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EDITORIAL

Neurofeedback training for major depressive disorder: recent developments and future directions

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1. Introduction

Major depressive disorder (MDD) is a prevalent, debilitating, and recurrent psychiatric disorder that is associated with enormous personal, societal, and economic costs [1–3]. MDD is characterized by sad mood and/or loss of pleasure (i.e. anhedonia), in addition to other affective, cognitive, and somatic symptoms. Although the underlying pathophysiology of MDD is not yet clear, neuroscientists are making significant progress in advancing our understanding of this disorder [4].

While a range of interventions have been used with MDD, researchers have recently begun to examine the effects of neurofeedback training (NFT) for this disorder. Indeed, findings suggest that NFT can reduce depression-related symptoms in MDD (e.g. [5–7]). NFT involves presenting individuals with feedback about their patterns of neural activation in real time in order for them to learn to control specific brain processes. These patterns are typically informed by previously identified relations between neural processes and depressive symptoms, affect, and/or behavior. The anatomic and functional specificity of NFT may lead to fewer side effects than is the case for pharmacological interventions for depression; NFT is also less invasive than are other brain manipulation procedures such as deep brain stimulation. Consequently, if it proves to be effective, NFT may hold considerable promise as a next-generation neuroscience-informed treatment for MDD.

In this article, we describe several recent developments in the application of NFT to MDD and offer recommendations for future studies using this procedure in the context of depression. Importantly, we do not attempt to provide a comprehensive review of the extant literature of NFT studies of MDD; rather, we focus on several new applications of NFT that we believe are particularly promising for future work in this area. These developments include using NFT to probe neural mechanisms of MDD, NFT, and large-scale neural functional connectivity and the application of NFT using signals derived through machine learning. We hope that these recommendations will generate further interest in the application of NFT to the study and treatment of depression.

2. Using NFT to test neural mechanisms underlying MDD

In addition to clinical applications of NFT, which focus on reducing symptoms of depression by modulating activity in specific brain regions, NFT can be used to test mechanistic hypotheses concerning this disorder. Researchers using functional neuroimaging in psychiatric disorders typically assess neural correlates of disorders; this approach tells us little, however, about causal relations among neural processes, symptoms, affect, and behavior. In contrast, because NFT involves the manipulation of neural activation, it allows investigators to assess sequelae of the neural activity, providing important information concerning causal functional relations between localized brain activity and specific characteristics of the disorder being studied [8].

We recently used this approach to examine the effects of altering patterns of neural activation in MDD [5]. In this real-time functional magnetic resonance imaging (fMRI) study, we used NFT to assess whether depressed individuals could modulate activity in the salience network (SN), which has been implicated in the orienting of attention and, importantly, is aberrant in MDD [9]. Importantly, we also assessed whether NFT-based modulation of the SN would reduce negative affective biases that are prominent in and posited to underlie MDD. We randomly assigned depressed individuals to receive either real NFT or sham NFT (receiving false neurofeedback from a 'real-NFT' participant's brain). Compared to participants in the sham NFT group, participants who received real NFT exhibited greater decreases in SN and affective responses to negative stimuli and in negative biases. These findings indicate that directly changing SN activity reduces negative biases in MDD, highlighting the use of NFT for examining mechanisms underlying this disorder. We are currently extending this procedure to examine whether using NFT to teach children who are at familial risk for depression to modulate SN activation reduces reactivity to stress and delays or prevents the onset of MDD. Despite obvious differences between children and adults, we are finding that NFT is reducing children's subsequent stress reactivity; we are continuing to follow-up these children to examine whether NFT also influences onset of MDD.

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3. Neural connectivity and NFT

There is increasing interest in understanding abnormalities in large-scale neural functional connectivity in MDD. A recent meta-analysis found that MDD is associated with specific anomalies in functional connectivity, including hypo-connectivity within the frontoparietal network and hyper-connectivity within the default mode network [10]. It will be important for investigators to leverage this information in using NFT in the treatment of depression. In this context, Yuan et al. (2014) assessed the effect of NFT on resting-state fMRI functional connectivity in individuals diagnosed with MDD [11]. Participants attempted to increase activity of the left amygdala while recalling positive autobiographical memories. Left amygdala activity to positive stimuli was chosen as the feedback signal in part because reduced activation in this structure has been found to be associated with symptoms of MDD, and it normalizes with remission of depression [11]. Yuan et al. found that hypo-connectivity of the left amygdala with pregenual anterior cingulate cortex and cuneus normalized following localized NFT, suggesting that NFT can change resting-state functional connectivity in this disorder.

It will be important in future research to examine the effects of NFT in which an index of neural connectivity is used as the feedback signal. Indeed, researchers have now begun to document the utility of using connectivity measures as feedback signals for NFT in samples of healthy individuals (e.g. [12,13]). And we should note that fMRI is not the only procedure that can be used to measure neural connectivity. Although electroencephalography (EEG) and magnetoencephalography (MEG) have lower spatial resolution than does fMRI, they have superior temporal resolution, which can be useful in the context of connectivity-based NFT. Drawing on this advantage, some investigators have developed procedures to use MEG to provide neurofeedback about functional connectivity [14], while other researchers have combined EEG and fMRI for simultaneous multimodal NFT [15]; both of these approaches might be usefully extended to the study of connectivity-based NFT for MDD.

4. Machine learning and NFT

Multivariate methods that can summarize highly complex neural features may provide opportunities to identify new neural targets for use with NFT. Machine learning can identify patterns in high-dimensional data that can be used for predictive modeling and classification. Conducting machine learning analyses on brain features allows researchers to summarize complex neural patterns and has the potential to improve the identification and characterization of complex brain signals that are associated with MDD and that can be used in NFT. Machine learning has recently been used with neuroimaging data to distinguish depressed from nondepressed individuals [16,17]. Sitaram et al. (2011) used machine learning to predict in real time whether individuals were feeling happiness, disgust, or sadness [18]. Future applications of machine learning-based NFT might utilize patterns defined from multimodal signals, such as those acquired through simultaneous EEG and fMRI. Investigators might also use machine learning to characterize specific neural patterns associated with cognitive or affective tasks that are associated with abnormal activity in MDD in order to improve functioning in these domains.

5. Summary

NFT is a promising next-generation research tool and treatment for MDD. We have highlighted three developments in the use of NFT with MDD: using NFT to assess mechanisms that link brain with cognition, affect, and behavior; NFT and the integration of large-scale neural functional connectivity; and the use of signals derived from machine learning in NFT. Although using NFT for the study and treatment of depressed individuals is still relatively novel, we propose that leveraging these three developments will significantly increase our understanding of neural aspects of MDD while simultaneously informing the development of more effective neuroscience-based prevention and treatment approaches for this debilitating disorder.

Declaration of interest

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