interindividual variability in tES effects on the human brain, and present recent data from our group to establish a link between individually induced electric fields with behavioral and neurophysiological effects of tES. This approach can help understand variability in responsiveness to tES interventions, potentially also distinguishing responders from non-responders, and can advance the understanding of underlying mechanisms in post-hoc (i.e., retrospective) analyses. I will further discuss the potential usefulness of this approach for prospective planning of stimulation parameters and development of individualized interventions.

Research Category and Technology and Methods

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

http://dx.doi.org/10.1016/j.brs.2023.01.243

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

OS11.3

NEURO-VASCULAR MODULATION AND BRAIN RESPONSE TO TRANSCRANIAL ELECTRICAL STIMULATION

Marom Bikson. *The City College of New York, New York, NY, USA*

Abstract

The development and validation of technology to apply energy non-invasively to the brain to treat disease and enhance learning is accelerating. This broad spectrum of research and development naturally focuses on how applied energy changes neuronal function, which in turn changes behavior and performance. For example transcranial Direct Current Stimulation (tDCS) generates static electric fields in the brain that boost neuronal plasticity. This talk presents an alternative mechanistic pathway for brain stimulation (Neuromodulation) technologies: namely that applied energy directly changes brain vascular function and clearance mechanisms, leading to secondary neuronal function changes. This “Neurovascular-Modulation” hypothesis is compelling as it suggests unique therapeutic pathways for a broad range of brain disorders, including age related cognitive decline.

Research Category and Technology and Methods

Translational Research: 19. Modeling and computational methods

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

OS11.4

TOWARD VALIDATED MULTI-SCALE MODELS FOR DOSE CONTROL IN NON-INVASIVE BRAIN STIMULATION

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Abstract

There are recent efforts developing multi-scale models for NIBS dose control. While the induced electric field is the key factor to determine dosing and target engagement, it is only a first step to model the physiological response. To advance these efforts we have developed a new multi-scale pipeline (NeMo-TMS) for modeling TMS effects across spatial scales. On the macro-scale, we simulate TMS electric fields using SimNIBS. Afterwards, electric fields are coupled with morphologically realistic neuronal models in the NEURON environment. These neuron-scale simulations allow the investigation of membrane voltage, action potential initiation and propagation, field intensity, and orientation necessary for modulating neuron response. Finally, we incorporate the membrane voltage data to simulate the calcium concentration induced by voltage-gated calcium-channels at the subcellular scale by solving the calcium dynamics equations. This allows us to model effects of rTMS protocols on somatic calcium accumulation, important for neural plasticity.

The experimental results of model validation based on invasive recordings in non-human primates will be presented. We stimulate different brain regions with TMS at different intensities and a sham protocol. Our key findings are a dose-dependent effect of TMS evoked potentials (TEP) at 50 ms in frontal contacts in FEF and TEM electrodes and coil location-dependent effect of center of activation. These results support the premise that TMS induces direct neural responses in a dose-dependent and targeted manner.

There are still existing challenges and limitations of computational models. Computational models have greatly improved our understanding of NIBS biophysics and can inform stimulation design and dosing. However, modeling technologies are still actively developed, and current models have several limitations. For example, tissue conductivities are often based on ex-vivo measurements and population averages. Individual differences in tissue conductivities are substantial and can result in significant uncertainty in the electric field estimates per individual.

Research Category and Technology and Methods

Translational Research: 10. Transcranial Magnetic Stimulation (TMS)

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

OS12.1

CELLULAR MECHANISMS OF TRANSCRANIAL MAGNETIC STIMULATION IN AN IN VITRO TURTLE CEREBELLUM

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Symposium title: Insights and challenges in preclinical models of transcranial magnetic stimulation: multimodal investigations across animal species

Symposium description: Transcranial magnetic stimulation (rTMS) has gained growing interest as an assessment of cortical excitability and function, as well as a treatment for brain-based disorders. Recent advances in TMS in animal models has laid the foundations for improved translational studies. Preclinical studies have the potential to shed light on mechanistic understanding of the neurobiological basis of TMS, and to help identify optimal stimulation protocols. This proposed panel aims to present on insights and challenges in TMS across different animal models from turtle, rodent, to nonhuman primate. Dr. Padma Sundaram from Massachusetts General Hospital will present on investigation of cellular mechanisms of TMS in in vitro turtle cerebellum. This work combines computational electric field modeling and electrophysiology to show TMS activation of Purkinje cells either directly or synaptically via the parallel fibers and climbing fibers. Dr. Jennifer Rodger from University of Western Australia will present on the use of multimodal imaging, including resting state functional MRI, diffusion MRI, magnetic resonance spectroscopy, and cfos immunohistochemistry, in rodent TMS. This work shows that TMS promotes anticorrelated functional connectivity between cortical and subcortical brain regions due to decreased GABA-ergic parvalbumin interneuron activation. Next, Dr. Hanbing Lu from the National Institute of Drug Abuse will present on a new TMS technique called high-density theta burst stimulation (hdTBS). Using a novel rodent TMS coil, and longitudinal motor evoked potential recording in awake rats, the results of this work suggest hdTBS can enhance the after-effects of TMS. Finally, Dr. Marc Sommer from Duke University will present on simultaneous single-unit recording and TMS in nonhuman primate. This work integrates neural recordings from awake macaques, simulations of the electric fields evoked in their brains, and data-driven models to understand the direct and indirect effects of TMS.

Abstract

The goal of this study is to help advance our understanding of how transcranial magnetic stimulation (TMS) activates neurons in the cerebellum at the cellular level. Even though TMS has been commercially available for a long time, more effort is required to understand the actions of TMS at the cellular level. We do this using TMS activation of the cerebellum in an in vitro preparation of an isolated turtle cerebellum and a computational study of TMS-induced electric field (E-field) in the tissue. The cerebellum of the turtle is basically a flat circular disk about 1 mm-thick and 5 mm in diameter and has a cellular geometry ideally suited for experimental analysis. The principal neurons and axons in the cerebellum