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ABSTRACT #3: TRANSCRANIAL MAGNETIC STIMULATION TO THE PREFRONTAL CORTEX: A NON-HUMAN PRIMATE STUDY

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Abstract: Transcranial magnetic stimulation (TMS) is a noninvasive neuromodulation method which enables in vivo perturbation of neural activity in humans through the application of electromagnetic fields to the brain. The repeated application of TMS (rTMS) to the dorsolateral prefrontal cortex (DLPFC) has been shown to be a non-invasive neuromodulation tool for the treatment of drug resistant depression and is FDA approved to be used clinically. However, significant variability in treatment outcomes across patients has been reported. Additionally, basic mechanisms underlying TMS effects on prefrontal neural circuitry is largely unknown. Therefore, it is necessary to improve current stimulation protocols by exploring the mechanism of such modulation. Several studies have investigated TMS effects using non-invasive imaging modalities such as electroencephalography (EEG). However, EEG suffers from low signal to noise ratio (SNR) and low spatial specify due to volume conduction. Therefore, in our study we investigate the effect of prefrontal TMS in a non-human primate model with implanted depth electrodes (32 electrode channels spanning the left hemisphere from frontal to occipital brain regions). This allows us to record high quality neural activity from the stimulation region as well as connected brain areas with a high spatio-temporal resolution. Several sessions of single-pulse TMS (100 pulses total per stimulation condition) to the prefrontal cortex were recorded while the monkey was under anesthesia. Data preprocessing involved TMS artifact removal including TMS artifacts and TMS induced muscle activity. Neural activity could be fully recovered at least 10 ms after stimulation. With further time-frequency analysis, we found decreased power mainly in low frequency oscillations, (2-4 Hz) shortly after the TMS stimulus followed by a recovery approximately one second after offset. This effect was strongest in prefrontal electrodes. We provide evidence that TMS is modulating intrinsic brain activity even under anesthesia through the suppression of low frequency oscillations. Future research will involve investigating the effect of changing TMS parameters (intensity, coil orientation) in further detail. Our research can provide a better understanding on how TMS affects neural activity in the prefrontal cortex and eventually can lead to more efficient treatment protocols to a variety of disorders such as depression.

ABSTRACT #4: PIPELINE VERIFICATION FOR THE IDENTIFICATION OF NONINVASIVE NEUROMODULATION TARGETS FOR PEDIATRIC STROKE REHABILITATION

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Abstract

Introduction: Ischemic perinatal stroke affects as many as 1 in 2,300 live births and may result in lifelong burden of care. Thus, better rehabilitation techniques are indicated to improve quality of life for individuals and families. Implementing interventions early in life can harness neuroplastic potential to promote recovery. Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) have shown promise as noninvasive cortical assessment and neuromodulation techniques for stroke rehabilitation; regaining motor control and function can be facilitated through the induction of plasticity. While mostly studied in adult populations, recent efforts have been made to translate these methods to pediatric populations. This is challenging because, in addition to the presence of a lesion, stimulation fields vary significantly due to head anatomy and size differences.

Methods: Here, we explore the integration of individual realistic head models to identify stimulation targets for synergistic neuromodulation and rehabilitation. Combining TMS motor mapping data with FEM models allows precise identification of motor representations in both affected and unaffected brain hemispheres. Using our computational motor mapping method, we are developing a system to predict individualized neuromodulation stimulation targets for stroke rehabilitation.

Results: We have successfully created pediatric stroke FEM head models by combining automated segmentation software and hand drawn lesion masks. Additionally, we have verified our software pipeline for building and running simulations based on actual experimental TMS coil positioning data.

Conclusion: A software pipeline that is able to simulate the electric field distribution for an actual TMS coil position and compare it to the resulting experimental MEP data from a pediatric stroke population will allow us to validate that the FEM models are able to accurately handle large lesions in simulations. Post validation, we expect that we will be able to determine coil positions to stimulate specific brain area targets in future studies based on individual MRI scans and simulation results.

ABSTRACT #5: FOCAL TRANSCRANIAL MAGNETIC STIMULATION (TMS) OF THE RAT BRAIN

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Abstract: TMS is emerging as a therapeutic tool for several neuropsychiatric disorders. Preclinical rodent studies are of great value in understanding the neurobiological mechanism of TMS. To draw spatially translatable neurobiological conclusions, and ultimately to inform clinical interventions to improve efficacy, it is critical that animal studies mimic human TMS conditions. Unfortunately, there is no commercial rodent TMS coil that can mimic the spatial focality of human TMS. We report here a novel system capable of inducing a brief twitch of a single limb when a TMS pulse is delivered to the motor cortex of the mouse and rat brain. Based on known cortical representation of the motor cortex, we estimate the focality of the TMS system is about 1 mm.

A key strategy in our coil design is the use of long magnetic core. Theoretically, the Maxwell equation $\nabla \times E = \partial B/\partial t + \mu 0 J$ dictates that the induced E field is a function of how fast the B field changes over time. $B(x,y,z) = \mu r(x,y,z) \times \mu 0 \times H(x,y,z)$, here $\mu 0$ is a constant; $\mu r(x,y,z)$ is relative permeability of the core material. $\mu r(x,y,z)=1$ for air; the theoretical value of μr is 5000 for silicon steel. H is the magnetic field strength produced by a coil in free space (air core). It is apparent that the intensity and spatial distribution of the B field of the coil in relation to the H field is shaped by $\mu r(x,y,z)$. By properly designing a silicon steel magnetic core, one can not only drastically enhance the B field, but can also guide and focus the magnetic flux to the region of interest, depending on the spatial distribution of $\mu r(x,y,z)$. Based upon this insight, we have developed a TMS coil and impedance-matched driver circuits specific for rats and mice. Experiments were performed on 6 awake rats. The coil was carefully adjusted to the motor cortex representation of the hindlimb region. We consistently observed contralateral hindlimb twitch to a single TMS pulse. We also measured motor evoked potential (MEP) in some of the animals via implanted microwires into the lateral gastrocnemius of the contralateral hindlimb muscle. We observed MEP signal with the delay, duration and amplitude consistent with the literature. We also mapped neural activity induced by TMS administration using c-fos immunochemistry (n=8 awake rats).Brains areas with Fos expressions are consistent with known projection pathways. The development of focal TMS system opens novel opportunity to investigate the neurobiological basis of TMS.