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).