



Sex-related differences in neural activity during emotion regulation

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ABSTRACT

The sex disparity in the development of depression has long been an important research topic, but the sex-related differences in neural activity during emotion regulation have been less thoroughly studied. It was hypothesized that, during the regulation of emotion, there would be more activation in the prefrontal regions implicated in cognitive processing for males, while there would be more activation in the prefrontal regions implicated in affective processing for females. This fMRI study recruited 12 females and 12 males who were required to view or to regulate the negative and positive emotion induced by some emotion-arousing pictures. During the regulation of negative emotion, both males and females had stronger activation in the left anterior cingulate gyrus, but males showed more activation in the prefrontal regions in general, including the left dorsolateral and lateral orbitofrontal gyrus as well as the right anterior cingulate gyrus, while females only showed stronger activation in the left medial orbitofrontal gyrus. For the regulation of positive emotion, both males and females showed stronger activation in the left dorsomedial prefrontal gyrus, but males were found to also have stronger activity in the left lateral orbitofrontal gyrus. It was concluded that there are common as well as sex-specific sets of brain regions involved in regulating negative and positive emotion, and the findings may have significant implications for females' vulnerability to developing depression.

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1. Introduction

Lifetime prevalence of major depressive disorders is much higher among females than among males, at a ratio of about 2:1 (Nolen-Hoeksema, 2001). The sex-related phenomenon of affective disturbances is multifactorial. Kessler (2003) suggested that the higher rate of depression in females could relate to the interplay of biological vulnerabilities and environmental stressful experiences. Others have conjectured that the differences between males and females in terms of their prevalence of affective disorders may be related to sex-specific emotion regulatory strategies for processing negative experiences (Nolen-Hoeksema, 2001; Thayer, Rossy, Ruiz-Padial, & Johnsen, 2003).

It is clear from the developmental literature that females respond to stress and distress very differently from males, even when they are at a young age. Rumination appears to be more frequently observed in females than males during stressful situations.

Nolen-Hoeksema and Girgus (1994) reported that teenage girls tend to respond to distress with rumination, a coping method that focuses inwardly on the feelings rather than directs action to any external agents for stress relief. Thomsen, Mehlsen, Viidik, Sommerlund, and Zachariae (2005) found that young females reported higher scores on negative affect mediated by rumination. Rumination does indeed increase the likelihood of developing depression by diminishing the individual's sense of mastery. It may also serve to sensitize the biological systems involved in the stress response (Nolen-Hoeksema, 2001). Further studies on sex differences in emotional regulation indicate that females with high depressive symptoms show greater attention to emotion, less anti-rumination emotional repair strategies, and higher reported depressive symptoms than do males with high depressive symptoms (Thayer et al., 2003). Matud (2004) reported that females show a significantly higher tendency to use emotional and avoidance-coping styles, and a lower tendency to use rational and detachment coping strategies.

Sex differences in the neural mechanisms subserving emotion recognition and perception for the processing of emotion have been reported. For example, Lee et al. (2002) suggested that males and females recruit different brain regions during emotion recognition of happy or sad facial expressions. Another study (Lee, Liu, Chan,

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Fang, & Gao, 2005) revealed that the right insula and the left thalamus were consistently activated in males, but not in females, during emotion recognition of affective stimuli. In a study on transient mood induction from viewing emotional pictures (Hofer et al., 2006), the females showed more neural activities in the right posterior cingulate, left putamen, and left cerebellum while viewing positive emotional pictures, and more neural activities in the bilateral superior temporal gyri and cerebellar vermis while viewing negative emotional pictures, relative to males. Studies on humor appreciation (Azim, Mobbs, Jo, Menon, & Reiss, 2005) and responses to disgusting visual stimuli (Caseras et al., 2007) have also demonstrated common and sex-related differential patterns of brain activation.

Sex differences in the neural mechanisms associated with various kinds of cognitive processing have been reported (Bell, Willson, Wilman, Dave, & Silverstone, 2006). In a study on autobiographical memory (Piefke, Weiss, Markowitsch, & Fink, 2005), in the process of retrieving autobiographical memories, activation in the left parahippocampal gyrus was observed in males while activation in the right dorsolateral prefrontal cortex was observed in females. Piefke et al. (2005) suggested that the sex-related difference in activation might reflect the different cognitive strategies employed for accessing autobiographical memories, since no significant sex differences were observed in memory performance, nor in the intensity of the emotion related to the memories. Cahill (2003) hypothesized that in the process of explicit recall of emotionally arousing events, males tend to recall the global/central aspects of a situation, which would relate to the right amygdala, whereas females tend to recall the local/fine detail aspects of a situation, which would be associated with the left amygdala.

Differences in the cognitive control of emotion between males and females have been relatively understudied. Koch et al. (2007) investigated the sex-related neural correlates of cognition and emotion interplay. They found that the interaction between negative emotion and working memory in females involved activation in the amygdala and the orbitofrontal cortex (OFC), while in males it involved activation in the prefrontal and superior parietal regions. This suggested that during the cognitive control of emotion, females mainly recruit the emotion-associated areas and males mainly recruit the brain regions important for cognitive processing. They concluded that this finding was associated with the increased emotional reactivity of females.

The discussions about the different cognitive strategies and emotion processing deployed for emotion regulation led to our hypothesis that there would be sex-related differences in neural activity when emotion regulation was exercised. However, this research question has rarely been addressed, and research to date has largely focused on the female population, probably due to the higher prevalence of affective disorders in this population. Emotion regulation involves inhibition or modulation of the primary emotion so as to produce contextually appropriate emotion and behavior (Phillips, Drevets, Rauch, & Lane, 2003a). The regulatory process is underlined by the involvement of control-appraisal system dynamics between the prefrontal cortex and other limbic-related regions (Ochsner & Gross, 2005). The prefrontal cortex plays a central role in cognitive control of behavior (Davidson & Irwin, 1999; Davidson, Putman, & Larson, 2000; Miller & Cohen, 2001; Ochsner & Gross, 2005; Phillips et al., 2003a; Phillips, Drevets, Rauch, & Lane, 2003b), while the limbic-related regions, such as the amygdala and insula, are implicated in the appraisal of emotion (Phan, Wager, Taylor, & Liberzon, 2002; Phillips et al., 2003a, 2003b). Several prior imaging studies have investigated the neural correlates of regulation of negative emotion (Le'vesque et al., 2003; Ochsner, Bunge, Gross, & Gabrieli, 2002; Ochsner et al., 2004; Phan et al., 2005). The participants viewed

probes depicting negative emotion-laden scenes. During regulation of the negative emotion, the participants were asked to either decrease (Le'vesque et al., 2003; Ochsner et al., 2002, 2004; Phan et al., 2005) or increase (Ochsner et al., 2004) their negative emotion induced by the emotional probes. Increased activity was then found in the prefrontal cortex, including the superior, lateral, and orbital prefrontal regions, and the anterior cingulate cortex, while decreased activity was found in the limbic-related regions, including the amygdala, the nucleus accumbens, and the insula.

Given the different prevalences of affective disturbances between males and females, we hypothesized that males would perform better than females in regulating negative emotion. We further hypothesized that males and females might show different patterns of neural activations in emotion regulation. The brain regions selected *a priori* were the prefrontal cortex and the limbic-related regions, regions that are associated with the dynamics of the control-appraisal system subserving the emotion regulatory process. Specifically, based on the findings of Koch et al. (2007) and studies on the relative tendencies to use rational and emotion-focused strategies to cope with stress in males and females, respectively (Matud, 2004; Nolen-Hoeksema, 2001; Thayer et al., 2003; Thomsen et al., 2005), we hypothesized that during emotion regulation, males would mainly recruit the dorsolateral prefrontal regions that are implicated in cognitive processes, while females would mainly recruit the orbitofrontal regions that are implicated in affective processes.

2. Methods

2.1. Participants

Twenty-four people, 12 females (age range = 20–27, mean age = 24, *sd* = 1.78 years) and 12 males (age range = 22–28, mean age = 24, *sd* = 1.68 years) participated in this study. They were all students from Shantou University, China. They were all right-handed and had no history of psychiatric illness, brain disease, or head trauma. They were assessed with the Chinese version of the Beck Depression Inventory-II (BDI-II; Chinese Behavioral Sciences Society, 2000) and only those whose scores were below the recommended clinical cut-off score (Beck, Steer, & Brown, 1996) were recruited. The study was approved by a local Institute Review Board. Written informed consent was obtained from each participant and the experimental protocol was explained to them.

2.2. Experimental stimuli

The potential stimuli for this study were 294 emotional pictures extracted from the International Emotion Picture System (IAPS) (Lang, Bradley, & Cuthbert, 1999) and the popular media. The stimulus set was tailored for each participant according to his or her rating of the 294 emotional stimuli. Stimuli selection was completed prior to scanning. Each participant viewed and rated all emotional pictures on a 9-point Likert scale according to his or her perceived emotional valence of the pictures (1 = very unpleasant, 5 = neutral, 9 = very pleasant), which were shown for 3 s in a random order. Only those pictures rated by the participants as highly negative (i.e. less than or equal to 3) and highly positive (i.e. greater than or equal to 7) were used in the subsequent fMRI study, so as to control the variation in intensity of the stimuli. The protocol of this study consisted of 48 negative, 48 positive, and 24 neutral pictures selected according to the participants' individual ratings of the pictures.

2.3. Experimental task

We adopted the block design of the emotion regulatory paradigm that was used in previous imaging studies of emotion regulation (Phan et al., 2005). Each block contained four components (see Fig. 1). Firstly, an arrow was displayed in the center of the screen for 3 s. The direction of this cue whether they should reduce their negative emotion (up arrow "↑") or positive emotion (down arrow "↓"), or whether they should simply view the pictures and perform no emotion regulation (equal sign "="). Secondly, four pictures for each emotion condition (positive, negative, or neutral) appeared in succession for 24 s (6 s per picture), and the participants responded to the pictures according to the cued instruction. Thirdly, they gave an average valence rating of the four emotion-arousing pictures that they had just viewed or regulated on a 9-point Likert scale, using the same procedure they had done in picture selecting by button pressing (9 s). Fourthly, a 21-s break then followed before the commencement of the next block.

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