imaging task

All participants took part in two eight-minute event-related fMRI scanning sessions of the Facial Emotional Valence Discrimination Task. In brief, Asian female faces with angry, fearful, happy or neutral expressions were presented and

participants were required to judge the presented facial expressions and press a button

of a response box (press the left button for angry or happy faces; press the right button

for fearful or neutral faces). This task has been used in a previous study and more

details could be found in Li et al.[54] (also see the Supplementary materials).

Imaging acquisition and preprocessing

All MRI scans were acquired on a Siemens Verio 3T MR scanner. Functional

imaging data were acquired using a T2-weighted echo planar imaging (EPI) sequence:

264 whole-brain volumes were collected with slice thickness = 4mm, echo time (TE)

= 28ms, repetition time (TR) = 2000ms, flip angle = 90°, matrix size = 64 x 64, 32

slices in coronal plane, field of view (FOV) = 210 mm, voxel size = 3 x 3 x 4 mm,

bandwidth = 2232Hz/Px. The T1-weighted images were scanned using a

three-dimensional magnetization-prepared rapid gradient-echo (MPRAGE) sequence,

with slice thickness=1mm, TE=2.34ms, TR=2530ms, flip angle=7 degree, 176 slices

in sagittal plane, field of view (FOV) =256mm, voxel size=1x1x1mm^3. The images

were screened by a radiologist to exclude any incidental clinical abnormalities before

further analysis.

The functional images were preprocessed using DPABI toolbox.[55] The toolbox

integrates the neuroimaging analysis packages (e.g., SPM

(http://www.fil.ion.ucl.ac.uk/spm/), AFNI (https://afni.nimh.nih.gov/) and FSL

(https://fsl.fmrib.ox.ac.uk/fsl/fslwiki), and was developed to be a user-friendly

toolbox for preprocessing of both resting state and task-based fMRI images. First, the

time differences for slices were corrected with the middle slice as the reference slice. Then head motion parameters were estimated using six-parameter rigid body transformation. The structural images were segmented into grey matter and white matter images using the Segmentation toolbox.[56] The DARTEL toolbox was used to create a study specific template.[57] Then, resting-state functional images were co-registered to the structural images and normalized into Montreal Neurological Institute (MNI) space. The normalized functional images were then smoothed with a full width at half maximum (FWHM) Gaussian kernel of 8mm. At last, wavelet despike was then applied to the preprocessed functional images to remove the effect caused by head motion.[58] We controlled for head motion by excluding participants with head motion exceeding 2 mm of translation, 2 degrees of rotation, or a mean framewise displacement (FD)[59] of > 0.3mm during any of the two scanning sessions. The six parameters were also entered as covariates in the subsequent first level analysis, while the mean FD of each participant was entered as a covariate in the second level analysis.

Statistical analysis

We first described the demographic information as well as the estimated IQ and scores on the self-reported scales of the participants. Performance in the facial emotion discrimination fMRI task (accuracy and reaction time) was also reported. Group comparisons were made using independent sample t test or chi-square test for all the variables mentioned above in SPSS v19. Significance was set at $p<0.05$.

Univariate analysis

In the first level analyses, a general linear model was used to estimate a blood oxygenation level-dependent (BOLD) response for each condition containing regressors depicting onset times of stimulus and six regressors for head movement parameters in the two sessions. We then calculated the BOLD signal change contrasts for each emotion condition relative to the neutral facial emotion condition using the general linear model, taking the six head motion parameters as covariates. Three contrast images were generated for each participant, including "Angry > Neutral", "Fearful > Neutral", and "Happy > Neutral", which were then used for the subsequent second level analysis in SPM12. First, one-sample t tests were conducted to examine the brain activation under each facial emotion contrasts in the whole sample, and significant clusters with FWE corrected p < 0.05 were reported (see **Supplementary materials** for the results). Secondly, independent sample t tests were conducted to examine the group differences between the high and low NS groups for each emotion contrast and neutral condition, with the participants' mean FD as covariate. The significant threshold was set as $p < 0.001$ as cluster defined threshold (CDT) and cluster level FWE corrected p <0.05.

Furthermore, the amygdala was chosen as a region of interest (ROI), 4mm radius spheres of the bilateral amygdala seeds were defined according to a previous meta-analysis[60] (left amygdala (ROI1): x=-20, y=-6, z=-12; right amygdala (ROI2): x=18, y=-6, z=-14 in MNI space) and the averaged percentages of signal changes of

ROIs were extracted for each emotion condition for each participant using MarsBar v0.44.[61] Group comparisons in brain activity of the bilateral amygdala were tested by repeated measured ANOVA, with hemisphere (left and right) and conditions (angry, fear, happy, neutral) as within-subject factors, and high /low NS groups as the between-subject factor. The main effect of group, condition and hemisphere, as well as the interactions were examined in SPSS v19, with $p < 0.05$ as the significance threshold. Post-hoc t tests were further conducted for each condition if a significant group effect was found.

Functional connectivity analysis

Beta-series correlations were calculated to measure functional connectivity using the BASCO (BetA Series COrrelation) software.[62] First, beta series of the bilateral amygdala were averaged across voxels within each sphere ROI we defined and correlated with the beta series of every other voxel in the whole brain. All correlation maps were normalized using an arc-hyperbolic tangent transform for further statistical inference. Flexible factor analyses were conducted with group as the between-subject factor and condition as the within-subject factor to examine the main effect of group and group by condition interaction using SPM12 with a mask of the mPFC/ACC generated using the WFU pickatlas software (http://www.nitrc.org/projects/wfu_pickatlas/), with small volume correction $p < 0.05$, FWE correction as threshold.

To examine other potential changes in functional connectivity, we took all the significantly activated brain regions as ROIs (4mm sphere) from the univariate analysis together with the bilateral amygdala and calculated the beta-series correlations between each pair of seeds (22 ROIs in total, see Supplementary Table S1). Brain networks were constructed using the beta-series correlations between each pair of seeds in each emotion condition as edges, which represented the strength of the connectivity. The network edges were then compared using permutation tests (10000 times) in the BASCO software. The results were reported based on a significance threshold of $p < 0.05$.

Results

1. Behavioural performance and self-reported scores

The high NS group scored significantly higher on the SPQ interpersonal factor than the low NS group. In the fMRI task, the two groups did not show any difference in accuracy and reaction time. The mean FD of head motion for the two groups was comparable.

Insert Table 1 About Here

2. Univariate Analysis

2.1 Group differences in brain activity

Independent sample t tests revealed significantly higher activity under the [angry > neutral] contrast in the high NS group, including the right insula (k = 42, x= 54, y= -21, z = 24), the left middle frontal gyrus (k = 44, x= -24, y= 0, z = 63), the right putamen (k = 36, x= 27, y= 3, z = 12) and the cingulate gyrus (k=22, x= -18, y= -15, z = 39). However, these did not survive multiple comparison correction. No significant differences were found in the other contrasts (fearful > neutral or happy > neutral). In addition, under the neutral condition, we found significantly reduced brain activity in the medial prefrontal cortex (k =145, cluster level FWE p <0.05, x= -6, y= 39, z = -15) in the high NS group (see Figure 1A).

2.2 Activation of the amygdala

Repeated measures ANOVA showed a significant decrease in brain activity at the amygdala in the high NS group (*F*=5.34, *p*=0.024, partial eta square = 0.079) (see Figure 1B). We also found a significant main effect for hemisphere (*F*=8.29, *p*=0.005, partial eta square = 0.118), indicating significantly stronger activation at the right amygdala than the left. The following post-hoc tests showed that the reduced amygdala activation corresponded to conditions with fearful faces (left amygdala: *p* = 0.049; right amygdala: *p* = 0.059) and neutral faces (left amygdala: *p* = 0.039; right amygdala: *p* = 0.049) in the high NS group.

3. Functional connectivity

3.1 Group comparison of functional connectivity of the amygdala

Flexible factor analyses showed that for the functional connectivity of the right amygdala, there was a significant main effect for group at the dorsal ACC (dACC, k=20, x=6, y=36, z=21, small volume correction, p <0.05 FWE corrected) (see Figure 1C). Further analyses showed a significant reduction of right amygdala-dACC functional connectivity in the high NS group under the happy faces condition (k=34, x=6, y=33, z=24, small volume correction, p <0.05 FWE corrected). We also found reduced functional connectivity between the right amygdala and the medial frontal gyrus (BA6, k=23, x= 3, y=0, z=60) under the fearful faces condition.

3.2 Group comparisons of network edges

Taking 22 seeds as nodes and beta-series correlations as edges, we created networks and compared the edges. The results showed increased functional connectivity between the insula and the superior frontal gyrus, and reduced functional connectivity between the amygdala and the mPFC, the middle temporal gyrus and the fusiform gyrus in the high NS group under the different conditions (permutation tests, $p < 0.05$) (see Figure 2). We also compared the network edges for each condition and the results can be found in the Supplementary Material.

Discussion

In this study, we examined changes in brain activity and functional connectivity during a facial emotion perception task in individuals with high and low levels of NS. At the behavioural level, we did not observe any significant group differences in accuracy or reaction time in the facial perception fMRI task. In the univariate analysis, reduced activity at the medial prefrontal cortex was found during neutral facial conditions in the high NS group. We also found significantly reduced activation of the amygdala in the high NS group, especially under the fearful faces condition. Secondly, functional connectivity analysis revealed hypoconnectivity between the amygdala and the dACC in the high NS group across different conditions. We also found reduced functional connectivity of the amygdala with the medial frontal gyrus (BA6) under the fearful faces condition. In the network edges comparison, we found significantly reduced functional connectivity between the left amygdala and the middle temporal gyrus and the medial frontal gyrus, reduced functional connectivity between the right amygdala and the fusiform gyrus; and increased connectivity between the superior frontal gyrus and the insula.

In terms of the behavioural performances, we did not find any group difference between high and low NS groups on the accuracy and reaction time in this study. Considering the positive and negative dimensions of schizotypy may have different effects on facial emotion perception,[63] a possible reason that we did not find any significant difference may be due to the fact that we only focused on the negative dimension of schizotypy in the present study. As the previous studies investigated the

deficits of facial emotion perception in schizotypy various tasks, researchers suggest

that schizotypy may not be necessary associated with abnormal facial emotion

perception,[30] more work needs to be carefully done in the future using comparable

tasks and measures to clarify this issue.

Brunet-Gouet and Decety[64] reviewed the results of functional imaging studies in

schizophrenia patients and concluded that the medial prefrontal cortex and the

amygdala are key regions involved in social cognition dysfunction in schizophrenia

patients. In our univariate analysis, the high NS group showed reduced activity in the

bilateral amygdala, especially during the fearful condition. This is consistent with

another functional imaging study which reported reduced amygdala activity during

emotion processing in individuals with negative schizotypal traits.[39] However,

previous studies have also reported increased amygdala activity while performing

facial emotion perception tasks in individuals with high level of positive schizotypy.[36]

The discrepancy reported in schizotypal studies may suggest that the positive and

negative dimensions of schizotypy might be related to opposite changes in the

activation of the amygdala during emotion processing. Hyperactivation of the

amygdala in individual with positive schizotypy and hypoactivity in individuals with

NS may contribute to the different emotional experiences in individuals with positive

and negative dimension of schizotypy.[48] On the other hand, behavioural studies in

schizophrenia patients have shown that different from other facial emotions, deficits

in fear recognition could be identified as early as in the first episode of

schizophrenia.[9] The ability to identify facial expressions associated with negative

emotions, such as fear, may be a potential access point for the investigation of early

brain changes in individuals with schizotypy in future research.

At the same time, we found hyperactivity of the insula, the middle frontal gyrus,

the putamen and the cingulate cortex in individuals with high NS under the angry >

neutral contrast. Hyper-responsiveness of the insula, the striatum and the ACC during

facial emotion perception has also been found in individuals with high positive

schizotypy in a recent study.[36] Another study found stronger activation in prefrontal

regions during the reappraisal of negative pictures in high schizotypy individuals

compared with controls.[65] Individuals with NS experience less pleasure in social

interaction and the insula has been shown to play an important role in the processing

of distressing stimuli.[66] Hyperactivation of the insula observed in the present study

may therefore suggest that there may be a stronger negative emotional response to

angry faces in social interaction in individuals with high NS. Since the prefrontal

cortex modulates activity of the amygdala to accomplish top-down regulation of

emotion, altered brain activity in prefrontal regions may result in the dysregulation of

negative emotions. In our study, there was no significant difference in behavioural

performance in the imaging task. The increased activation at the paralimbic and

cognitive control regions might be related to possible protective or compensatory

mechanisms in schizotypy as suggested by previous studies.[67] Together with previous

studies, our findings suggest that both positive and NS might be correlated with brain

activity changes in prefrontal regions and the insula. Moreover, brain structural

changes associated with schizotypy have been observed in the posterior cingulate, the

medial prefrontal, the orbitofrontal and the temporal cortical regions as well as the precuneus.[68–70] Whether these functional changes are related to any underlying structural changes should be further examined in future studies.

Using the beta-series correlations to investigate functional connectivity, we observed decoupling of the amygdala with the dorsal ACC/mPFC in the high NS group during facial emotion processing in this study. Abnormal functional connectivity between the amygdala and the PFC/ACC has been reported in patients with schizophrenia and has been associated with the deficit syndrome.[23] The amygdala is involved in processing the salience of emotional stimuli and the mPFC/ACC are involved in emotion appraisal and regulation.[21] Hence, the weaker connectivity of the amygdala with the mPFC/ACC may be suggestive of abnormal top-down regulation of the prefrontal cortex. Recently, a study examining the age-related changes in connectivity during an emotional face matching task in healthy subjects (7-25 years old) found a shift from positive functional connectivity between the amygdala and the ACC/mPFC in children to negative connectivity in adults.[71] This was taken as evidence suggesting the development of top-down inhibitory control of the ACC/mPFC to the amygdala with age. This reduced functional connectivity between the amygdala and the mPFC/ACC has been found in patients with schizophrenia and clinically-defined high risk individuals as well.[16,72] This may suggest an abnormality in the development of prefrontal inhibition in individuals along the schizophrenia spectrum and might be related to changes in emotion processing or trait-like anhedonia, underlie by activity and connectivity of the

amygdala. The vigilance-avoidance hypothesis[73] proposes that when aversive threat is present, attention would be first allocated towards it but then diverted away from it in order to reduce the distress caused by this threat. This theory may also be helpful in interpreting our findings of reduced functional connectivity under fearful conditions.

This study has several limitations. First, our facial perception task took the neutral faces as the control condition. However, we observed a significant group difference in activation at the medial prefrontal cortex during the neutral faces condition. As such, the comparison on emotional vs. neutral contrasts may be affected by this effect. In fact, abnormal brain activity at the amygdala and the medial PFC/ACC when processing neutral faces has been found in patients with schizophrenia, major depression and bipolar disorder.[74] Future studies may include participants with other conditions as controls to further investigate this issue. Secondly, our participants were college students and they were median split into two groups based on their scores on self-reported scales. A more rigorous approach adopting an interview-based measure together with self-reported scale to capture NS should be incorporated in future studies. In addition, using extreme groups to examine the group difference in behavioural performance would be an alternative way to clarify this issue. Thirdly, we did not record the daily use of alcohol or tobacco of our participants, which might affect brain activation and connectivity. This issue should be taken into consideration in future study. Fourthly, social anxiety might be related to NS and may have a potential effect on brain activation during the social cognition

task. Future studies should consider including measures of social anxiety to control for this effect.

It should be noted that participants with schizotypy may not necessarily be associated with negative outcomes or go on to develop schizophrenia.[28] Our findings only suggest that individuals with social anhedonia (NS) may be associated with altered brain activity and functional connectivity at the amygdala during facial emotion processing. Future study should also examine the positive aspect of schizotypy such as creativity.

In conclusion, the present findings suggest that individuals with schizotypy showed altered brain activity and functional connectivity at the amygdala during facial emotion processing. These findings highlight the underlying neural mechanism of social cognition in these individuals.

Acknowledgement

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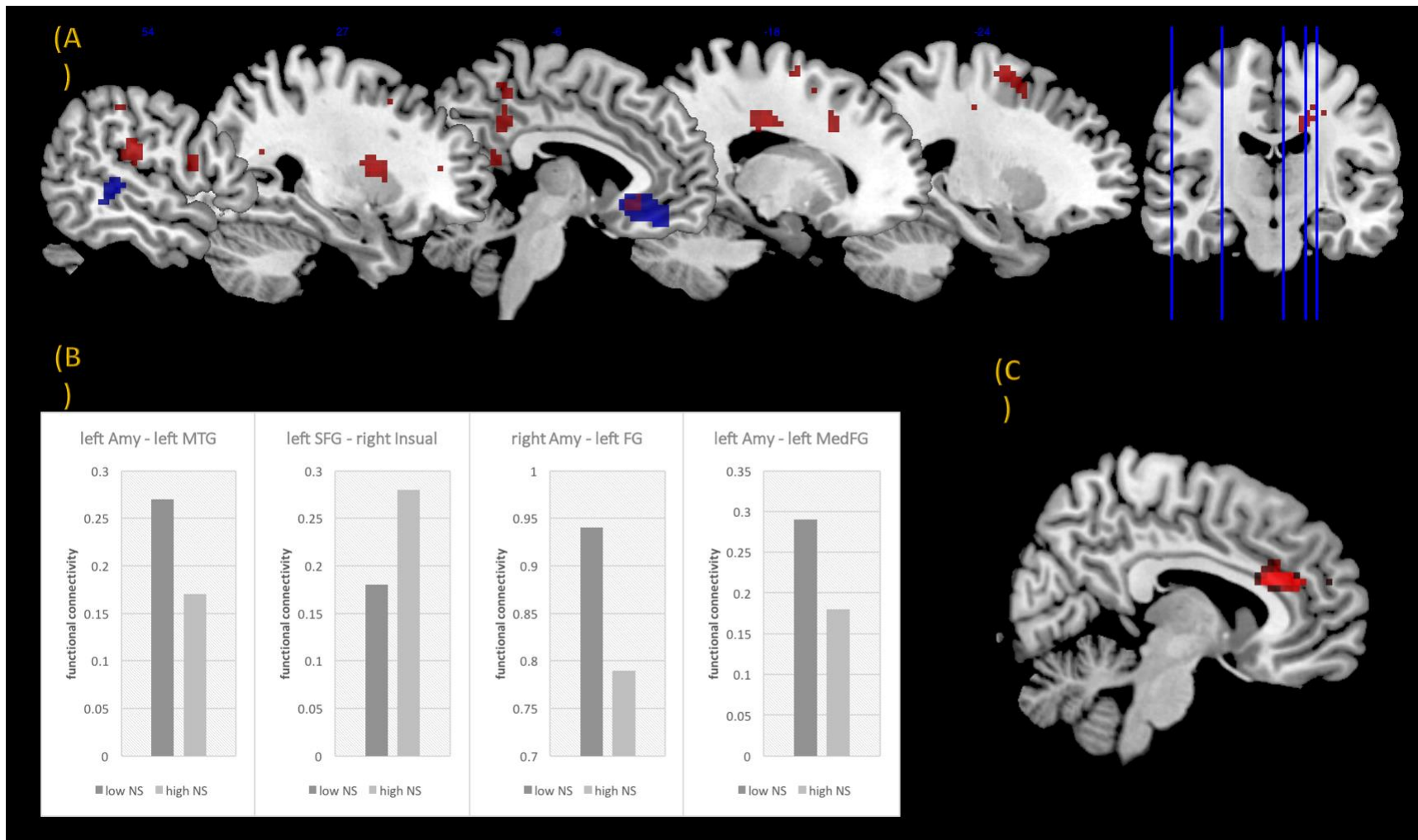
Figure Legends

Figure 1. Group differences on brain activity and functional connectivity of amygdala during the facial emotion task. (A). Compared with the low NS group, high NS group showed reduced activity at the ACC/mPFC (blue) and increased activation at the posterior insula, the putamen, the posterior cingulate and the middle frontal gyrus (red) (B). The group effects of amygdala activation under each condition. The mean percent signal change was extracted using MarsBar and group comparison was conducted by SPSS (C). Group effect on the functional connectivity of the right amygdala was found at the dorsal ACC.
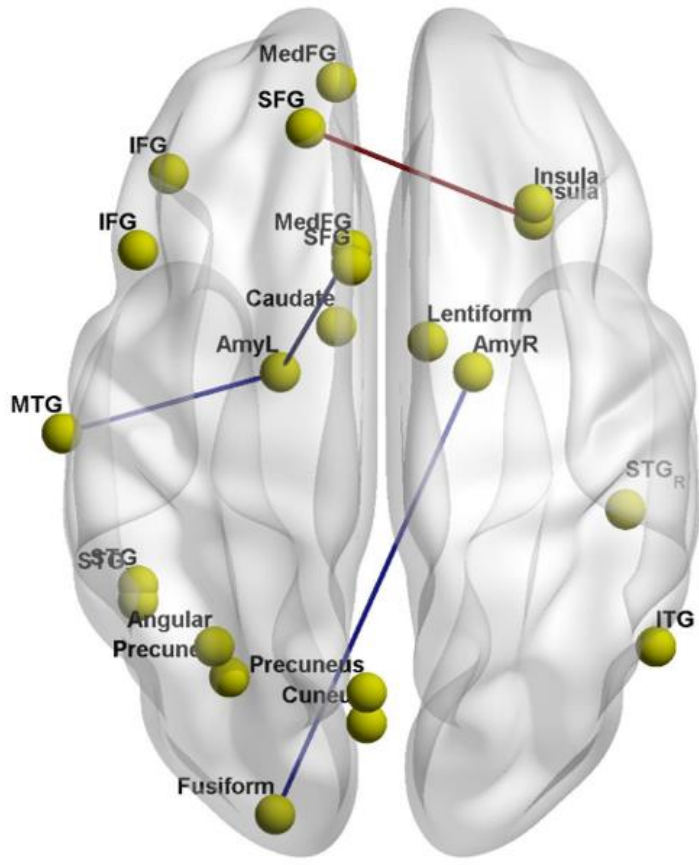
Figure 2. Illustration of group difference on the network edges. Increased functional connectivity between the insula and the superior frontal gyrus, and reduced functional connectivity of the amygdala with the mPFC, the middle temporal gyrus and the fusiform gyrus in the high NS group under different emotional conditions were found.

Table 1. Demographic description and self-reported scores

	high NS (n=34)		low NS (n=30)		t/chi-square	p
	Mean	SD	Mean	SD		
age	19.21	0.95	19.23	0.86	-0.12	0.904
gender	17:17		13:17		-0.53	0.601
years of education	13.09	0.52	13.00	0.37	0.79	0.433
IQ estimates	117.41	9.99	116.43	10.29	0.39	0.701
Schizotypy, Chapman						
Social anhedonia	11.24	5.89	4.23	2.62	6.00	<0.001
Physical anhedonia	18.74	10.11	6.00	3.83	6.50	<0.001
Perceptual aberration	5.65	5.43	6.83	7.87	-0.71	0.481
Magical ideation	9.62	4.76	10.97	6.21	-0.98	0.330
fMRI task performance						
Mean accuracy	0.83	0.08	0.82	0.07	0.42	0.678
Mean reaction time	1130.58	123.35	1129.00	121.62	0.05	0.960
Head motion						
Mean SP	0.14	0.07	0.13	0.07	0.70	0.485
Mean FD	0.12	0.05	0.14	0.05	-1.72	0.091

Note. FD: framewise displacement; SP: spike percentage; NS: negative schizotypy.

(A)

(B)

left Amy - left MTG

left SFG - right Insual

right Amy - left FG

left Amy - left MedFG

(C)

Supplementary materials

1. Description of the fMRI task

All participants took part in two 8-minute event-related fMRI scanning sessions of **facial emotional valence discrimination**. Participants underwent a training session before fMRI data acquisition and were given about 5 min to familiarize with the task procedure. During the facial emotional valence discrimination scanning, they were presented with five different facial identities, each with a fearful, happy or neutral facial expression (Ekman et al., 1976). The faces were presented in a pseudo random order, and there were no successive presentation of the same identity or facial expression. In total, there were 20 facial expressions for each emotional valence, including angry, fearful, happy and neutral faces. Each emotional face was presented four times for 2 s, while the inter stimulus intervals varied from 4 s, 6 s, or 8 s in a pseudo random order, the average interval was 6 s, with a fixation cross presented. The participants were required to judge whether the presented facial expressions were positive or negative, and pressed one of two buttons accordingly.

2. Brain activation in the whole sample

The brain activation of each facial emotional contrast to neutral faces were examined by one sample t tests. The results were shown in Table S1 and Figure S1. For the Angry > Neutral contrast, inferior and superior frontal gyrus, insula, lentiform gyrus,

cuneus gyrus, superior and inferior temporal gyrus were activated; under the fearful >

neutral contrast, inferior frontal gyrus, fusiform, superior temporal gyrus, medial

frontal gyrus, insula and precuneus gyrus were significant stronger activated; for the

happy > neutral contrast, superior and medial frontal gyrus, middle temporal gyrus

were found significant activated. Besides, we also found the amygdala activation

under each of emotion conditions using a mask of bilateral amygdala in AAL
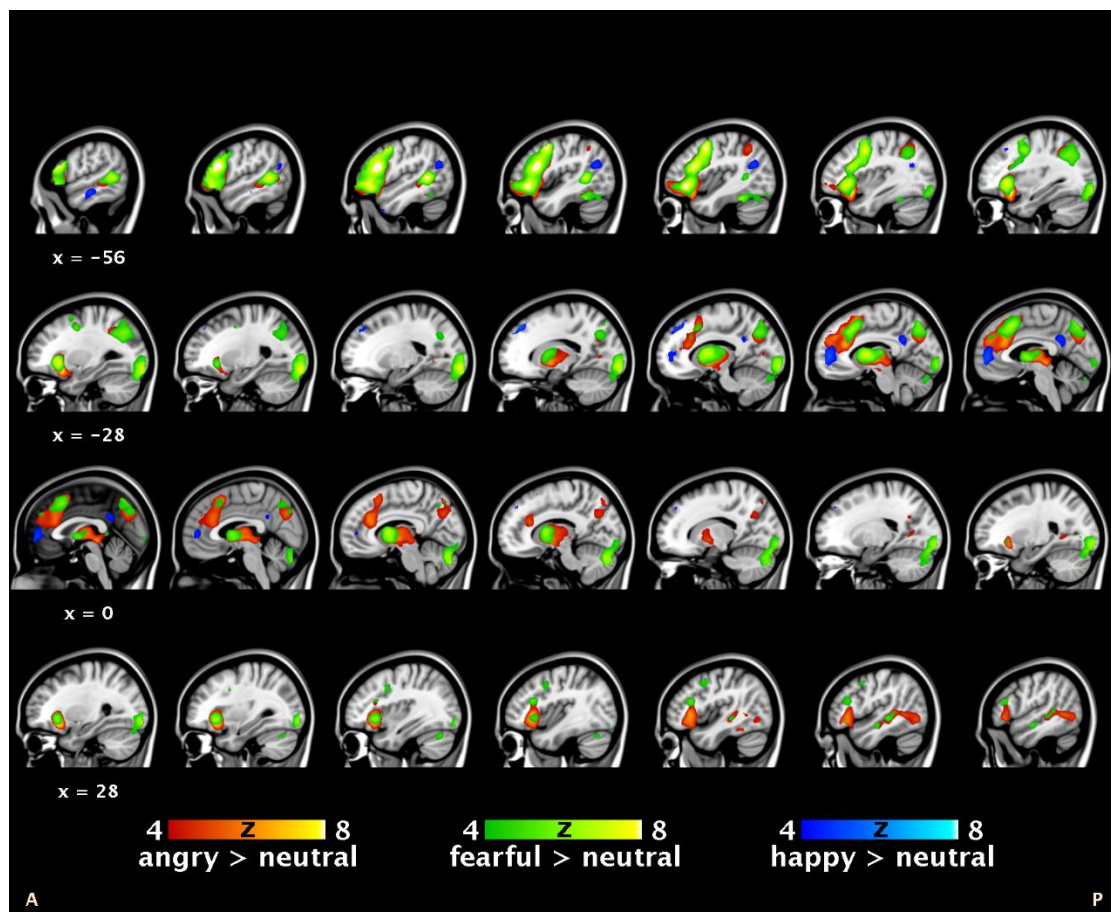
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Figure S1. Brain activation of emotional expressions compared to neutral faces. The contrasts of the facial emotion identification task were plotted at the threshold of 8> Z > 4, including: Angry minus Neutral (red), Fearful minus Neutral (green), and Happy minus Neutral (blue).

Table S1. The Brain activation of different emotional faces

	cluster	peak	MNI coordinates				
	k	T	X	Y	Z	label	
Angry > Neutral							
ROI6	1308	10.51	-42	33	-9	Inferior Frontal gyrus, BA47	IFG_L
		9.30	-30	21	-12	Insula, BA47	
		9.28	-48	21	18	Inferior Frontal gyrus, BA9	
ROI7	305	8.63	30	24	-9	Insula, BA13/Clsustrum	Insula_R
		6.16	48	30	-9	Inferior Frontal gyrus, BA47	
ROI8	585	8.00	-6	15	51	Superior Frontal gyrus, BA6	SFG_L
		7.23	-9	24	30	Cingulate gyrus, BA32	
		6.70	-9	30	21	Cingulate gyrus, BA32	
ROI9	640	7.41	9	0	-3	Lentiform nucleus, pallidus	Lentiform_R
		7.41	-12	3	9	Caudate body	
		7.13	-9	-12	0	Thalamus	
ROI10	84	6.34	-33	-60	39	Angular gyrus, BA39	Angular_L
ROI11	175	6.11	-3	-75	36	Cuneus, BA7	Cuneus_L
		5.97	-6	-75	45	Precuneus, BA7	
		5.79	-9	-66	36	Cuneus, BA7	
ROI12	27	5.67	48	-33	0	Superior Temporal gyrus, BA41	STG_R
ROI13	53	5.62	-48	-51	6	Superior Temporal gyrus, BA39	STG_L
		5.27	-54	-36	0	Middle temporal gyrus, BA22	
ROI14	30	5.49	54	-60	0	Inferior Temporal gyrus, BA19	ITG_R
		5.45	51	-51	3	Middle temporal gyrus, BA37	
		5.20	48	-69	-6	Fusiform gyrus, BA19	
fear > neutral							
ROI15	1163	8.97	-48	18	21	Inferior Frontal gyrus, BA9	IFG_L
		8.65	-42	33	-9	Inferior Frontal gyrus, BA47	
		8.46	-42	3	51	Middle Frontal gyrus, BA6	
ROI16	156	8.35	-48	-48	6	Superior Temporal gyrus, BA39	STG_L
ROI17	327	8.04	-21	-93	-12	Fusiform gyrus, BA18	FG_L
ROI18	281	7.66	-9	3	9	Caudate body	Caudate
		7.19	9	6	6	Caudate body	
		5.47	-9	-18	12	Thalamus	
	276	6.99	9	-78	-30	Cerebellum	
		6.93	24	-93	-9	Fusiform gyrus, BA18	
		6.03	21	-87	-18	Cerebellum	
ROI19	128	6.67	-6	18	45	Medial Frontal Gyrus, BA32	MedFG_L
	30	6.66	-42	-45	-21	Cerebellum	
ROI20	56	6.60	30	27	-6	Insula, BA13/Clsustrum	Insula_R

ROI21	93	6.18	-3	-69	51	Precuneus, BA7	Precuneus_L
		5.58	-15	-66	36	Precuneus, BA7	
ROI22	107	5.99	-30	-66	36	Precuneus, BA39	Precuneus_L
		5.85	-30	-57	36	Middle Temporal BA39	
happy > neutral							
ROI3	21	5.79	-15	42	45	Superior frontal gyrus, BA8	H_SFG_L
ROI4	22	5.54	-63	-18	-15	Middle Temporal gyrus, BA21	H_MTG_L
ROI5	35	5.51	-9	51	3	Medial frontal gyrus, BA10	H_MedFG_L

Note. The one-sample t tests were performed using SPM, clusters with p < 0.05 after
FWE correction, k>20 were reported.

3. Comparisons on network edges

We took all the significantly activated brain regions as ROIs (4mm sphere, see Table
S1) from the univariate analysis together with the bilateral amygdala, and calculated
the beta-series correlations between each pair of the seeds (22 ROIs in total). Brain
networks were constructed using the beta-series correlations between each pair of
seeds in each emotion condition as edges. The network edges were then compared
using permutation tests (10000 times) in BASCO software. The results were reported
based on a significance threshold of $p < 0.05$.

Table S2. group differences on the network edges under each facial emotion

			high NS	low NS	
Facial conditions	**Seed1**	**Seed2**	**r**	**r**	**p**
ANGRY	Amy L (ROI1)	MTG L (ROI4)	0.20	0.35	0.039
	Amy R (ROI2)	MedFG L (ROI5)	0.30	0.15	0.045
	SFG L (ROI3)	Insula R (ROI7)	0.29	0.14	0.018
	Insula R (ROI7)	Lentiform R (ROI9)	0.32	0.14	0.026
	SFG L (ROI3)	Angular L (ROI10)	0.29	0.16	0.043
	IFG L (ROI6)	Cuneus L (ROI11)	0.15	0.02	0.043
	SFG L (ROI8)	Cuneus L (ROI11)	0.32	0.18	0.047
	Insula R (ROI7)	STG L (ROI13)	0.34	0.17	0.041
	Angular L (ROI10)	STG L (ROI13)	0.24	0.10	0.042

	Amy R (ROI2)	ITG R (ROI14)	0.29	0.14	0.049
	Angular L (ROI10)	IFG L (ROI15)	0.25	0.09	0.035
	Cuneus L (ROI11)	IFG L (ROI15)	0.18	0.06	0.050
	SFG L (ROI8)	FG L (ROI17)	0.31	0.16	0.043
	IFG L (ROI6)	Caudate (ROI18)	0.32	0.15	0.016
	Lentiform R (ROI9)	Caudate (ROI18)	0.40	0.16	0.004
	Cuneus L (ROI11)	MedFG L (ROI19)	0.26	0.12	0.050
FEARFUL	Amy L (ROI1)	IFG L (ROI6)	0.11	0.32	0.003
	MedFG L (ROI5)	Lentiform R (ROI9)	0.28	0.47	0.037
	SFG L (ROI3)	STG R (ROI12)	0.11	-0.02	0.046
	SFG L (ROI8)	STG R (ROI12)	0.21	-0.01	0.004
	Amy L (ROI1)	IFG L (ROI15)	0.13	0.35	0.002
	Amy L (ROI1)	MedFG L (ROI19)	0.11	0.27	0.027
	MedFG L (ROI5)	MedFG L (ROI19)	0.18	0.35	0.046
	FG L (ROI17)	Precuneus L (ROI22)	0.14	0.01	0.033
HAPPY	MedFG L (ROI5)	Lentiform R (ROI9)	0.25	0.43	0.022
	SFG L (ROI8)	Lentiform R (ROI9)	0.15	0.31	0.039
	IFG L (ROI6)	Cuneus L (ROI11)	0.05	0.24	0.011
	Insula R (ROI7)	Cuneus L (ROI11)	0.08	0.28	0.007
	MedFG L (ROI5)	STG R (ROI12)	0.06	0.20	0.045
	Cuneus L (ROI11)	ITG R (ROI14)	0.06	0.20	0.045
	MedFG L (ROI5)	STG L (ROI16)	0.12	0.27	0.033
	Cuneus L (ROI11)	Insula R (ROI20)	0.18	0.34	0.030
EMOTION	Amy L (ROI1)	MTG L (ROI4)	0.17	0.27	0.027
	SFG L (ROI3)	Insula R (ROI7)	0.28	0.18	0.043
	Amy R (ROI2)	FG L (ROI17)	0.79	0.94	0.044
	Amy L (ROI1)	MedFG L (ROI19)	0.18	0.29	0.039