Social Anxiety Disorder

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Social anxiety disorder (SAD; previously called social phobia) has been defined as the experience of constant fear, nervousness, and avoidance in the presence of a stranger, or in social situations that involve being observed.

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1. Introduction

Previous studies found that social anxiety often begins in adolescence and, if left untreated, can lead to comorbidity with depression, substance abuse, and other anxiety disorders [1]. More and more researchers are using neuroimaging technology (especially magnetic resonance imaging technology) to explore the cognitive neural mechanism of SAD. This basic research may one day have applied value in the diagnosis and treatment of the disorder.

However, not all these studies have obtained concordant conclusions. First, there is no consensus on which brain regions are related to SAD. Some researchers believed that a large-scale system of neural activity should be concerned in the diagnosis of SAD, while others considered that some distinct brain regions (e.g., right amygdala and superior temporal sulcus) are related to SAD [2][3]. Besides, researchers have no agreement on how the activities of brain regions change in SAD. For example, Gentili et al. found that the activity of the left fusiform gyrus of individuals with social phobia was significantly increased in their research, however, Frick et al. derived the opposite conclusion in their study, in which the activity of the bilateral fusiform gyrus of individuals with SAD significantly increased [4][5]. A possible explanation for inconsistent conclusions could be that there are different experimental paradigms in these studies. In previous task-state fMRI studies of SAD, researchers mostly used emotional face stimuli, social context stimuli, memory tasks, emotional Stroop tasks, and speech tasks to explore the relationships between activation of different brain structures and SAD. The results of these studies appear to differ based on task. For example, in one study using a speech task, activation of the pons, ventral striatum, amygdala, insula, and temporal polar regions of persons with SAD increased significantly, while the activations of dorsal anterior cingulate cortex and prefrontal cortex decreased significantly [4].

There have been many meta-analyses that included results regarding the relation between brain activation and SAD. For example, Etkin et al. published the first meta-analysis of neuroimaging results in samples of participants with anxiety disorders, including post-traumatic stress disorder, SAD, specific phobia, obsessive-compulsive disorder, generalized anxiety disorder, and comorbid pain disorder. They concluded that there may be a general “fear circuit” centered in the amygdala and the insula, and abnormal activities in these brain regions may cause

SAD [5]. Later, in 1999, Hattingh et al. published a meta-analysis exploring the affective cognition ability of persons with SAD and found that the average activations of the amygdala, temporal lobe, parahippocampal gyrus, anterior cingulate gyrus, globus pallidus, and posterior central gyrus in SAD groups were significantly lower than those in control groups [6]. Gentili et al. studied the face perception ability of patients with SAD and found that the face stimulation task led to increased activations of the amygdala, globus pallidus, superior temporal sulcus, visual cortex, and prefrontal cortex of patients with SAD [7]. Binelli et al. found abnormal activation of the limbic system in patients with SAD [8].

Although these meta-analyses found associations between SAD and abnormalities in certain brain regions, as a group they had limitations. Each included only seven or eight articles. They also used inconsistent methods of data analysis (some used analysis of region of interest (ROI)), the literature searches were not comprehensive, and a focus on the experimental tasks that assess the processing of emotional faces but not memory tasks, speech tasks, and situation presentations. These inconsistent results and limitations of previous studies and meta-analysis indicate that more comprehensive meta-analyses using innovative methods need to be taken to further clarify the cognitive neural mechanism of SAD.

2. Anterior Cingulate Cortex

The anterior cingulate gyrus belongs to the medial prefrontal cortex (mPFC) group. It is an important structure of the limbic system and plays an important role in the generation and regulation of emotions. The cingulate gyrus is the main brain area that helps information from focused attention enter the conscious level, and its activation state has been confirmed in various experiments [9]. For example, in simple and easy processing, the anterior cingulate gyrus is less able to cope with selective attention, and the posterior cingulate gyrus is less able to promote the execution of appropriate responses and/or inhibit the execution of unsuitable responses. These weakening effects may result in a decline in the anti-interference ability of individuals with SAD, making them feel more anxious.

The anterior cingulate gyrus is also an important connection node between the prefrontal cortex and limbic system. It plays an important role in perceiving and processing social rejection, and research on the activity of this structure provides evidence that social pain and physical pain share a common neurocognitive function [10]. The anterior cingulate gyrus is also important in a person's coping with social stressors [11]. For example, Wang et al. found that a reduction in the connection between the left anterior cuneate/posterior cingulate and the gyrus-anterior cingulate gyrus in anxious patients will lead to weakened emotion regulation, and finally cause anxiety [12].

3. Angular Gyrus/Supramarginal Gyrus

The meta-analysis found that the angular gyrus activity was significantly lower in individuals with SAD than in healthy controls when performing a situational stimulus task. The angular gyrus plays a very important role in mental constructs such as thoughts, feelings, and beliefs related to oneself and others [13]. Qiu et al. reported that during the resting state without external stimuli, individuals with SAD had emotional and attentional deviations and

distorted negative self-belief [14]. The results of this study support previous researchers' conclusions that individuals who hold negative beliefs about themselves show abnormal angular gyrus activity [15]. We also found that the activity of the upper right supramarginal gyrus of individuals with SAD was significantly lower than that of healthy controls in situational stimulus tasks. Previous studies reported that when individuals with SAD recognized their own faces, they also showed significant reductions of activity in the supramarginal gyrus. Therefore, some researchers believe that the cognitive bias of individuals with SAD when performing a situational stimulus task may be related to the cognitive distortion of their own faces [16].

4. Cerebellar Slope/Fusiform Gyrus

This meta-analysis showed that the activation of the left cerebellar slope of individuals with SAD was significantly lower than that of the healthy controls when performing face recognition tasks. The cerebellum is an important part of the motor network, and structurally it is closely connected with the limbic system. It is also an important part of emotional processing [17]. Previous studies found that the cerebellar area showed abnormal changes when individuals with SAD spoke in public, watched angry faces, performed confrontational computing tasks, and were exposed to different social tasks. The results of these previous studies are consistent with those of the current research [18].

The meta-analysis also showed that there was significantly lower activity of the fusiform gyrus in the SAD groups than in the healthy control groups during emotional faces tasks. This may indicate that the individuals with SAD adopted an avoidance strategy and reduced their fixation on emotional facial stimuli. The results of several previous studies support this finding. For example, Gentili et al. found that the activity of the left fusiform gyrus of individuals with social phobia was significantly reduced when watching emotional and neutral faces, compared with watching garbled pictures [7]. However, other studies reported opposite results. For example, Frick et al. found that the activity of the bilateral fusiform gyrus of individuals with SAD significantly increased when they looked at scared faces [19]. A reasonable explanation for this inconsistency is that the activity of the fusiform gyrus depends on whether individuals with SAD adopt avoidance strategies, but also on the type of research paradigm the study used. Future research could use eye tracking to test the hypothesis that individuals with SAD avoid looking at the emotional face, leading to reduced activity in the fusiform gyrus.

5. Different Task Types Affect Activation Patterns in Brain Regions

In the emotional face stimulation task, previous studies found abnormal activity in the limbic system of individuals with SAD [5]. Specifically, compared to healthy controls, people with SAD showed significantly higher activity in the amygdala, sulcus, and the parahippocampal gyrus when viewing angry and contemptuous faces. The hippocampus' response to emotional faces is positively correlated with the severity of social anxiety symptoms [20]. This meta-analysis excluded studies that only analyzed a specific brain region of interest and studies that did not report the coordinates of the brain regions showing abnormal activity. Using these exclusion criteria, we found a

significant decrease in the activation of the left cerebellar slope, providing new insights for research in this field. That is, SAD may involve dysfunction of a wide range of neural networks, including the limbic system and cerebellum.

In the specific situational stimulus paradigm, the activation of the upper right supramarginal gyrus in the SAD groups was significantly lower than that of the control groups. The upper right supramarginal gyrus plays an important role in regulating empathy for others. When this area works abnormally, people are unable to make rapid judgments about other people's emotions and have difficulty feeling empathy. Dysfunction in this area can also lead to more self-centeredness because of high levels of cognition at the expense of emotion, known as intellectualization [21]. Previous research found that people with SAD were not incapable of recognizing other people's emotions, but they still had low ability for empathy. One reason may be that they have problems with mentalization [22]. Compared with emotional facial stimuli, certain situational stimuli may be more likely to create a sense of an interpersonal environment, which serves as an important condition for the creation of empathy [23].

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