Medical Xpress

# Cognitive behavioral therapy enhances brain circuits to relieve depression

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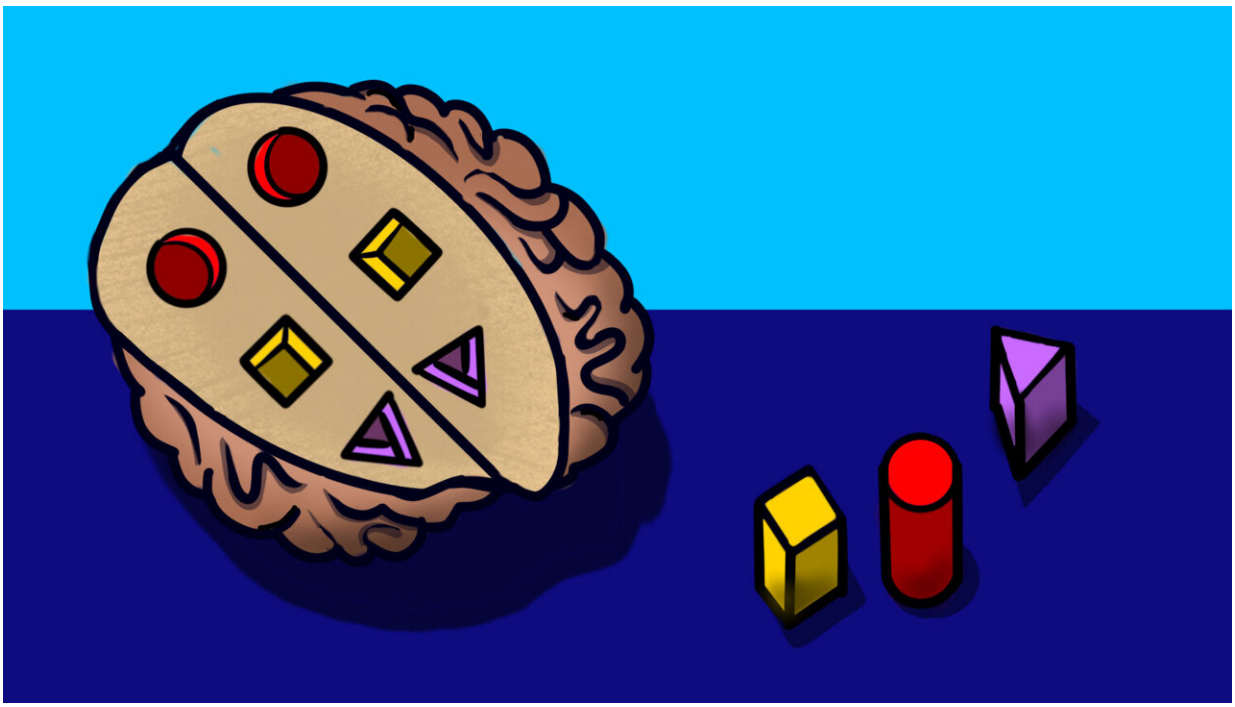

Stanford Medicine researchers and their colleagues have found that choosing treatments based on the type of a patient's depression increases the odds of success. Credit: Emily Moskal/Stanford Medicine

Cognitive behavioral therapy, one of the most common treatments for depression, can teach skills for coping with everyday troubles, reinforce healthy behaviors and counter negative thoughts. But can altering thoughts and behaviors lead to lasting changes in the brain?

New research led by Stanford Medicine has found that it can—if a therapy is matched with the right patients. In a study of adults with both depression and obesity—a difficult-to-treat combination—cognitive behavioral therapy that focused on problem solving reduced depression in a third of patients. These patients also showed adaptative changes in their brain circuitry.

Moreover, these neural adaptations were apparent after just two months of therapy and could predict which patients would benefit from long-term therapy.

The findings add to evidence that choosing treatments based on the neurological underpinnings of a patient's depression—which vary among people—increases the odds of success.

The same concept is already standard practice in other medical specialties.

"If you had chest pain, your physician would suggest some tests—an electrocardiogram, a heart scan, maybe a blood test—to work out the cause and which treatments to consider," said Leanne Williams, Ph.D., the Vincent V.C. Woo Professor, a professor of psychiatry and behavioral sciences, and the director of Stanford Medicine's Center for Precision Mental Health and Wellness.

"Yet in depression, we have no tests being used. You have this broad sense of emotional pain, but it's a trial-and-error process to choose a treatment, because we have no tests for what is going on in the brain."

Williams and Jun Ma, MD, Ph.D., professor of academic medicine and geriatrics at the University of Illinois at Chicago, are co-senior authors of the study published Sept. 4 in *Science Translational Medicine*. The work is part of a larger clinical trial called RAINBOW (Research Aimed

at Improving Both Mood and Weight).

## Problem solving

The form of cognitive behavioral therapy used in the trial, known as problem-solving therapy, is designed to improve cognitive skills used in planning, troubleshooting and tuning out irrelevant information. A therapist guides patients in identifying real-life problems—a conflict with a roommate, say—brainstorming solutions and choosing the best one.

These cognitive skills depend on a particular set of neurons that function together, known as the cognitive control circuit.

Previous work from Williams' lab, which identified six biotypes of depression based on patterns of brain activity, estimated that a quarter of people with depression have dysfunction with their cognitive control circuits—either too much or too little activity.

The participants in the new study were adults diagnosed with both major depression and obesity, a confluence of symptoms that often indicates problems with the cognitive control circuit. Patients with this profile generally do poorly on antidepressants: They have a dismal response rate of 17%.

Of the 108 participants, 59 underwent a year-long program of problem-solving therapy in addition to their usual care, such as medications and visits to a primary care physician. The other 49 received only usual care.

They were given fMRI brain scans at the beginning of the study, then after two months, six months, 12 months and 24 months. During the brain scans, the participants completed a test that involves pressing or not pressing a button according to text on a screen—a task known to

engage the cognitive control circuit. The test allowed the researchers to gauge changes in the activity of that circuit throughout the study.

"We wanted to see whether this problem-solving therapy in particular could modulate the cognitive control circuit," said Xue Zhang, Ph.D., a postdoctoral scholar in psychiatry who is the lead author of the study.

With each brain scan, participants also filled out standard questionnaires that assessed their problem-solving ability and depression symptoms.

## Working smarter

As with any other depression treatment, problem-solving therapy didn't work for everyone. But 32% of participants responded to the therapy, meaning their symptom severity decreased by half or more.

"That's a huge improvement over the 17% response rate for antidepressants," Zhang said.

When researchers examined the brain scans, they found that in the group receiving only usual care, a cognitive control circuit that became less active over the course of the study correlated with worsening problem-solving ability.

But in the group receiving therapy, the pattern was reversed: Decreased activity correlated with enhanced problem-solving ability. The researchers think this may be due to their brains learning, through the therapy, to process information more efficiently.

"We believe they have more efficient cognitive processing, meaning now they need fewer resources in the cognitive control circuit to do the same behavior," Zhang said.

Before the therapy, their brains had been working harder; now, they were working smarter.

Both groups, on average, improved in their overall depression severity. But when Zhang dug deeper into the 20-item depression assessment, she found that the depression symptom most relevant to cognitive control—"feeling everything is an effort"—benefited from the more efficient cognitive processing gained from the therapy.

"We're seeing that we can pinpoint the improvement specific to the cognitive aspect of depression, which is what drives disability because it has the biggest impact on real-world functioning," Williams said.

Indeed, some participants reported that problem-solving therapy helped them think more clearly, allowing them to return to work, resume hobbies and manage social interactions.

## Fast track to recovery

Just two months into the study, brain scans showed changes in cognitive control circuit activity in the therapy group.

"That's important, because it tells us that there is an actual brain change going on early, and it's in the time frame that you'd expect brain plasticity," Williams said. "Real-world problem solving is literally changing the brain in a couple of months."

The idea that thoughts and behaviors can modify brain circuits is not so different from how exercise—a behavior—strengthens muscles, she added.

The researchers found that these early changes signaled which patients were responding to the therapy and would likely improve on problem-

solving skills and depression symptoms at six months, 12 months and even one year after the therapy ended, at 24 months. That means a brain scan could be used to predict which patients are the best candidates for problem-solving therapy.

It's a step toward Williams' vision of precision psychiatry—using brain activity to match patients with the therapies most likely to help them, fast-tracking them to recovery.

"It's definitely advancing the science," Zhang said. "But it's also going to transform a lot of people's lives."

Researchers from University of Washington, University of Pittsburgh School of Medicine and The Ohio State University also contributed to the work.

**More information:** Xue Zhang et al, Adaptive cognitive control circuit changes associated with problem-solving ability and depression symptom outcomes over 24 months, *Science Translational Medicine* (2024). DOI: 10.1126/scitranslmed.adh3172

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