Selectively rewiring the brain's circuitry to treat depression

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On Star Trek, it is easy to take for granted the incredible ability of futuristic doctors to wave small devices over the heads of both humans and aliens, diagnose their problems through evaluating changes in brain activity or chemistry, and then treat behavior problems by selectively stimulating relevant brain circuits.

While that day is a long way off, transcranial magnetic stimulation (TMS) of the left dorsolateral prefrontal cortex does treat symptoms of depression in humans by placing a relatively small device on a person's scalp and stimulating brain circuits. However, relatively little is known about how, exactly, TMS produces these beneficial effects.

Some studies have suggested that TMS may modulate atypical interactions between two large-scale neuronal networks, the frontoparietal central executive network (CEN) and the medial prefrontal-medial parietal default mode network (DMN). These two functional networks play important roles in emotion regulation and cognition.

In order to advance our understanding of the underlying antidepressant mechanisms of TMS, Drs. Conor Liston, Marc Dubin, and their colleagues conducted a longitudinal study to test this hypothesis.

The researchers used functional magnetic resonance imaging in 17 currently depressed patients to measure connectivity in the CEN and DMN networks both before and after a 25-day course of TMS. They also compared the connectivity in the depressed patients with a group of 35 healthy volunteers.

TMS normalized depression-related hyperconnectivity between the subgenual cingulate and medial prefrontal areas of the DMN, but did not alter connectivity in the CEN.

Liston, an Assistant Professor at Weill Cornell Medical College, further details their findings, "We found that connectivity within the DMN and between nodes of the DMN and CEN was elevated in depressed individuals compared to healthy volunteers at baseline and normalized after TMS. Additionally, individuals with greater baseline connectivity with subgenual anterior cingulate cortex – an important target for other

antidepressant modalities – were more likely to respond to TMS."

These findings indicate that TMS may act, in part, by selectively regulating network-level connectivity.

Dr. John Krystal, Editor of Biological Psychiatry, comments, "We are a long way from Star Trek, but even the current ability to link brain stimulation treatments for depression to the activity of particular brain circuits strikes me as incredible progress."

Dubin, also an Assistant Professor at Weill Cornell Medical College, adds, "Our findings may inform future efforts to develop personalized strategies for treating depression with TMS based on the connectivity of an individual's default mode network. Further, they may help triage to TMS only those patients most likely to respond."

More information: The article is "Default Mode Network Mechanisms of Transcranial Magnetic Stimulation in Depression" by Conor Liston, Ashley C. Chen, Benjamin D. Zebley, Andrew T. Drysdale, Rebecca Gordon, Bruce Leuchter, Henning U. Voss, B.J. Casey, Amit Etkin, and Marc J. Dubin (DOI: 10.1016/j.biopsych.2014.01.023). The article appears in *Biological Psychiatry*, Volume 76, Issue 7 (October 1, 2014)

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