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Brain response during visual emotional processing: an fMRI study of alexithymia

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ABSTRACT

Alexithymia is found in up to 10% of the general population and is associated with lower quality of life. Alexithymia is a major risk factor for a range of medical and psychiatric problems. Although a deficit involving the anterior cingulate cortex (ACC) deficit is thought to offer the most promising neurobiological model of alexithymia, current studies have yielded inconsistent findings. In this study, neural activity was investigated in well-controlled alexithymic individuals subjected to emotional stimuli. Fifteen individuals with high Toronto Alexithymia Scale (TAS-20) scores (high-alexithymic group) and 15 individuals with low TAS-20 scores (low-alexithymic group) were screened from 432 female college students. Depressive and anxious behaviors were scored using self-rating depression scale (SDS) and self-rating anxiety scale (SAS) questionnaires, respectively. Emotional stimuli consisted of pictures with positive, negative, or neutral pleasantness and high or low arousal of emotional intensity. Regional cerebral activation was measured by functional magnetic resonance imaging (fMRI). The anterior cingulate, mediofrontal cortices, insula and temporal lobe were significantly activated by intense emotional stimuli (negative or positive pictures) in high-alexithymic individuals compared to low-alexithymic individuals. Conversely, high-alexithymic and low-alexithymic individuals showed similar brain activity when subjected to neutral stimuli. **A**lexithymia is associated with activation in anterior cingulate and mediofrontal cortices during emotional stimuli processing. Therefore, our findings support the hypothesis that altered ACC function may be implicated in alexithymia.

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1. Introduction

Alexithymia is a term used to describe people who have deficiencies in understanding, processing, or describing their emotions (Moriguchi et al., 2009). The deficiencies in emotional regulation in alexithymia are characterized as follows: (1) difficulty in identifying and describing subjective feelings; (2) difficulty in distinguishing between feelings and bodily sensations of emotional arousal; (3) reduced imagining capacity; (4) an externally oriented cognitive style; and (5) social conformity (Mantani et al., 2005; Reker et al., 2010; Miyake et al., 2012; Borsci et al., 2009). The ability to successfully regulate emotion is essential to psychological, social, and physical health (Goldin et al., 2008). A high prevalence of alexithymia has been reported in individuals with somatoform disorders, anxiety, chronic pain, depression, and substance dependence (Heinzel et al., 2012). Recently, alexithymia has been described not as a discrete disorder but rather as a personality construct that is expressed with variable intensity in up to 10% of the general population (Sturm and Levenson, 2011). Alexithymia is thought to be a transdiagnostic deficit, a major risk factor for a range of medical and psychiatric problems that is associated with lower quality of life (Aleman, 2005). The study of alexithymia can offer new perspectives in determining the pathological mechanisms and vulnerability factors leading to clinical disorders associated with poor social skills and deficits in the processing of facial expressions of emotion (Grynberg et al., 2012). It is therefore important to elucidate the neural mechanism underlying the development of alexithymia.

Several neurobiological models of alexithymia have been proposed (Larsen et al., 2003). Among them, the model of a deficity in the function of the anterior cingulate cortex (ACC) has attracted a considerable amount of attention in neuroimaging studies of alexithymia (Aleman, 2005; Schafer et al., 2007; Dorard et al., 2008). For example, Lane et al. (1997a) demonstrated that alexithymia is associated with a deficit in the participation of the ACC during emotional arousal. They therefore conceptualized alexithymia as an emotional equivalent of blind sight and coined the term “blind feel”. According to the “blind feel” hypothesis, subcortical limbic structures should remain unaffected by alexithymia (Lane et al., 1997a). Indeed, several studies observed no differences in the limbic structures between alexithymic and non alexithymic

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individuals (Heinzel and Schäfer, 2010; Berthoz et al., 2002; Kano et al., 2003). However, Leweke et al. (2004) reported lower activations of the right amygdala in alexithymic individuals. Recent studies on healthy volunteers also demonstrated a negative correlation between amygdala activity and scores of the 20-item Toronto Alexithymia Scale (TAS-20) (Kugel et al., 2008; Reker et al., 2010).

There are several functional imaging studies comparing visual emotional processing in individuals with or without alexithymia, but yielding inconclusive findings (Pouga et al., 2010). For example, Berthoz et al. (2002) found reduced cerebral activation in the left mediofrontal–paracingulate cortex in response to highly negative stimuli and more activation in the anterior cingulate, mediofrontal cortex, and middle frontal gyrus in response to highly positive stimuli in men with alexithymia than in men without alexithymia. Kano et al. (2003) observed significant decreases in regional cerebral blood flow in individuals with alexithymia in response to angry but not to sad or happy facial stimuli. Heinzel and Schäfer (2010) found increased activation of the supragenual ACC for different emotional valences as well as for different emotional stimuli. Leweke et al. (2004) observed decreased activation in the right medial prefrontal cortex and in the right amygdala in response to disgusted but not fearful facial stimuli. Liemburg et al. (2012) in a study using resting state functional magnetic resonance imaging (fMRI), found that alexithymia was associated with stronger functional connections between the default mode network and brain areas involved in sensory input and control of emotion. Collectively, both structural and functional imaging studies of alexithymic brains revealed inconsistent findings.

The reasons for inconsistent findings between different studies are currently unclear. We hypothesize that the inconsistency may be caused by differences in age, gender, emotional stimuli, and homogeneity in sample characteristics. In this study, we performed a whole brain analysis of neural activity under emotional stimuli in a well-defined homogeneous sample of female alexithymic individuals while minimizing the influences of anxiety or depression.

2. Materials and methods

2.1. Participants

Participants comprised 432 female college students with an average age of 20.53 ± 1.28 years (range=18–23 years), who completed the 20-item Toronto Alexithymia Scale Chinese edition (TAS-20). The TAS-20 scale is a 20-item self-administered questionnaire. The items are scored on a 5-point scale from strongly disagree to strongly agree. The TAS-20 has a three-factor structure. Factor 1 assesses difficulty in identifying and distinguishing between feelings and bodily sensations. Factor 2 assesses difficulty in describing feelings. Factor 3 assesses externally oriented thinking (Bagby et al., 1994; Yao et al., 2005). Classification was based on combined factor 1 and factor 2 scores (sum score) (Berthoz et al., 2002). Among the 432 female college students, 18 individuals with the highest TAS-20 sum scores and 18 individuals with the lowest TAS-20 sum scores were recruited for this study. Signed informed consent forms were obtained from all subjects. However, only 15 individuals with the highest (high-alexithymic, sum score=65.27) and 15 with lowest (low-alexithymic, sum score=29.73) TAS-20 sum scores completed the MRI scan and then visited a psychiatrist for the diagnosis of alexithymia, depression, and anxiety as well as to verify the inclusion criteria, such as right handedness and good or corrected visual acuity. All subjects with a history of medical, neurological, or psychiatric disorder were excluded. Individuals in both the high-alexithymic and low-alexithymic group completed the Self-rating Depression Scale (SDS) (Zung, 1972) and the Self-rating Anxiety Scale (SAS) questionnaires (Zung, 1971) just before the MRI scan. The study was approved by the institutional ethics board of Central South University.

2.2. Experimental design

In this study, emotional pictures were used as stimuli. All pictures were selected according to their pleasantness (positive, negative, or neutral valence) and emotional intensity (high or low arousal) on the basis of Chinese Affective Picture System norms (Bai et al., 2005). Five sets of pictures (12 pictures per set) were used in the study: (1) positive valence (v) with high-arousal (a) intensity (The score of v and a: 7.24 and 6.69); (2) positive valence with low-arousal intensity (the score of v and a: 7.07 and 5.77); (3) negative valence with high-arousal intensity (the score of v and a: 1.44 and 5.87); (4) negative valence with low-arousal intensity (the score of v and a: 2.75 and 3.82); and (5) neutral valence with neutral intensity (the score of v and a: 5.06 and 4.54). The intensity was defined by 9-point scales for both arousal (1=completely calm, 9=completely aroused) and valence (1=completely unpleasant, 9=completely pleasant). Control stimuli were created by scrambling the initial pictures to suppress their emotional tenor. Levels of Cerebral activation in response to pictures that were positive, negative, or neutral were compared with their corresponding control stimuli.

Pictures were presented to subjects for four runs and each run consisted of five sets of pictures. One set consisted of three blocks of three pictures with identical emotional valence, identical emotional intensity, and corresponding control pictures. Four control pictures (scambled pictures, control stimuli) were presented at the beginning of each run and were excluded from the analyses. Each picture and its control were presented for 6 s (one block=18 s), with no interval between the blocks. To minimize cognitive and motor interference on emotional processing, participants were instructed to maintain their attention as long as the stimuli were displayed. To ensure the participants were viewing the pictures passively, participants were given prior instructions and practices. During the test, the vision of the participant was corrected and the head was fixed to reduce movement. The order of the blocks was counterbalanced across runs and across subjects. During fMRI, the pictures were presented on a monitor inside the scanner room.

2.3. Image acquisition and data analysis

All subjects were imaged using a 1.5-Tesla Siemens Sonata scanner. A scan was completed in 10 min in a quadrature head coil. Foam pads were used to limit head motion and reduce scanner noise. Every patient received a whole brain scan. A series of 22 axial slices of 5-mm thickness were collected using a fast echo-planar image sequence with a repetition time of 2000 ms and 90-degree flip angle, a 64×80 matrix, and a 24×30-cm field of view.

Image processing and statistical analyses were carried out using SPM5 (http://www.fil.ion.ucl.ac.uk). The images were corrected for differences in slice acquisition time, realigned to the first volume of the time series to correct for subject movement between scans, and corrected for motion artifacts. The mean was adjusted by proportional scaling, resliced and normalized into standard stereotactic space (MNI EPI template) using a nonlinear discrete cosine transform. Images were smoothed with a 4-mm full-width-at-half-maximum Gaussian kernel. Low frequency noise was filtered out by using a high-pass filter with a cutoff frequency of 1/216 Hz.

Regionally specific effects were assessed in terms of t values. For each experimental condition, differences were assessed between high-alexithymic and low-alexithymic individuals on cerebral regional activation in response to stimulating pictures compared with scrambled pictures. Regional activity was assessed for each subject. Activity in high-alexithymic and low-alexithymic groups was compared by T maps using SPM 5. Variance across subjects was computed following a random-effect-analysis procedure. The statistical thresholds were set as $p < 0.005$, uncorrected and cluster size > 30 voxels as previously described (Berthoz et al., 2002; McRae et al., 2008).

3. Results

3.1. Behavioral measures

Individuals with high (high-alexithymic group) or low (low-alexithymic group) TAS-20 scores completed the TAS-20 questionnaire again before the fMRI scan. Although significant differences in TAS-20 scores were observed between high-alexithymic and low-alexithymic individuals ($p=0.000$), no significant differences were observed in TAS-20 scores collected during screening and before fMRI scans in the two groups. The high-alexithymic group showed significantly higher average SDS ($p=0.000$) and SAS ($p=0.032$) scores compared to low-alexithymic controls (Table 1). However, no individual in either group scored higher than the cutoff score for depression and anxiety. Also, psychiatrists diagnosed these patients to be free from depression or anxiety.

3.2. The fMRI data

At a threshold of $p < 0.005$ and cluster size > 30 voxels for statistical significance, no difference was observed between high-alexithymic and low-alexithymic individuals in response to neutral

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