

Fear of anxiety and the brain response to threatening stimuli in panic disorder

Panic attacks are periods of very sudden intense fear, accompanied by bodily or cognitive symptoms (such as heart palpitations, dizziness, shortness of breath, or feelings of unreality) that can last from 10 minutes to hours and are often unexpected and very disabling. Many people have just one or two panic attacks in their lifetimes that solve spontaneously. But recurrent, unexpected panic attacks associated to constant fear of another attack is a condition called panic disorder (PD). Although panic attacks themselves aren't life-threatening, they can be frightening and impair the quality of life. The tendency to fear all those sensations that are related to anxiety, typical of PD is called anxiety sensitivity (AS). Subjects with high AS believe that experiencing anxiety or fear will cause severe negative consequences (i.e., heart attack); pay much attention to stimuli that signal anxiety (i.e., increased heart rate); worry about becoming anxious; and avoid stimuli that provide anxiety.

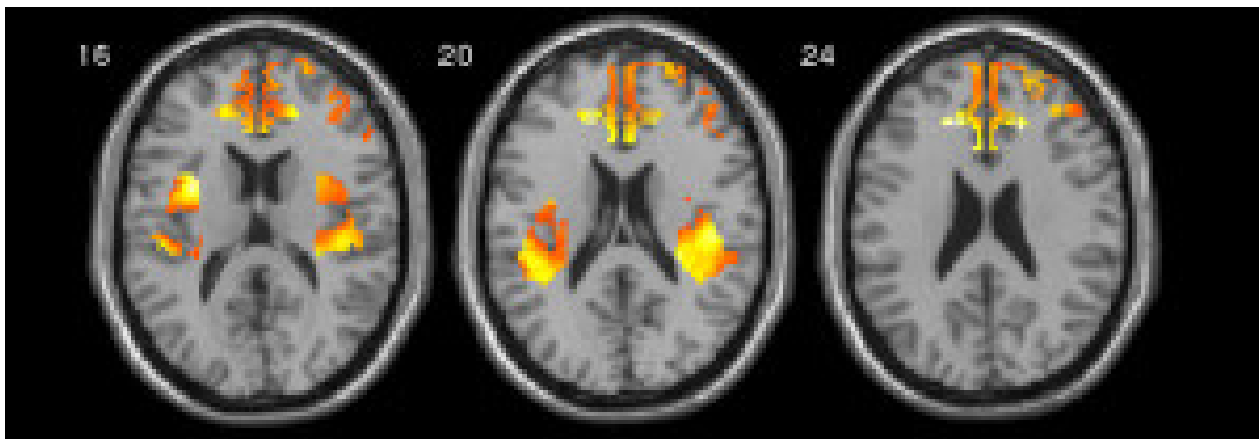


Fig.1. Response of the anterior cingulate cortex and the amygdala to negative emotional stimuli.

Patients suffering from PD show deficits in emotion processing, including the tendency to interpret ambiguous stimuli as threatening and give catastrophizing interpretation. Underpinning these deficits there is a network of neural structures called cortico-limbic network.

Here we used a functional magnetic resonance imaging (fMRI) technique in a sample of 18 patients affected by PD to investigate if AS could influence the brain response to emotion-related stimuli. fMRI enables to indirectly detect the activity of brain areas in response to stimuli, by observing changes in the blood flow. Blood is more oxygenated when neural activity increases and MR signal is sensitive to the different magnetic properties of the oxygen-rich and oxygen-poor blood, fMRI can thus produce activation maps showing which parts of the brain are involved in a particular mental process. To study the neural correlates of implicit emotional processing we chose

a face-matching paradigm where patients had to match picture of human faces with fearful or angry expressions. Each scenario is made up of two pictures in the lower side and one in the upper part. Participants had to choose which of the two images displayed in the lower side of the picture matched the one in the upper part. Higher levels of AS associated to a greater activation of the anterior cingulate cortex and the insula in response to emotional faces. Both these areas are part of the cortico-limbic network and are also involved in the processing of threat related stimuli. The anterior cingulate cortex is particularly involved in the appraisal and expression of fear, but also in evaluative judgment and anticipation of emotional stimuli. The insula has been implicated in the perception of internal bodily sensations and its hyperactivity in response to emotional faces in individuals with high anxiety may thus be specifically due to their sensitivity to the physical symptoms of anxiety. Furthermore, insula hyper-reactivity has been associated to the processing of negative emotional information, to threat relevant cues and symptom severity in anxiety.

This is the first study suggesting that core characteristics of PD such as unjustified fear of anxiety could depend on maladaptive changes in neurons connections that activate without a real threat. Several therapeutic approaches try to reverse these changes through the reduction of maladaptive thinking and behaviors (i.e. avoidance or anticipatory anxiety) that sustains or triggers the panic attacks (cognitive behavioural therapy) or directly promoting changes in brain activity as neurofeedback or neurostimulation do. These techniques should especially focus on the neural underpinnings of AS as a target for the treatment of panic disorder. Indeed, these techniques help in the extinction process of anxiety symptoms and increase the efficacy of conventional treatment strategies to improve quality of life of PD patients.

Publication

[Neural correlates of anxiety sensitivity in panic disorder: A functional magnetic resonance imaging study.](#)

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