S1b.3

BRAIN STIMULATION AND NEUROSCIENCE ROBOTICS FOR INDUCTION AND ASSESSMENT OF HALLUCINATIONS

Olaf Blanke. *Swiss Federal Institute of Technology (EPFL), Switzerland*

Abstract
Although hallucinations are essential and frequent symptoms in major psychiatric and neurological diseases, little is known about their brain mechanisms. Moreover, hallucinations are unpredictable and private experiences, making their investigation, quantification, and assessment challenging. A significant shortcoming in hallucination research is the absence of methods able to induce specific and short-lasting hallucinations, which resemble clinical hallucinations, which can be elicited repeatedly and vary across experimental conditions. By integrating results on specific hallucinations from cortical stimulation in epilepsy patients with recent advances in cognitive neuroscience and robotics, we have designed a robotic procedure able to repeatedly induce a specific, clinically relevant hallucination in healthy individuals: presence hallucination (PH). Patients with Parkinson's disease (PD), who frequently experience PH in daily life, were shown to have abnormally elevated sensitivity to the robotic PH procedure, reflecting their abnormal cortical-subcortical networks. In ongoing clinical research, we are combining neuroscience robotics with deep brain stimulation, targeting control of hallucinations and related cognitive dysfunction in PD.
Research Category and Technology and Methods
Basic Research: 1. Deep Brain Stimulation (DBS)

http://dx.doi.org/10.1016/j.brs.2023.01.019

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

S1b.4

STUDYING THE PHYSIOLOGY OF MIND WITH INTRACRANIAL ELECTRICAL STIMULATION

Itzhak Fried. *UCLA, USA*

Abstract
Direct electrical stimulation of the brain has been used as an investigative tool in the study of human mind physiology, and as a therapeutic mean to modulate higher cognitive and affective functions. Unique insights into human experience in states of mind including volition, spontaneous recollection, laughter, and guilt are obtained by electrical stimulation during awake neurosurgical procedures. Systematic modulation of memory during wake and sleep cycles is enabled by closed-loop brain stimulation based on hippocampal-neocortical physiology. The chief strength of brain stimulation lies in the combination of causal inference and self-report of human experience, albeit the lack of anatomic, physiological and functional specificity remains a major challenge.
Research Category and Technology and Methods
Basic Research: 1. Deep Brain Stimulation (DBS)

http://dx.doi.org/10.1016/j.brs.2023.01.020

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

S2a.1

ROBOTIC-GUIDED MULTI-LOCUS TMS FOR AUTOMATED, FAST, AND ACCURATE BRAIN NETWORK STIMULATION

Victor Hugo Souza. *Aalto University School of Science, Finland*

Symposium title: The ConnectToBrain Project: On the way to multi-locus closed-loop brain stimulation
Symposium description: The ConnectToBrain Project is funded by the European Research Council Synergy program. The three project partners (Aalto University Finland, Chieti-Pescara University Italy, Tübingen University Germany) contribute complementary expertise to develop a radically novel approach to stimulate the human brain with TMS. They will develop a helmet-like multi-channel coil (Aalto) to enable multi-site stimulation of distributed brain networks, utilize EEG real-time information on brain network excitability and connectivity (Chieti-Pescara) to read brain states, and use this information for brain-state-dependent and closed-loop stimulation (Tübingen) to highly effectively modify brain networks, eventually for treating network disorders of the human brain. This symposium will provide insights into the most recent advancements three years into the ConnectToBrain Project.
Abstract
Our recently developed 5-coil multi-locus TMS (mTMS) device enabled, for the first time, the operator to electronically control the stimulus location and orientation without manually moving the transducer. However, the increase in the number of coils makes the transducer heavy and inconvenient for manual operation, limiting its applicability in clinical settings. Thus, we developed and validated a robotic-guided control of mTMS transducers. Our system automatically and safely positions the multi-coil transducers and accurately stimulates user-specified cortical targets based on closed-loop automated algorithms, compensating for the subject's head movement. The presentation will provide performance data and applications of this novel technology.
Research Category and Technology and Methods
Translational Research: 7. Responsive (Closed-Loop) Stimulation
Keywords: TMS, Multi-locus TMS, Multi-channel coil, Robotic-guided TMS

http://dx.doi.org/10.1016/j.brs.2023.01.021

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

S2a.2

REPETITIVE TMS DURING SPECIFIC PHASES OF THE DORSOMEDIAL PREFRONTAL THETA OSCILLATION HAS DIFFERENTIAL EFFECTS ON NETWORK EXCITABILITY AND WORKING MEMORY PERFORMANCE

Pedro Caldana Gordon. *Eberhard Karls University Tübingen, Germany*

Abstract
Brain-state-dependent rTMS has been used for phase-specific stimulation of the μ-rhythm in motor cortex, and revealed differential efficacy of plasticity induction depending of the phase stimulated. We extended this method based on real-time analysis of EEG to target prefrontal theta, a rhythm associated with cognitive functions. By applying rTMS to the dorsomedial prefrontal cortex during different phases of the local theta oscillation, we obtained TMS-EEG excitability increase and working memory performance improvement specifically when stimulating the trough of dorsomedial prefrontal theta. This novel method may have potential for therapeutic applications in patients with cognitive disorders.
Research Category and Technology and Methods
Translational Research: 7. Responsive (Closed-Loop) Stimulation
Keywords: EEG-TMS, Brain-state-dependent stimulation, Dorsomedial prefrontal cortex, Working memory

http://dx.doi.org/10.1016/j.brs.2023.01.022

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

S2a.3

EEG BRAIN NETWORKS IDENTIFIED BY HIDDEN MARKOV MODEL AND THEIR RELATION TO TMS-EVOKED MEP AMPLITUDES

Laura Marzetti. *University "G. d'Annunzio" of Chieti-Pescara, Italy*

Abstract
Recent work using time delay embedded hidden Markov model applied to magnetoencephalography resting-state data revealed a distinct set of brain states, with each state engaging a specific set of cortical regions and featuring different functional roles. Here, we apply this approach to EEG-TMS data to the purpose of understanding whether the characteristics of

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.