

People with anxiety disorder less able to regulate response to negative emotions, study shows

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People with generalized anxiety disorder, or GAD, have abnormalities in the way their brain unconsciously controls emotions. That's the conclusion of a new Stanford University School of Medicine study, and the study authors say the findings could open up new avenues for treatments and change our understanding of how emotion is regulated in everyday life.

The work is published online in this month's [American Journal of Psychiatry](#).

According to the National Institute of Mental Health, 18 percent of Americans have an anxiety disorder. GAD in particular is marked by extreme feelings of fear and uncertainty; people with the disorder live in a state of non-stop worry and often struggle getting through their daily lives. "Patients experience anxiety and worry and respond excessively to emotionally negative stimuli, but it's never been clear really why," said Amit Etkin, MD, PhD, acting assistant professor of psychiatry and behavioral sciences and first author of the study.

Etkin said clinical data have suggested that adult GAD patients initially register negative stimuli in a largely normal way, but have deficits in how they then control [negative emotions](#). He and his colleagues conducted their research to better understand these potential abnormalities and to shed light on two theories dating back to Sigmund

Freud: that most emotion regulation is done unconsciously, and that a disturbance in unconscious emotion regulation leads to psychiatric symptoms.

For the study, Etkin recruited 17 people with GAD and 24 healthy participants and used [functional magnetic resonance imaging](#) and a behavioral marker to compare what happened when the two groups performed an emotion-based task. The task involved viewing images of happy or fearful faces, overlaid with the words "fear" or "happy," and using a button box to identify the expression of each face. Not all the words matched up — some happy faces featured the word "fear," and vice versa — which created an emotional conflict for participants.

The authors' previous work involving the task has shown that it takes study subjects longer to identify the correct expression when the expression and word contradict one another. But the slowdown in reaction time is lessened if the previous image was also incongruent, demonstrating that an emotion regulatory process kicked in to help the brain react faster to the conflicting emotional information. "We can see through the reaction-time effect that people are adapting their emotional processing" from image to image, Etkin explained.

In the current study, Etkin and his colleagues found that both healthy participants and GAD patients were able to identify the expressions. Healthy participants, as was expected, reacted more quickly to incongruent images when the previous image was also incongruent. When later asked if they were aware of any pattern that might have helped or hindered their performance, the volunteers said they were not; Etkin said this demonstrated that this process was carried out unconsciously.

However, the researchers found that in the GAD patients, the reaction-time effect seen in healthy patients was absent — and in the most

anxious patients, reaction time actually worsened when there were two incongruent images in a row. "GAD patients had decreased ability to use emotional content from previous stimuli to help them with the task," said Etkin.

He said the differences between the two groups were striking. "By looking at reaction times alone, we could classify who was a patient and who was a control," he said, adding that this represented the first solid demonstration that a psychiatric population has a deficit in a form of unconscious emotion regulation.

Earlier work from Etkin and colleagues had shown that when healthy subjects encountered the emotional conflict during this task, the pregenual anterior cingulate, a part of the brain's prefrontal cortex, was activated. That part of the brain then inhibited the amygdala, which acts to dampen or regulate negative emotion.

During this study, the brains of health participants reacted as expected. But for patients with GAD, the pregenual anterior cingulate failed to light up and to inhibit the amygdala, showing something went awry with this circuit. This has never been shown before, Etkin noted.

Understanding that the prefrontal cortex is an important site of abnormality could potentially lead to advances in more accurate diagnosis and effective treatment. By targeting this region more directly, clinicians might be able to improve regulation function in GAD patients. Etkin also suspects that a faulty pregenual cingulate-amygdala circuit during unconscious [emotion regulation](#) is involved in other psychiatric disorders, such as post-traumatic stress disorder, so the work could lead to a better understanding of those conditions.

Senior study author Alan Schatzberg, MD, the Kenneth T. Norris, Jr. Professor and chair of psychiatry and behavioral sciences, noted that the

findings bring new insight into the biology of psychopathology, as well as potentially the mechanisms underlying the response to psychotherapy. They could, he said, provide a new way also to gauge the efficacy of therapy.

Etkin said he'll continue his investigations in this area, and use these findings to identify brain signatures that differ among psychiatric disorders, as well as to track the effects of psychotherapy. A grant from the national stimulus package, which was signed into law last year and included \$8.2 billion in extramural funding for the National Institutes of Health, will help him continue and expand this work.

Provided by Stanford University Medical Center

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