Where do fears come from? How can new insights enhance treatment?

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Exposure therapy is a major treatment option used by clinicians to help patients face and get past their distressing and impairing fears. However, the fears can return in as many as 50% of patients.

University of Colorado researchers recently published a study that presents groundbreaking behavioral health models. The study, published in *Computational Psychiatry*, showed that fears are likely to linger because fear memories outlast competing safety memories gained in exposure therapy.

In the following Q&A, Joel Stoddard, MD, associate professor in the Department of Psychiatry at the University of Colorado School of Medicine, explains where our fears come from and how the new research and mathematical modeling will help strengthen exposure therapy, based on the individual patient's experience. He also explains how the research was made possible by strong collaboration across two University of Colorado campuses with Sarah Kennedy, Ph.D., and Sam Paskewitz, Ph.D., at CU Anschutz and Matt Jones, Ph.D., at CU Boulder.

As a clinician and researcher, how do you define fear?

Fear is a person's whole-body response to a threat.

You're walking in the forest, and you see a snake. Your body responds, "This is dangerous!" Your whole mind-body response to the snake is typically a fear response. So, you're going to have the response you've come to label as fear, a mixed state of feelings, thoughts, behaviors, and physiologic changes. Everyone experiences fear a bit differently based on how they integrate the component responses.

It's your whole response to the threatening situation, not just how you feel about it. Classically, your body gets ready to deal with the threat with a "freeze, flight or fight" response.

The freeze: "Don't notice me, please." Flight: "I'm going to run away while I still can." And fight, our last resort.

A snake on a hike seems like an innate response. What about learned or conditioned fears?

So that's the next step. When we're talking about fear, we're talking about basically a type of threat response. Things that are threatening to you are things that are going to harm you.

There's a bunch of stuff in the world that may evoke a fear response where we don't exactly know why it does. Some people are afraid of snakes even though they were never harmed by one. That's called an unconditioned fear.

Conditioned fears are different in that they are learned. For example, a car accident is a huge, life-threatening event. A lot of times, folks will learn to fear certain things that were not scary before the car accident. Like the steering wheel. Steering wheels don't typically hurt people. But our car accident victim was focused on the wheel at the time of the accident. And so now whenever they see a steering wheel, they have a significant life-or-death response. Steering wheels are now part of a new threat memory. The reaction to steering wheels is a conditioned fear response.

So taking conditioned fears into account, what are the different kinds of fear that you see in your work?

First off, let's be clear here and differentiate different disorders of the threat response:

- Post-traumatic stress (PTSD). When you have one event, you have a distressing and impairing reaction to the experience of trauma including fear of things you learned to fear during that traumatic event. This can be like the car accident example I

mentioned, or post-traumatic fear responses experienced by soldiers in conflict zones.
- Anxiety disorders. Anxiety disorders are a fear response to a threat you haven't encountered yet or to an anticipated threat. "I didn't do well on that test," for example.
- Panic disorders. That's like having a severe fear reaction out of the blue. To many, this can feel like a heart attack.

Broadly, those exemplify different types of disorders where people have problems with their fear responses. Panic: fear response without the threat. Anxiety: fear response to an anticipated threat. Post-traumatic stress: response to a threat memory.

What is exposure therapy, and historically has it been the best treatment option for fear?

Exposure therapy is a very efficacious, highly evidence-based intervention that came out of mid-20th century psychiatry.

Let's say you are afraid of heights. There's this ladder, and you've got to climb it in order to fix something. But you're paralyzed by your fear. You just can't get up that ladder. It's just too scary for you to do that.

In general, the therapy is placing yourself in a situation to do what you're afraid of while being in a safe environment. You learn that you're safe, then carry forward that learned safety memory. The safety memory competes with the threat association to heights.

Our work has much broader implications to just exposure therapy. Exposures are actually a technique which are an active ingredient in many therapies that target a threat association.

In PTSD, for example, indicated therapies can include trauma-focused cognitive behavioral therapy, narrative therapy, or eye movement desensitization and reprocessing. These are all very different kinds of therapies that in looking under the hood, one finds that they have some sort of exposure element to target the threat association. They bring the individual closer to their feared threat memory, but they also empower the individual and provide safety memories that compete with the threat memories through different ways.

Why did you and your team decide to research improving exposure therapy?

It really was a serendipitous, chocolate-meets-peanut butter moment. I was recruited to CU Anschutz to learn different mathematical models of the mind and how we can apply them to treatment.

Exposure therapy is generally super effective, but for 50% of people it's not as effective and for many it is not long-lasting. That's because their fears can come back over time. Without an enduring safety memory, a patient's memories are tenacious and lead to recurrent fear responses. A fear response can come back if the person gets threatened again or maybe finds themselves triggered in a different context. Sometimes their symptoms are milder. Unfortunately, full-blown symptoms can return.

My colleagues and I were in Matt Jones's office chatting. Matt is a prolific genius of rigorously mapping psychological processes to math. He and Sam Paskewitz had been working on how stimuli compete to trigger memories. I had already studied the brain basis of threat/safety memory competition in humans. Lightbulbs were going off. So, when I heard about their new experiment, I immediately asked them to apply it to threat learning. We later asked Sarah Kennedy for help because she had a deep understanding of how fear learning theory may be applied to

therapy and is a leading behavioral experimental therapeutics expert on campus. It was just all here at CU.

We had to figure out a mathematical framework that explained all of that—what is observed in people and experiments. All of it with no exceptions. Once you get it mathematically expressed, it means now you have a precise theory. This is a hot topic, and people have been trying to understand how we can map this for some time mostly because the basic science is so good. Luckily, we have connections between CU Boulder and CU Anschutz, and AB Nexus, in both the modeling and clinical health aspects. So, to avoid pulling punches and honor my colleagues' work, they frankly integrated a profound body of work into a coherent theory of treating fear, expressed in math.

What is the takeaway from your math and equations? How does it show a new model and paradigm for exposure therapy to make it more durable?

The big takeaway has been the potential for precision medicine in behavioral health, to borrow a popular phrase.

What if instead of months of exposure therapy, we could tell you within a week or two whether it is the right therapy? What if you are in exposure therapy, are very invested, but are having trouble with threat learning? We can tell you that early as well.

Mathematically, this research is analogous to Newton's equations in physics. These are simple, elegant equations that help describe motion and force. They aren't perfect, but they are powerfully predictive for day to day gross motion. You can land a person on the moon with them. More complex elaborations, like relativity and quantum physics, exist for narrow problems. We actually did stress test elaborate models for

therapy, but found they need a little more work.

We were successful because we built on a tremendous body of experimental and mathematical work—translating and in some places revising the Rescorla-Wagner family of equations. This is specifically for use in measuring and predicting learning processes involving threat memories. By detailing a set of equations to measure and predict how people acquire and forget both safety and threat memories, we may be able to better help individuals who have trouble with their fear responses to threat memories. That impacts on a staggering percentage of people over the lifetime and is a leading cause of disability worldwide, accounting for all diseases.

Already we have preliminary evidence that we can use this family of equations to predict how well patients will respond to treatment by how much they learn in their treatment sessions.

Let's say you're in your therapist's office: You're associating your therapist and that office with safety. It's really those safety signals that are helping you prevent that threat response. And so, as soon as you're out of your therapist's office, if you don't learn to generalize those safety memories your fear response can return. Unfortunately, experiments and models suggest that safety memories are less stable than threat memories.

Because the equations summarize all of our theory in compact form, it's easy to see how things precisely relate. It's an exciting future for behavioral health research. There are actually numerous implications for practice and predicting individual responses for those who brave reading the paper. It's the beginning of an exciting new program of research to test a theory integrating over 50 years of work in threat learning to patient care.

More information: Samuel Paskewitz et al, Explaining the Return of Fear with Revised Rescorla-Wagner Models, *Computational Psychiatry* (2022). DOI: 10.5334/cpsy.88