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Engaging Neuroplasticity in Depression with Cognitive-Emotional Training

Announcer:
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Here's your host, Dr. Charles Turck.

Dr. Turck:
This is ReachMD, and I'm Dr. Charles Turck. Today, we'll be discussing cognitive-emotional training, which leverages neuroplasticity of the brain, as a potential digital therapeutic to treat depression.[1-3] Joining me is Dr. Brian Iacoviello, who's an Assistant Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai in New York City.

Dr. Iacoviello, welcome to the program.

Dr. Iacoviello:
Thank you for having me.

Dr. Turck:
Before we dive into digital therapeutics for depression, I'd like to learn a bit more about your research background, Dr. Iacoviello. What inspired you to focus on cognitive control as a target for treating depression?

Dr. Iacoviello:
Thanks for asking. So I'm a clinical psychologist, meaning that I have a PhD in psychology that included training both as a psychotherapist and as a researcher. Actually, my clinical and research interests have always centered on trying to understand the experience of depression and anxiety, as well as the treatments that we have for people who are struggling with these conditions—especially focusing on the cognitive and behavioral patterns involved.

One aspect of depression and anxiety that seemed challenging to tackle was the perseverative thinking. This could include constantly thinking about sad or worrisome things, ruminating or dwelling on the past, or obsessing or worrying about current or future concerns. Getting stuck in these negative thoughts, and holding them in our minds, keeps our moods down and our worries up.[1]

So I began to explore and study what was going on for people with depression regarding what we would call cognitive control capability.[1] This describes the ability to exert some control over our thinking and emotions to be able to pull ourselves out of the perseverative thinking. And I was particularly interested in targeting cognitive control to develop effective treatments for depression.[1]

Dr. Turck:
Thank you for sharing your background in this area. Turning to therapeutic options, can you briefly walk us through how we currently approach these negative thinking patterns in depression?

Dr. Iacoviello:
Sure. For people with depression, the treatment options thus far have been medications and psychotherapy.[4]Antidepressants, such as selective serotonin reuptake inhibitors, or SSRIs, seem to help reduce the intensity of persistent negative, perseverative, or emotional thinking.[5]Studies have found that the amygdala, the part of the brain that's responsible for processing emotions and detecting danger, appears to be hyperactive in people with depression.[1,6] So part of how antidepressants might work is by quieting down the hyperactivity

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of the amygdala.[5]

As far as psychotherapy, research has shown that cognitive behavioral therapy, or CBT, can be effective for many people with depression.[5] CBT focuses on thought patterns in an explicit way. And by explicit, I mean that we're looking at the content of the thinking and trying to question and change any problematic or biased patterns, such as persistent negative thoughts about yourself or a tendency to catastrophize.[1] CBT can help teach you to challenge those negative automatic thoughts and replace them with healthier thoughts.[1]

Notably, brain imaging research suggests that part of what might be going on with CBT includes activation of the brain areas, such as the prefrontal cortex, or the PFC, that are involved with the cognitive control capability that I was talking about earlier, or the ability to influence our thinking and our attention instead of just being on autopilot.[7]

As with antidepressants, CBT may also quiet down the amygdala, the emotion-processing part of the brain that tends to be hyperactive in depression, which could stem from having more control over your emotions and thinking patterns.[5] So when we consider how CBT is effective for depression, it appears to help train patients in cognitive control, as well as affect the brain regions involved in both cognitive control and emotion processing.[7]Approaches other than CBT might target cognitive control in an implicit way, by which I mean targeting the problematic cognitive process itself rather than the content of the thinking.[1]

An example of this is a treatment called attention bias modification, where the tendency to hyperfocus one's attention on a perceived danger or threat-related cue can be trained to be a bit more balanced.[1]In this intervention, a patient wouldn't focus quite so much on the perceived danger cues that aren't actual danger cues in their environment. And as a result of attention bias modification, the patient potentially wouldn't experience quite as much anxiety.[1]

Turning back to depression, clinicians and researchers have been considering for some time how to approach the dysfunction in cognitive control, or the inability to pull oneself out of rumination or very sad/negative thoughts.[1]Interestingly, researchers have designed and studied trainings in cognitive control, but these only targeted the cognitive aspect or the ability to hold, process, and work with information in the mind.[2] As a result, we saw that the cognitive control training may help strengthen people's cognitive abilities, but we weren't seeing much improvement in their mood or other symptoms of depression.[2] We also didn't see much improvement in the negative emotional thinking patterns, such as rumination.[2]

Dr. Turck:
So how did you approach going beyond these training methods to propose cognitive-emotional training for the treatment of depression?

Dr. Iacoviello:
Well to start, I think it's important to note that the unhelpful thinking patterns of depression don't involve getting stuck on just any thoughts, but specifically, the sad or negative thoughts. So we realized that we needed to focus on improving the cognitive control of emotional information processing, specifically.[2] And this aligns with findings from brain imaging research in people who are depressed that show increased activity in the emotion-processing regions, such as the amygdala, and reduced activity in the cognitive control regions, such as the PFC.[2]

Our theory was that we needed to target both parts of this neural network—both the emotion-processing and cognitive-control parts—to help the brain learn, or *relearn*, a more balanced activation pattern.[2] But instead of using explicit training or psychotherapy, we wanted to create an implicit training that could be used like an exercise for these brain regions. Additionally, we wanted to develop a training intervention that could be administered digitally by computer or smartphone.[2]

Dr. Turck:
For those just tuning in, you're listening to a Medical Industry Feature on ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Brian Iacoviello about leveraging neuroplasticity to digitally deliver cognitive-emotional training to treat depression.

Now let's dive further into delivering cognitive-emotional training digitally, Dr. Iacoviello. Why is this important?

Dr. Iacoviello:
Unfortunately, people with depression may still encounter barriers to accessing mental health care.[8] For example, accessing medication or psychotherapy treatment for depression can be difficult for a number of reasons, including finding a local provider. Even after connecting with a provider, financing the costs of treatment and staying consistent with medications or therapy sessions can also pose challenges for patients.[8] We've seen that these and other barriers can actually prevent some people from receiving effective treatment

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for depression.[8] So we wanted to develop a therapeutic that could overcome some of these barriers, and digital interventions offered a potential option.[9]

Since digital interventions are portable and they can be accessed from your own device, hopefully, patients find them convenient and easier for adherence.[9] Also, digital interventions allow people to access treatment wherever and whenever they want, potentially, making for an appealing option for depression treatment.[9] These delivery aspects may help patients overcome some of the barriers they face when trying to access mental health treatment.

Dr. Turck:
And with that in mind, could you break down the steps that you followed to develop a cognitive-emotional training intervention?

Dr. Iacoviello:
I'd be happy to. We started out by identifying exactly what we wanted to target with this treatment. In this case, we wanted to target the ability to exert some control over perseverative thinking on negative or sad emotional content.[1] And we worked with the model of neural networks in depression where the amygdala, which is responsible for emotion processing, is hyperactive and the cognitive control regions, including the PFC, are underactive.[1]

So we then devised a training exercise, called the Emotional Faces Memory Task, or EFMT, to challenge both the emotion processing and cognitive control capabilities. We designed the exercise intending to not only activate both regions of the brain simultaneously but also to keep those brain regions engaged by consistently challenging them.[1,2] The hope was that with enough of this training, the brain would learn, or *relearn*, to activate those brain regions in a more balanced manner—what we would call neuroplasticity.[1,2]

So first, we developed some prototypes for the exercise and tested them out to make sure they functioned properly. We also figured out the correct parameters for things like difficulty and timing in order to keep the person and their brain networks consistently challenged during the intervention.[2]

Next, we tested the prototype in a small sample of patients with depression. Our goal was to see if using the training exercise would result in improved symptoms of depression, which it indeed appeared to do.[2]

With those early findings showing promise, we then conducted a larger clinical trial to further study the effects of the training, and once again, we saw an improvement in depression symptoms.[3]

Additionally, we collected some brain imaging data, specifically, from functional MRIs or fMRIs, which further confirm that the training exercise successfully activated the emotion processing and cognitive control regions of the brain, and perhaps even altered the connectivity patterns between them.[10]

Dr. Turck:
Lastly, Dr. Iacoviello, what are the next steps for this type of cognitive-emotional training intervention? Are there plans for further research on digitally-delivered therapeutics for depression?

Dr. Iacoviello:
I believe there's a lot of potential for cognitive-emotional training interventions in the future. Right now, there's a lot of excitement in the field to develop digital therapeutics for depression using this mechanism of action that leverages neuroplasticity. Currently, academia, digital health technology companies, and pharmaceutical companies are all involved in developing digital therapeutics for depression.[11] Some are even developing interventions with the same level of rigor as traditional drug development and approval pathways.[12] So it's really exciting to think that in the not too distant future, these types of interventions could be in the hands of people with depression who could benefit from them.

Dr. Turck:
Those are some great considerations for us to think on as we come to the end of today's program.

I want to thank my guest, Dr. Brian Iacoviello, for helping us better understand cognitive-emotional training as a potential digital therapeutic to treat patients with depression.

Dr. Iacoviello, it was great speaking with you today.

Dr. Iacoviello:

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It was my pleasure.

Dr. Turck:
I'm Dr. Charles Turck.

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