



5th International Brain Stimulation Meeting – Plenary Abstracts

[PL01]

TARGETED MODULATION OF NEURAL POPULATION DYNAMICS TO IMPROVE MOVEMENT CONTROL

Karunesh Ganguly. *University of California San Francisco, USA; San Francisco VA Health Care System, USA*

Stroke is a leading cause of motor disability in the world. While brain stimulation to enhance motor function after stroke has shown promise, large clinical trials in human stroke patients have not found consistent benefits. These trials were conducted using open-loop stimulation, where the neural responses to stimulation were not measured. It remains unclear how to precisely tailor brain stimulation to effectively modulate neural dynamics in the motor network in order to improve motor control after stroke. Our recent studies have demonstrated that the reliability of single trial population dynamics associated with low-frequency oscillatory activity are important for movement control and can serve as a target for modulation using electrical stimulation (e.g., Ramanathan et al., *Nature Medicine*, 2018; Lemke et al., *Nature Neuroscience*, 2019; Khanna et al., *Cell*, 2021). Specifically, epidural cortical stimulation was found to both boost low-frequency power in animals recovering from injury and increase neural co-firing; this also reliably improved movement control during recovery from stroke. Our results have also demonstrated that relatively high electrical field strengths (~ 3 mV/mm) were effective in regulating neural spike entrainment and co-firing. More recently, we have also studied how activity associated with movement preparation changes with recovery. We find that the reliable transition from preparation to movement control appears to be governed by 'bistable' transition dynamics. Notably, improvements in transition dynamics were closely correlated with recovery of prehension. Moreover, epidural electrical stimulation was found to be capable of modulating both preparatory and movement related dynamics. Our work provides insight into how to design therapeutic stimulation that selectively targets population dynamics in the distributed motor network and to improve dexterity after stroke. The information gained may also help improve approaches for non-invasive brain stimulation for stroke.

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[PL02.1]

HOME-BASED TRANSCRANIAL ELECTRICAL STIMULATION TO SCALE CLINICAL TRIALS: METHODOLOGY, SAFETY, AND BEYOND

Giuseppina Piloni. *NYU Grossman School of Medicine, USA*

Clinical trials of transcranial electrical stimulation (tES) are rapidly increasing in number as research explores potential therapeutic uses across a wide range of neurological and psychiatric conditions. Both human and mechanistic studies have shown that tES can have a cumulative benefit across multiple stimulation sessions, but this presents a practical challenge for investigators when participants are required to travel to a clinic or lab for daily treatment. The ability to deploy tDCS and other emerging TES at home is a key advantage in scaling clinical trials.

Home-based tES delivery has the potential to increase participation and accommodate a larger number of tES sessions, which may be necessary for a thorough evaluation of its effects. However, there are several important factors to consider such as methodology, safety, and ethical aspects when conducting home-based tES clinical trials.

This lecture will provide a comprehensive review of the methodology, instruments, and safety considerations surrounding the growing body of home-based tES trials. The discussion will also include the current regulatory landscape surrounding the home use of tES devices, addressing some of the concerns such as the lack of oversight, and how to ensure patient safety when using tES devices at home. Additionally, it will provide insights into how home-based tES clinical trials can support the scaling up of tES and its long-term benefit for patients.

Research Category and Technology and Methods: Clinical Research: 9. Transcranial Direct Current Stimulation (tDCS)

Keywords: Scalability, tES, tDCS, home use

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[PL02.2]

MODULATION OF BRAIN-LUNG INTERACTIONS USING HD-TDCS: MECHANISMS, CLINICAL PRACTICE, AND RECENT ADVANCES

Suellen Andrade¹, Eduardo França¹, Joao Sato², Larissa Costa¹, Maria Eduarda Bezerra¹, Egas Caparelli-Dáquer³, Abhishek Datta⁴, Marom Bikson⁴. ¹Paraíba Federal University, Brazil; ²Federal University of ABC, Brazil; ³Rio de Janeiro State University, Brazil; ⁴The City College of New York, USA

The pathophysiology of the brain-lung interactions are complex and involve inflammation, neurodegeneration and disruptions into the respiratory control system. Recently, it has been suggested that noninvasive brain stimulation could be a valuable tool for the management of the early and post acute phase of patients with respiratory dysfunction. In this session, we will provide data that supports the use of HD-tDCS as an useful therapeutic approach for modulating the respiratory function at the neurophysiological and clinical levels.

Research Category and Technology and Methods: Clinical Research: 9. Transcranial Direct Current Stimulation (tDCS)

Keywords: Brain–lung interactions, Respiratory modulation, Non-invasive brain stimulation, Rehabilitation

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[PL03]

RESPONSIVE NUCLEUS ACCUMBENS DEEP BRAIN STIMULATION FOR LOSS-OF-CONTROL EATING

Casey Halpern. *University of Pennsylvania Perelman School of Medicine, USA*

Loss of control (LOC) eating is pervasive in eating disorders and obesity. The presence of this phenotype appears to predict treatment-resistance, including to gastric bypass surgery. Cravings that precede LOC over food consumption present an opportunity for intervention in patients with the binge eating disorder (BED). Responsive deep brain stimulation (DBS)

guided by low frequency changes in the nucleus accumbens was previously found to block binge-like eating behavior in mice. Following this preclinical work, in a first-in-human pilot study, we recorded nucleus accumbens electrophysiology during food cravings preceding LOC eating in two patients with BED and severe obesity (trial registration no. NCT03868670). We observed increased bilateral ventral NAc low frequency power and connectivity that appeared selective for states of food craving. We then used the peaks in nucleus accumbens electrophysiological signal that corresponded to increased low-frequency power to guide DBS delivery. Over 6 months, we observed improved self-control of food intake and weight loss in both patients. These findings provide early support for restoring inhibitory control with electrophysiologically-guided NAc DBS in the context of LOC. Further work with increased sample sizes is required to determine the scalability of this approach.

Research Category and Technology and Methods: Translational Research: 1. Deep Brain Stimulation (DBS)

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[PL04]

PAST, PRESENT (AND ?FUTURE) OF TMS

John Rothwell. *University College London, UK*

Of the many methods now available for non-invasive transcranial stimulation of the human brain, we have the clearest understanding of the mechanism of action of TMS. Yet the application of TMS, like high voltage electrical stimulation of the brain that preceded it, was a chance event that had never been predicted, and which might have had a difficult time these days obtaining funding. Similarly, most of the major TMS methods (intracortical inhibition, cortico-cortical and cerebello-cortical connectivity, “virtual lesioning”, rTMS and even TMS-EEG) were explored in the 10 years following, a rate of progress that would probably halve in the present regulatory environment. So has TMS reached a plateau of development where it is just one of several tools to probe and interact with brain function, or will developments in TMS-EEG, EEG-TMS or novel designs of stimulator open new and unexpected avenues of research?

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[PL05]

TMS-EEG: A WINDOW ON CORTICAL CIRCUITS IN SEVERE AND FOCAL BRAIN INJURY

Marcello Massimini. *University of Milan, Italy*

TMS in combination with EEG (TMS-EEG) enables a direct assessment of the electrophysiological state of cortical circuits with unprecedented degrees of freedom whereby both primary and associative areas can be directly stimulated with a wide range of stimulation parameters. In this way, TMS-evoked potentials (TEPs) can both inform on the local input-output properties of different neuronal population and assess large-scale remote and re-entrant activations within thalamocortical networks. Furthermore, unlike resting EEG-based measures of connectivity, TMS-EEG measures are causal in nature and unconfounded by common inputs or spurious correlations. In my talk, I will first highlight the principles and caveats of TMS-EEG as well as the tools and procedures that can reliably facilitate the acquisition of high-quality TEPs. Then, I will review a series of recent studies in which TMS-EEG was used to probe the state of cortical circuit after brain injury. I will show how measures derived from TEPs can assist the diagnosis of patients with disorders of consciousness, inform on the state of the perilesional cortex after stroke and bear prognostic value for motor recovery and for the subsequent development of delirium. Finally, I will argue that TMS-EEG data can have a key role in driving a paradigm shift in our understanding of the electrophysiological consequences of brain injury and diaschisis.

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[PL06]

MEASURING INHIBITORY ENGRAMS IN MEMORY STORAGE AND RECALL USING CONCURRENT TDCS-FMRI

Helen Barron. *University of Oxford, UK*

Memories are thought to be represented in the brain by activity in groups of neurons described as memory engrams. Although memory engrams are typically thought to be made up of excitatory neurons, several recent studies suggest that inhibitory neurons also play a critical role. Indeed, by matching their excitatory counterparts, selective inhibitory interneurons may facilitate a stable storage system that allows memories to lie quiescent unless the balance between excitation and inhibition is perturbed. Here I will present a set of studies that show evidence for selective neocortical inhibition in the human brain using ultra-high field 7T MRI and concurrent non-invasive brain stimulation. I will show that matched excitatory-inhibitory engrams provide a stable storage mechanism for neocortical associations, and protect memories from interference. I will then show how neocortical memory engrams interact with brain regions such as the hippocampus during recall, to selectively perturb excitatory-inhibitory balance. To conclude, I will discuss how concurrent MRI and non-invasive brain stimulation can be used as a tool to demonstrate the importance of neural inhibition for computations that underlie higher-order cognition.

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[PL07]

THE ROLE OF CHRONIC BRAIN SENSING TECHNOLOGY FOR INDIVIDUALIZED DEEP BRAIN STIMULATION THERAPY

Andrea Kühn. *Charite University Hospital Berlin, Germany*

Deep brain stimulation is an established therapy for patients with severe movement disorders. Over the last decades invasive recordings from the human basal ganglia were used to characterize disease pattern and symptom specific neuronal signatures as biomarkers for PD and dystonia. This has helped to further elucidate the underlying pathophysiology of these network disorders. Recently, new technological advances in deep brain stimulation devices allow to chronically record neuronal activity from the target structures. Neuronal activity can be used as a feedback signal to inform DBS for closed loop stimulation. I will give an overview on what we have learnt from invasive recordings for movement disorders and how we can use neuronal signatures to inform parameter selection and timing of stimulation in order to better adapt DBS treatment to the individual symptoms in each patient in the future.

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[PL08]

A 12 STEP JOURNEY TO FIND A (TMS) TREATMENT FOR DRUG AND ALCOHOL ADDICTION: FROM DISCOVERY SCIENCE TO CLINICAL TRIALS

Colleen Hanlon. *Wake Forest University School of Medicine, USA; BrainsWay Ltd, USA*

Nearly 3 million people die annually from alcohol abuse. While several pharmaceutical options are available, the side effects are high and medication is not well-tolerated. Through recent innovations in neuroimaging and neuromodulation we, as a scientific community, are now uniquely positioned to evaluate transcranial magnetic stimulation (TMS) as a novel, non-invasive therapeutic tool to help improve the lives of people with alcohol use disorder (AUD).

This talk will cover a series of 12 decision making steps that led from discovery science to clinical trials in AUD. The talk will integrate studies from multiple laboratories and highlight moments that led us to rethink our hypotheses as well as findings that moved us forward. Briefly, our first step was to identify the neural circuits of interest (Target Identification).