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### FS3e.3

#### EFFECTS OF DIFFERENT FREQUENCIES OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION ON SIMULTANEOUSLY RECORDED ELECTROCORTICOGRAMS AND MOTOR EVOKED POTENTIALS IN MONKEYS

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#### Abstract

Repetitive transcranial magnetic stimulation (rTMS) is now widely used as a means of neuromodulation, but the exact mechanisms by which rTMS works remain unclarified. As a step forward to unveiling the neural phenomena occurring underneath the TMS coil, we conducted an electrophysiological study using awake and unanesthetized monkeys with subdural electrocorticogram (ECoG) electrodes implanted over the primary motor cortex (MI). We evaluated the effects of 0.5, 1, 2, 5, 10, and 20 Hz rTMS on the resting-state ECoG signals in the stimulated MI, as well as the motor evoked potentials (MEPs) in the contralateral hand. Only the 1-Hz rTMS yielded a significant decrease of the MEP amplitude. The 10- and 20-Hz rTMS yielded a significant increase of the MEP amplitude. Furthermore, the changes in MEP amplitudes were consistent with the changes in ECoG power. Decreases in MEP amplitude coincided with decreases in ECoG power centering on the beta frequency range, whereas increases in MEP amplitude coincided with increases in ECoG power centering on the high-gamma frequency range. Given that beta and high-gamma activities respectively reflect synchronous firing and the firing frequency of cell assemblies in local neural circuits, these results suggest that low-frequency rTMS inhibits neural activity by desynchronizing the firing activity of local circuits, whereas high-frequency rTMS facilitates neural activity by increasing the firing rate of cell assemblies in local circuits.

#### Research Category and Technology and Methods

**Basic Research:** 10. Transcranial Magnetic Stimulation (TMS)

**Keywords:** rTMS, ECoG, MEP, monkey

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### FS3e.4

#### IS IT POSSIBLE TO SEPARATE INTRA-CORTICAL EVOKED NEURAL DYNAMICS FROM PERIPHERAL EVOKED POTENTIALS DURING TRANSCRANIAL MAGNETIC STIMULATION?

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#### Abstract

When TMS is applied over motor cortex, it elicits movements that can be recorded in humans as motor-evoked muscle potentials, as well as in patterns in EEG. A discussion has been started recently in the community that TMS may not only excite neuronal structures in the central nervous system, but also cause peripheral co-stimulation of sensory and motor axons of the meninges, blood vessels, skin, and muscle. These structures may also excite the same cortical site that TMS was meant to stimulate in the first place, resulting in contamination of the TMS-induced cortical response. Therefore, many efforts are made to identify and isolate peripheral evoked potentials (PEPs) from TMS-induced cortical responses in EEG-Data. However, it is very difficult to develop an appropriate sham

stimulation for humans that closely reflects auditory, somatosensory, and motor responses accompanying TMS. An obvious route to clarify the issue is the blockade of cranial nerves, which requires animal models where invasive experiments to discover putative areas of origin can be done.

In recent years, we have developed a method to demonstrate the direct effect of a TMS pulse at the cellular level. We have transferred single pulse and repeated stimulation protocols from humans to a rat model. With selective blockade of PEP, we were able to show that the trigeminal nerve is a major contributor to TMS-evoked neuronal signals in motor cortex, represented by a prominent excitatory peak at around 20 ms after stimulation. TEPs starts much earlier and lasts up to 6 ms after the stimulus pulse. Both inputs then merge into a canonical inhibition-excitation pattern lasting more than 350 ms.

#### Research Category and Technology and Methods

**Basic Research:** 10. Transcranial Magnetic Stimulation (TMS)

**Keywords:** TMS, TMS evoked potential (TEP), Peripheral evoked potential (PEP), trigeminal nerve

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### FS3e.5

#### DISENTANGLING STRUCTURAL PATHWAYS THAT ARE RELATED TO RESPONSE TO ACCELERATED ITBS

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**Symposium title:** The potential of microstructural brain imaging in the field of non-invasive brain stimulation

**Symposium description:** Repetitive transcranial magnetic stimulation (rTMS) is a tool that can be used to treat various neuropsychiatric disorders. The mechanisms of action of rTMS are not yet fully understood but are thought to rely on the principles of long-term depression and long-term potentiation. The effectiveness of rTMS moreover relies on the interaction between the TMS-induced electric field and the neuronal populations within the brain. This symposium will focus on different aspects of structural brain connections, reconstructed from microstructural brain imaging, and show how these could aid in the application and understanding of rTMS. Firstly, Debby Klooster (Ghent University, Belgium) will give a short introduction about microstructural imaging and talk more about the methods to disentangle structural pathways that are related to responses to rTMS. Secondly, Davide Momi (Krembil Centre for Neuroinformatics, Canada) will focus on the spatio-temporal pattern of the propagation of TMS effects throughout the brain. Then, Baran Aydogan (University of Eastern Finland, Finland) will talk about a real-time tractography-based TMS neuronavigation system to improve TMS targeting. He will particularly focus on the promises and challenges of this method. The symposium will end with a presentation from Hartwig Siebner (Danish Research Center for Magnetic Resonance, Denmark). He will focus on deepening the understanding of the relationship between stimulating the hand area and motor evoked potentials using microstructural properties derived from high resolution MRI data. This symposium will shed light on the broad potential of combining microstructural imaging techniques with TMS. This knowledge is highly valuable to broaden the overall understanding about the mechanisms of action of TMS and could potentially lead to improved clinical efficacy when implemented in clinical practice.

#### Abstract

Transcranial magnetic stimulation (TMS) is a tool that can be used to non-invasively modulate brain activity. Repetitive TMS (rTMS) is FDA approved as a treatment for major depressive disorder (MDD). Because of the high inter-subject variability in the responses to rTMS treatment there is a pressing need for biomarkers that can predict individual treatment outcome. Previous work showed that the effects of TMS might propagate via structural connections rather than functional connections. Hence in this work, the potential of structural connections to predict response and remission to accelerated intermittent theta burst stimulation (iTBS, a particular rTMS paradigm) will be investigated.