What's really going on in PTSD brains? Experts suggest new theory

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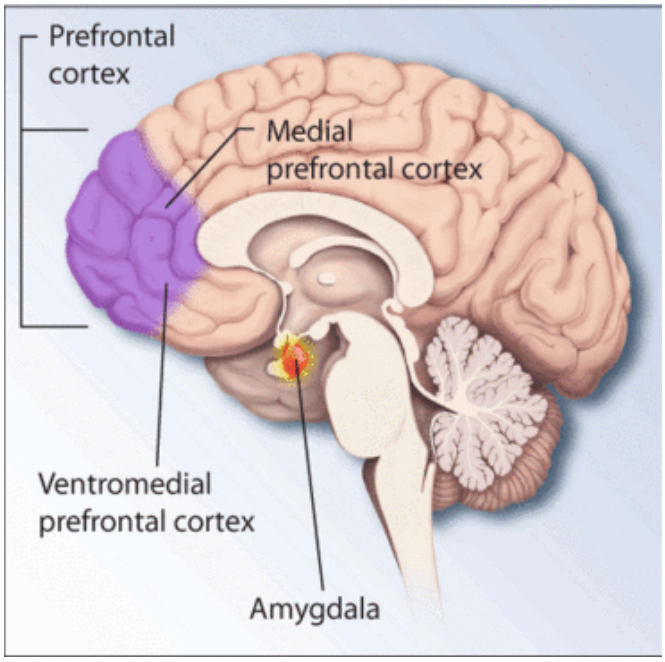

Regions of the brain associated with stress and posttraumatic stress disorder. Credit: National Institutes of Health

For decades, neuroscientists and physicians have tried to get to the bottom of the age-old mystery of post-traumatic stress disorder, to explain why only some people are vulnerable and why they experience so many symptoms and so much disability.

All experts in the field now agree that PTSD indeed has its roots in very real, physical processes within the brain - and not in some sort of psychological "weakness". But no clear consensus has emerged about what exactly has gone "wrong" in the brain.

In a Perspective article published this week in *Neuron*, a pair of University of Michigan Medical School professors—who have studied PTSD from many angles for many years—put forth a theory of PTSD that draws from and integrates decades of prior research. They hope to stimulate interest in the theory and invite others in the field to test it.

The bottom line, they say, is that people with PTSD appear to suffer from disrupted context processing. That's a core brain function that allows people and animals to recognize that a particular stimulus may require different responses depending on the context in which it is encountered. It's what allows us to call upon the "right" emotional or physical response to the current encounter.

A simple example, they write, is recognizing that a mountain lion seen in the zoo does not require a fear or "flight" response, while the same lion unexpectedly encountered in the backyard probably does.

For someone with PTSD, a stimulus associated with the trauma they previously experienced - such as a loud noise or a particular smell—triggers a fear response even when the context is very safe. That's why they react even if the noise came from the front door being slammed, or the smell comes from dinner being accidentally burned on the stove.

Context processing involves a brain region called the hippocampus, and its connections to two other regions called the prefrontal cortex and the amygdala. Research has shown that activity in these brain areas is disrupted in PTSD patients. The U-M team thinks their theory can unify wide-ranging evidence by showing how a disruption in this circuit can interfere with context processing and can explain most of the symptoms and much of the biology of PTSD.

"We hope to put some order to all the information that's been gathered about PTSD from studies of human patients, and of animal models of the condition," says Israel Liberzon, M.D., a professor of psychiatry at U-M and a researcher at the VA Ann Arbor Healthcare System who also treats

veterans with PTSD. "We hope to create a testable hypothesis, which isn't as common in mental health research as it should be. If this hypothesis proves true, maybe we can unravel some of the underlying pathophysiological processes, and offer better treatments."

Is this mountain lion in a zoo, or your backyard? You'd respond differently to it depending on how your brain processes the context in which you're encountering it. But a new theory of PTSD suggests that people with that condition have disrupted context processing -- which could lead to the kinds of symptoms and responses they exhibit. Credit: University of Michigan

Liberzon and his colleague, James Abelson, M.D., Ph.D., describe in their piece models of PTSD that have emerged in recent years, and lay out the evidence for each. The problem, they say, is that none of these models sufficiently explains the various symptoms seen in patients, nor all of the complex neurobiological changes seen in PTSD and in animal models of this disorder.

The first model, abnormal fear learning, is rooted in the amygdala - the brain's 'fight or flight' center that focuses on response to threats or safe environments. This model emerged from work on fear conditioning, fear extinction and fear generalization.

The second, exaggerated threat detection, is rooted in the brain regions that figure out what signals from the environment are "salient", or important to take note of and react to. This model focuses on vigilance and disproportionate responses to perceived threats.

The third, involving executive function and regulation of emotions, is mainly rooted in the prefrontal cortex - the brain's center for keeping emotions in check and planning or switching between tasks.

By focusing only on the evidence bolstering one of these theories, researchers may be "searching under the streetlight", says Liberzon. "But if we look at all of it in the light of context processing disruption, we can explain why different teams have seen different things. They're not mutually exclusive."

The main thing, says Liberzon, is that "context is not only information about your surroundings - it's pulling out the correct emotion and memories for the context you are in."

A deficit in context processing would lead PTSD patients to feel "unmoored" from the world around them, unable to shape their responses to fit their current contexts. Instead, their brains would impose an "internalized context"—one that always expects danger—on every situation.

This type of deficit, arising in the brain from a combination of genetics and life experiences, may create vulnerability to PTSD in the first place, they say. After trauma, this would generate symptoms of hypervigilance, sleeplessness, intrusive thoughts and dreams, and inappropriate emotional and physical outbursts.

Liberzon and Abelson think that testing the context processing theory will enhance understanding of PTSD, even if all of its details are not verified. They hope the PTSD community will help them pursue the needed research, in PTSD patients and in animal models. They put forth specific ideas in the Neuron paper to encourage that, and are embarking on such research themselves.

The U-M/VA team is currently recruiting people with PTSD - whether veterans or not - for studies

involving brain imaging and other tests.

In the meantime, they note that there is a growing set of therapeutic tools that can help patients with PTSD, such as cognitive behavioral therapy mindfulness training and pharmacological approaches. These may work by helping to anchor PTSD patients in their current environment, and may prove more effective as researchers learn how to specifically strengthen context processing capacities in the brain.

More information: Israel Liberzon et al, Context Processing and the Neurobiology of Post-Traumatic Stress Disorder, *Neuron* (2016). DOI: 10.1016/j.neuron.2016.09.039

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