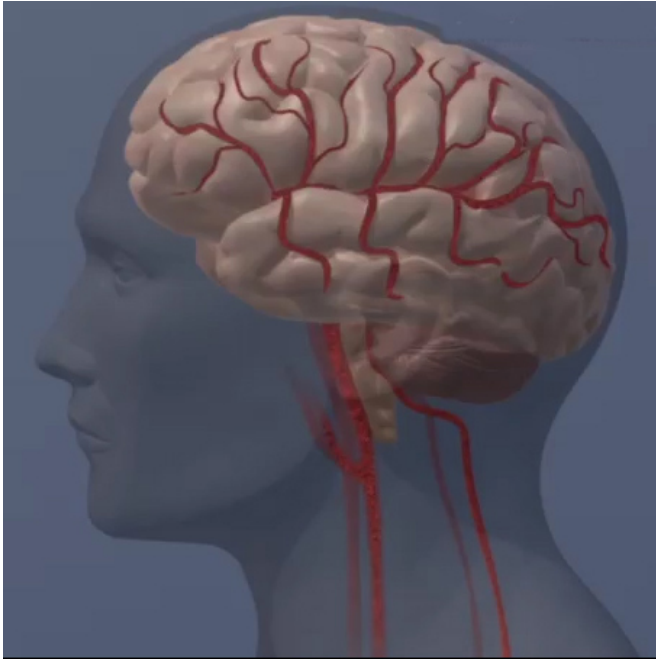


# Imaging reveals how well PTSD patients will respond to psychotherapy, researchers find

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A pair of studies led by researchers at the Stanford University School of Medicine demonstrates that scientists can predict, with a high degree of accuracy, which patients with post-traumatic stress disorder will respond to a method of psychotherapy often used to treat the condition.

The researchers showed how the treatment, prolonged exposure [therapy](#), works in the brains of PTSD patients and linked [brain](#) activity patterns to how well patients responded. The results could lead to personalized treatment for PTSD. The studies will be published online July 18 in *The American Journal of Psychiatry*.

"We understand vanishingly little about how psychotherapy works and for whom it works well," said Amit Etkin, MD, PhD, the senior author of both studies and an associate professor of psychiatry

and behavioral sciences at Stanford. "It's not even a knowledge gap—more like a knowledge ravine. This is especially an issue for PTSD because the only effective treatment is psychotherapy."

Lead authorship of the papers is shared by Stanford postdoctoral scholar Gregory Fonzo, PhD, and former Stanford postdoctoral scholar Madeleine Goodkind, PhD, now a psychologist at the New Mexico Veterans Affairs Health Care System and an adjunct assistant professor of psychiatry at the University of New Mexico School of Medicine.

## Revisiting traumatic experiences with psychotherapy

PTSD is a serious mental disorder that can develop after a dangerous or traumatic event. Patients experience recurring memories of the event; avoid situations, people or thoughts that remind them of the event; and experience altered mood and thinking patterns. Nearly 7 percent of people in the United States will suffer from PTSD at some point in their lifetime, according to the National Institute of Mental Health.

Prolonged exposure therapy for PTSD consists of a series of sessions and homework assignments that lead patients to gradually approach trauma-related memories and situations. Patients begin by imagining scenarios that trigger their PTSD symptoms—such as a crowded park. Then, they work up to deliberately putting themselves in those scenarios. Revisiting traumatic experiences in this manner can, over time, allow the brain to slowly reduce its response to emotional triggers. However, not all PTSD patients derive benefit from the treatment, and about a third drop out of the arduous process, according to Etkin, who is also an investigator at the Veterans Affairs Palo Alto Health Care System. About two-thirds of patients receiving prolonged exposure therapy see a 50 percent reduction in symptoms, and 40 percent of them

achieve remission, he said.

To learn how prolonged exposure therapy works in the brain, the studies used functional magnetic resonance imaging to measure the brain activity of 66 patients diagnosed with PTSD as they completed five tasks tapping a variety of emotional and cognitive functions. During these tasks, patients would view, for example, images of faces or scenes—like happy, neutral or scared faces or a scene depicting an event meant to induce negative emotions, such as an argument or physical violence—and either respond to questions about the images or try to control their response to the image's content.

After the initial brain imaging, about half the participants underwent nine to 12 sessions of prolonged exposure therapy; the remainder did not. At the end of the trial, all participants went through the same emotional response and regulation tests while researchers measured brain activity.

### **A step closer to personalized treatment**

One of the studies focused on whether brain activity levels before treatment could help scientists predict which participants would respond well to prolonged exposure therapy. The researchers measured how active certain brain regions were during the five tasks and looked for associations with reduced symptoms post-treatment.

Prior to receiving prolonged exposure therapy, patients with both lower activity in the amygdala and higher activity in various regions of the [frontal lobe](#) while viewing faces with fearful expressions showed a larger reduction in PTSD symptoms following therapy. Fonzo refers to the amygdala, seated deep within a primitive region of the brain, as the brain's alarm system, as it plays an important role in fear and other emotional responses. The frontal lobe is the outer layer of the human brain in the area behind the forehead; it plays a role in complex functions such as behavior, personality and decision-making.

The researchers also found that patients with greater activation in a deep region of the frontal lobe when ignoring the distracting effects of

conflicting emotional information—such as a picture of a scared face with the word "happy" written across it—responded better to exposure therapy.

"The better able the brain is at deploying attention- and emotion-controlling processes, the better you respond to treatment," said Fonzo.

Using this information about how the brain responds in emotional regulation and processing tasks, the team was able to predict how effective prolonged exposure therapy treatment would be for patients with up to 95.5 percent accuracy. This kind of screening approach, perhaps using the less expensive and more widely available electroencephalogram rather than fMRI, could help doctors determine the best course of PTSD therapy in the future, the researchers said.

"Not only could it provide a ray of hope for patients who would benefit from prolonged exposure to make it through the tough course," said Goodkind, "it means patients who wouldn't derive a benefit wouldn't have to start the treatment."

### **Therapy changes the brain**

In the second study, the researchers found that prolonged exposure therapy led to lasting changes in participants' brains that were associated with improvement in PTSD symptoms. About four weeks after therapy ended, fMRI showed elevated activity in the front-most region of the frontal lobe, an area called the frontopolar cortex. This region is the most recently evolved part of the human brain. It balances internal and external attention and helps coordinate multiple processes in the brain simultaneously, said Fonzo, as would occur when multitasking and remembering future to-do list items.

The role the frontopolar cortex plays in prolonged [exposure therapy](#) was surprising, Fonzo said, because much of the scientific attention on emotional processes in PTSD has centered on the amygdala.

Specifically, the changes the researchers observed in frontopolar cortex activity occurred when participants were instructed to regulate their

emotional response to an image of a negative or stressful scenario, such as one depicting an argument. The researchers also noted changes in frontopolar cortex activity in these participants during a resting, nonfocused state. The changes in frontopolar cortex activity indicate a shift in frontopolar function following therapy, according to the authors.

The post-therapy brain changes also included increased connectivity between the frontopolar cortex and deeper brain regions closer to emotional processing areas. The authors wrote that psychotherapy may train the frontopolar cortex "to better evoke or amplify attention toward an internal regulatory process that mediates successful emotion regulation."

The degree to which activity in the frontopolar cortex increased following therapy was associated with the degree of improvement in PTSD symptoms and emotional well-being.

#### Exploring use of transcranial magnetic stimulation

To confirm whether the frontopolar cortex controls important brain regions for emotional processing, the team used a noninvasive method of stimulating brain activity called [transcranial magnetic stimulation](#), or TMS, to activate the frontopolar cortex in healthy people. They simultaneously recorded [brain activity](#) with fMRI and confirmed that the frontopolar cortex modulated downstream activity in lower cortical regions closer to emotion-processing parts of the brain.

They also explored whether TMS might help PTSD patients respond to prolonged exposure treatment. Building off their findings that greater frontal lobe and less amygdala activation predicts better treatment outcome, the researchers activated a region of the frontal cortex with TMS probes while imaging the brain. They found that doing so inhibited activity in the amygdala, and the degree to which that happened also predicted the degree to which a patient's symptoms improved. In the future, stimulating this region may help increase [patients'](#) responsiveness to psychotherapy, they said. Indeed, some small-scale studies in which therapeutic TMS was used daily on the same

region of the frontal cortex, without the addition of psychotherapy, have already shown promising results.

"These findings put a place marker in our understanding of psychotherapy writ large. We can really put psychiatric disorders on the map in terms of hard science and help fight the stigma that surrounds these illnesses and their treatment," said Etkin. "Within the field of PTSD, it gives a concrete sense of hope for people undergoing treatment and starts laying the groundwork for new treatments based on understanding brain circuitry."

Provided by Stanford University Medical Center

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