EEG brain states occurring before the stimulation impact response to TMS. Our results show that specific brain states, with a motor network spatial and spectral signature, feature larger Motor Evoked Potential amplitude. These findings enable brain-state-dependent TMS based on real-time excitability and connectivity information, a critical step towards individualized therapeutic brain stimulation.

Research Category and Technology and Methods

Translational Research: 7. Responsive (Closed-Loop) Stimulation

Keywords: EEG-TMS, Hidden Markov model, Brain-state-dependent TMS, Motor cortex

http://dx.doi.org/10.1016/j.brs.2023.01.023

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

S2a.4

ENHANCING THE CONNECTIVITY IN A 2-NODE MOTOR NETWORK USING REINFORCEMENT LEARNING-BASED CLOSED-LOOP RTMS

Dania Humaidan. *Eberhard Karls University Tübingen, Germany*

Abstract

TMS has been extensively used to investigate the physiology of the central nervous system in health and disease. However, there is a strong need for a personalized, multi-locus, real-time stimulation procedure, which can be adaptively fine-tuned based on case-specific feedback. Here, we modulate the effective connectivity of the 2-node brain network from supplementary motor area (SMA) to primary motor cortex (M1) by closed-loop stimulation, optimized by application of an online reinforcement learning algorithm. This algorithm learns to identify the individually optimal phase of the ongoing μ-rhythm to be targeted by paired SMA-M1 TMS for maximized long-term enhancement of facilitatory effective connectivity between SMA and M1. This is one of the first demonstrations of true closed-loop stimulation, a crucially important step towards individualized highly-effective brain stimulation for therapeutic modulation of dysfunctional brain networks, e.g., the deficient SMA-M1 connection in motor stroke.

Research Category and Technology and Methods

Translational Research: 7. Responsive (Closed-Loop) Stimulation

Keywords: EEG-TMS, Machine Learning, Closed-loop stimulation, Motor cortex

http://dx.doi.org/10.1016/j.brs.2023.01.024

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

S2b.1

EFFECTS OF REPEATED TDCS ON FEAR EXTINCTION IN MICE

Andries Van Schuerbeek [1], Marie-Anne Vanderhasselt [2], Chris Baeken [2,1], Anouk Pierre [1], Ilse Smolders [1], Vincent Van Waes [3], Dimitri De Bundel [1]. [1] *Vrije Universiteit Brussel, Belgium;* [2] *Universiteit Gent, Belgium;* [3] *Université Bourgogne Franche-Comté, France*

Symposium title: Brain stimulation in fear and anxiety disorders

Symposium description: Anxiety disorders, together with depression, are the most common mental health disorders in the world. Although evidence-based treatments for anxiety disorders exist, more than half of treated individuals do not show sufficient improvement in clinical symptoms after therapy or show a relapse after successful therapy. Therefore there is a continuing need to develop novel and effective treatments for anxiety. The use of non-invasive brain stimulation represents a promising approach to complement current evidence-based treatments as therapeutic tools. This symposium takes a bench-to-bedside approach covering both basic and clinical studies using the two most common non-invasive brain stimulation techniques, transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS), in the context of fear and anxiety disorders. First, Dimitri de Bundel will demonstrate in an animal model that tDCS is capable of modulating fear extinction in mice. Next, Mascha van 't Wout-Frank will cover the use of tDCS to modulate fear extinction and anxious habituation during exposure in individuals with posttraumatic stress disorder (PTSD). This will be followed by Martin Herrmann who will present a clinical study investigating whether rTMS can be used to improve exposure therapy in phobic patients. The symposium will conclude with a lecture by Sara Borgomaneri who will demonstrate that rTMS can be used to disrupt the consolidationand reconsolidation of fear memory, providing a novel option for the treatment of anxiety disorders.

Abstract

Exposure-based psychotherapy is a first line treatment for fear-related disorders. Not all patients achieve long-term remission but adjunctive non-invasive neuromodulation may be a promising strategy to enhance the efficacy of exposure therapy. In a proof of concept study, we explored whether tDCS over the prefrontal cortex (PFC) could enhance fear extinction in mice. While this preclinical model of exposure therapy is appealing for in-depth exploration of mechanisms of action, it comes with technical challenges that may hamper direct comparisons of online with offline tDSC effects and the translation towards applications in humans. Nevertheless, we found that repeated offline anodal tDCS (0.2 mA, 20 min, twice daily for five consecutive days) over the PFC resulted in enhanced fear extinction when extinction training followed one day after the last stimulation session. We found that tDCS was most effective in experimental conditions corresponding to high fear expression. Our data provide a rationale to further explore anodal tDCS over the PFC as potential support for exposure-based psychotherapy.

Research Category and Technology and Methods

Basic Research: 9. Transcranial Direct Current Stimulation (tDCS)

Keywords: Fear extinction, mice, tDCS

http://dx.doi.org/10.1016/j.brs.2023.01.025

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

S2b.2

UTILIZING TDCS TO AUGMENT THE FORMATION OF SAFETY SIGNALS FOR FEAR INHIBITION IN POSTTRAUMATIC STRESS DISORDER

Mascha van 't Wout-Frank [1,2,3], Sydney Brigido [2], Julia Cole [3], Noah Philip [4,1]. [1] *Warren Alpert Medical School of Brown University, USA;* [2] *VA Providence Healthcare System, USA;* [3] *COBRE Center for Neuromodulation, Butler Hospital, USA;* [4] *VA Providence Healthcare System, USA*

Abstract

Posttraumatic stress disorder (PTSD) can be understood as a disorder in the processing of traumatic fear memories due to hyperactivity in amygdala-based threat reactivity, exacerbated by a failure to down-regulate this threat responding attributed to hypoactivity in ventromedial prefrontal cortex (VMPFC) and hippocampal aberrations. Here we test whether transcranial direct current stimulation (tDCS) targeting the VMPFC can augment the inhibition of fear responses in the context of extinction learning and recall as well as exposure to trauma cues in individuals with PTSD. In all experiments, tDCS involved 2 mA intensity with the anode placed around EEG locations Fp1/AF3 and the cathode over EEG location P08, and we assessed skin conductance reactivity (SCR) as a biologically relevant measure of emotional arousal. First, we demonstrate that the modulation of extinction learning and memory by tDCS may depend on the timing of stimulation, such that when applied during synaptic consolidation immediately following extinction learning of conditioned fear tDCS may prevent the return of fear during extinction recall. Yet we also observed a possible generalization of the fear response because of tDCS. Next, we demonstrate that the repeated application of tDCS during exposure to virtual reality trauma cues may bolster anxious habituation in individuals with warzone PTSD. Yet again we appear to observe a seemingly initial increase in emotional arousal before a more rapid reduction of emotional arousal and subsequent reduction of PTSD symptom severity. Taken together this research highlights the importance of the application of tDCS in context, including the timing of stimulation in relation to safety learning and memory processing and the importance of repeated sessions for clinical benefit.