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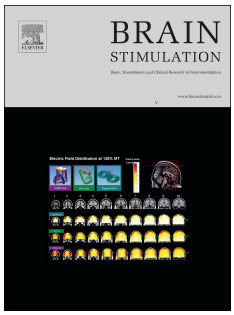

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PII: S1935-861X(20)30084-X

DOI: https://doi.org/10.1016/j.brs.2020.04.005

Reference: BRS 1714

To appear in: *Brain Stimulation*

Received Date: 30 March 2020

Accepted Date: 7 April 2020

Please cite this article as: Caulfield KA, George MS, Treating the Mental Health Effects of COVID-19: The Need for At-Home Neurotherapeutics Is Now, *Brain Stimulation*, https://doi.org/10.1016/j.brs.2020.04.005.

Treating the Mental Health Effects of COVID-19: The Need for At-Home Neurotherapeutics Is Now

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Word count: 996/1000
Thursday, March 26, 2020 KAC version

Author's Note: COVID-19 is a rapidly evolving situation. The data reported in this manuscript will be out of date by the time of publication. We reported the most up-to-date figures available at the time of submission.

To the Editor:

COVID-19 is a global pandemic that is expected to infect millions and kill up to hundreds of thousands of people, with a troubling rise in cases each day(1). It is first and foremost a deadly virus. However, what many have not yet considered are the secondary mental health effects that will likely occur the ongoing efforts to reduce the impact of COVID-19. Here we discuss how at-home neurotherapeutics, including telehealth and self-administered brain stimulation, could help to curtail some of the possible mental health ripple effects caused by COVID-19.

Currently, billions of people worldwide have been told to self-isolate to limit the spread of COVID-19. To be clear, this self-isolation strategy is the correct and necessary one and is supported by modeling that highlights how reducing human-to-human contact could help to lessen the impact of the disease(2). However, the call for self-isolation has resulted in the reduction of in-person social interactions on a magnitude that the world has not experienced since the Spanish Flu pandemic of 1918-1919. This social isolation will likely lead to an increase in depression, a link that has been established with previous studies in humans(3) and non-human mammals such as prairie voles(4). Social isolation secondarily limits access to mental health resources, preventing many who need psychological help from getting it. Put together, there is an urgent demand for more accessible mental health services during this COVID-19 self-isolation period.

The need for at-home neurotherapeutics is now. The current toolbox for at-home mental health treatments is largely limited to telehealth, where providers remotely communicate with patients over the phone or using video. There is a need for the rapid production and dissemination of other tools such as self-administered, at-home brain stimulation, which could help to curtail the mental health effects from self-isolation.

One option could be to adopt existing clinical brain stimulation technologies that are used for depression to at-home settings. For instance, high frequency (>5Hz) repetitive transcranial magnetic stimulation (rTMS) is a United States Food and Drug Administration (FDA) approved for treatment resistant depression (TRD). Treatments typically require a TMS operator to hold a TMS coil over the left dorsolateral prefrontal cortex (DLPFC) to noninvasively pass electromagnetic pulses into this brain region that is under-activated in depression. A recent variant of this treatment for depression is using 360 pulses of daily low frequency (1Hz) rTMS to the right DLPFC, with the specific intention of evaluating this treatment paradigm for at-home administration(5). Preliminary results using this approach have been promising, with 37.2% of patients having a 50% or greater reduction in depression symptoms after four weeks of daily treatments(5).

A similar method that could help to translate TMS into an at-home setting uses high frequency, 10Hz rTMS over the left DLPFC with modified, “miniature” TMS machines with head-worn TMS coils. These head-worn TMS coils could possibly allow future patients to self-administer treatment without the presence of a TMS operator, opening up the possibility for at-home use. These head-worn TMS coils also appear to be effective. In a single-blind trial, 15 daily sessions of rTMS with head-worn TMS coils significantly reduced depression scores compared to a sham stimulation condition and were non-inferior to standard TMS coils(6). Other researchers have investigated the use of custom-built helmets that could hold existing, commercially available TMS coils over a stimulation target such as the DLPFC(7). These possibilities are intriguing but need further evaluation, particularly for the feasibility of self-administered TMS. Thus, at-home rTMS should be further developed but may not translate quickly to at-home use during the COVID-19 pandemic.

There are other forms of noninvasive brain stimulation that have been used to treat depression and could be more easily and immediately adaptable to at-home use. Transauricular vagus nerve stimulation (taVNS) uses a portable stimulation device that passes small electrical

pulses (typically 1-12mA) through an electrode that is placed on vagal nerve afferents that project from the ear to the cortex. taVNS for depression builds on implanted cervical VNS, which is an effective and durable treatment for depression. In a recent single-arm feasibility trial, 10 sessions of 30 minute, 12mA taVNS to the bilateral mastoid processes produced an average drop of 19.75 points on the Hamilton Depression Rating Scale (HDRS) in 12 patients with major depressive disorder(8). There is a push for moving taVNS technology to at-home settings, which could help in this instance to mitigate the likely mental health burden of self-isolation to combat COVID-19. However, more evidence of the feasibility of self-administration and efficacy of this approach are needed before it is used at home.

Perhaps the most appealing current potential option for at-home brain stimulation is transcranial direct current stimulation (tDCS). tDCS is a cheap, handheld stimulation device that passes small amounts of electrical current (typically 1-2mA) through two electrodes that are placed on the scalp. Several large, double-blind, randomized-controlled tDCS trials for depression have been conducted with mixed but promising results. In one trial, 22 sessions of daily 30 minute, 2mA tDCS over bilateral DLPFCs reduced depression scores by 9.0 points on the HDRS, significantly more than in a sham stimulation condition and non-inferior to the 11.3 point drop from escitalopram(9). tDCS is particularly compelling as it has already been evaluated for at-home, self-administered use for multiple conditions including Parkinson's Disease(10) and could be easily adopted for depression due to self-isolation during the COVID-19 pandemic.

In sum, the mental health ripple effects from COVID-19 remain to be seen and will likely depend on how long the pandemic and self-isolation period lasts. Nevertheless, COVID-19 is underscoring a growing need for at-home neurotherapeutics, which could additionally help those in underserved or rural areas gain access to mental healthcare. Now is the time for an at-home neurotherapeutics revolution, with tDCS, taVNS, and TMS as strong candidate options.

Conflict of Interest Statement **Conflict of Interest Statement:** We confirm that there are no known conflicts of interest associated with this publication and there was no financial support for this work that could have influenced its outcome.

Financial Support: We received no funding for this study.

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