

## P2.136

**REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) FOR COMPLEX REGIONAL PAIN SYNDROME (CRPS)**

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**Abstract**

**Background:** Complex regional pain syndrome (CRPS) is a chronic pain condition occurring after trauma, even minor injuries. CRPS can be difficult to diagnose and treat, and its pathophysiology is incompletely understood. Diagnosis of CRPS is based on history and clinical examination. It is clinically divided in CRPS 1 (no nerve injury) and CRPS 2 (with nerve injury). Neuroplastic reorganization within the sensorimotor cortex is associated to and aggravates chronic pain in CRPS, leading to secondary motor symptoms and apraxia/neglect similar to stroke, as well as possible spread of the symptoms to additional extremities.

Repetitive transcranial magnetic stimulation (rTMS) is in clinical use for e.g. neuropathic pain, stroke rehabilitation, and depression. Neuro-navigated rTMS utilizing estimation of the induced electrical field (E-field) improves efficacy in neuropathic pain and depression, but it has not been studied in CRPS patients. The optimal cortical target site(s) and rTMS protocol for CRPS are neither known.

**Objectives:** To study the efficacy of E-field-navigated rTMS with a new protocol targeted to the right parietal operculum on pain and function in CRPS patients in acute and long-term maintenance therapy compared with sham stimulation. To study the pathophysiological mechanisms of CRPS, and patient characteristics influencing rTMS-treatment results.

**Methods:** In this prospective, randomized, placebo-controlled parallel group trial, we studied the therapeutic effects of rTMS with a 3-month follow-up at the Turku and Helsinki University Hospitals. Patients underwent clinical examinations before and after a 10-session serial treatment. Neurophysiological tests, mood, sleep and function were assessed at baseline and during follow-up.

**Results:** 71 patients were recruited, 62 participated. Sixty patients underwent one-month control after the treatment period. Of these patients 45 had CRPS 1 and 15 CRPS 2. The results comparing the effects of sham and active treatment will be analyzed with repeated measures ANOVA, and presented in the poster.

**Research Category and Technology and Methods**

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

**Keywords:** Repetitive transcranial magnetic stimulation (rTMS), E-field navigation, Complex regional pain syndrome (CRPS)

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## P2.137

**ALTERATIONS IN THE SENSE OF SELF CAUSED BY DIRECT ELECTRICAL STIMULATION OF THE HUMAN PRECUNEUS**

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**Abstract**

Self-dissociation is an altered state of consciousness where the integrity of the sense of self is disrupted. We explored the phenomenology of self-dissociation in 10 human subjects without epileptic abnormality in the precuneus region. Using direct bipolar 50Hz electrical stimulation of different sites within the posteromedial cortex (i.e., posterior cingulate, retrosplenial, and precuneus regions) in each subject's brain, we replicated our prior findings that the majority of sites in the PMC are silent to

electrical stimulation (i.e., do not cause a change in the conscious subjective state of the subject). Interestingly, we discovered a region in the anterior PMC, i.e., in the mid-anterior precuneus, where 50Hz electrical stimulation consistently caused an alteration in the subject's sense of bodily self. We used resting-state fMRI and seed-based functional connectivity (FC) analysis in the native brain space and intracranial 0.5Hz single pulse electrical stimulation (SPES) to provide a map of connectivity of the responsive sites. Our findings clearly distinguished cortical and thalamic connectivity profiles and marked a critical functional watershed from the neighboring PMC areas. Self-dissociation-causing sites were not part of the default network (DMN) but causally and bilaterally connected with DMN sites. Our findings feature an extraordinary functional anatomical architecture of the PMC with the addition of a new unexplored region that represents an anatomically and functionally distinct subregion within the human PMC.

**Research Category and Technology and Methods**

**Basic Research:** 1. Deep Brain Stimulation (DBS)

**Keywords:** consciousness, sense of self, default mode network, posterior cingulate

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## P2.138

**A PILOT STUDY LEVERAGING LARGE SCALE DATASETS FROM INTERNET-CONNECTED TRANSCRANIAL MAGNETIC STIMULATORS: CIRCADIAN MODULATION OF CORTICAL EXCITABILITY**

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**Abstract**

**Background:** Transcranial Magnetic Stimulation (TMS) research has been historically dominated by single, academic center research. Recent advances in TMS devices have introduced a new generation of internet-connected that collects anonymized data from geographically diverse medical clinics. Retrospective analysis of this data may afford unique opportunities to improve neuroscience understanding or treatment efficacy due to both the different environments and possible scale. For example, circadian rhythms affect brain function, and many neuropsychiatric disorders represent circadian fluctuations of their symptomatology. The available dataset includes resting motor threshold (rMT) values at different times of day. Although the measurement of rMT by TMS is a relatively stable measure over time, several small-sample studies have shown that circadian rhythms can impact rMT. This pilot study therefore aims to demonstrate the ability to use large, internet-connected data sets by investigating the effect of the measurement time on rMT.

**Methods:** Magstim Horizon 3.0 systems, including the Horizon biphasic pulse stimulator, MT and EZ coils, StimGuide+ neuronavigation systems, and Magstim Connect with Analytics software were used to collect data from 22 clinics in different states of the USA, for 454 individuals.

**Results:** The measured rMTs were clustered into three groups: 08:00-11:59, 12:00-15:59, and 16:00-20:00 in local times. The average threshold and standard deviation for each group were calculated as 60%±10.6%, 57.7%±11.4%, and 63%±11.5% respectively. A significant difference was observed between the groups ( $F(2,451) = 6.19, P < 0.05$ ). The largest difference between the rMTs was determined between groups two and three as a medium effect (Cohen's  $d = 0.46$ ) and the smallest difference between groups one and two ( $d = 0.2$ ).

**Conclusions:** The integrated dataset revealed considerable circadian effects of TMS-inferred corticospinal excitability. The growing data set shown here will be a useful tool to assess variability factors in TMS, which may have clinical implications.

**Research Category and Technology and Methods**

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

**Keywords:** Transcranial magnetic stimulation, Circadian Modulation, resting motor threshold, Cortical Excitability

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## P2.139

### NEUROMODULATION USING CROSS-FREQUENCY COUPLING TACS: PRELIMINARY DATA

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#### Abstract

Non-invasive brain stimulation (NIBS) techniques are widely used in both clinical and experimental settings because they can modulate and provide information about ongoing cortical activity. It is well known that our brain works in networks and that frequency changes probably sustain communication among different cortical areas. In particular, the cross-frequency coupling (CFC) phenomenon is thought to mediate large-scale integration and communication by synchronizing the discharge frequencies of other neuronal populations in time.

Based on the CFC hypothesis, this study aimed to interfere with the spontaneous cortical activity of primary motor cortices (M1) using an innovative transcranial alternating current stimulation (tACS) protocol. Seven healthy subjects underwent two experimental sessions in which we applied either 20 minutes of theta-gamma tACS ( $\theta$ - $\gamma$  tACS) or 20 minutes of sham tACS (s-tACS).

To assess the aftereffects induced with this protocol, we used transcranial magnetic stimulation (TMS) over left M1 to evaluate cortical changes in different intracortical circuits before and after the intervention. In particular, we tested motor evoked potentials (MEP), Short Intracortical Facilitation (SICF), and Short Intracortical Inhibition-Intracortical Facilitation (SICI-ICF) before and after the stimulation. We expected there to be a shift in the balance between inhibitory and excitatory activity only following the  $\theta$ - $\gamma$  tACS stimulation. The main result of the study is that  $\theta$ - $\gamma$  tACS exerted an effect on SICI, leading to a lower inhibition after the stimulation ( $p < 0.05$ ), whereas no changes were found in the MEP and ICF following stimulation ( $p > 0.05$ ). Importantly we found no statistically significant differences in any of the neurophysiological measures (i.e. MEP, SICF, SICI-ICF) following the sham condition.

These preliminary data suggest that combining different frequencies for tACS interventions may effectively induce changes in cortical activity. Understanding the neural underpinnings of such neuromodulation may shed light on the future therapeutic application in clinical settings.

#### Research Category and Technology and Methods

**Basic Research:** 8. Transcranial Alternating Current Stimulation (tACS)

**Keywords:** tACS, TMS, cross-frequency, neurophysiology

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## P2.140

### RTMS OF THE SMA: A SYSTEMATIC REVIEW OF CLINICAL AND FUNDAMENTAL APPROACHES

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#### Abstract

The supplementary motor area (SMA) is a multifunctional brain region divided into two subregions: the pre-SMA and SMA-proper. Non-invasive brain stimulation was applied to both regions and reported to be successful in treating various neurological and psychiatric conditions. Here we systematically review studies involving repetitive transcranial magnetic stimulation (rTMS) applied over the SMA-proper/pre-SMA in healthy and clinical populations to leverage information about the future outlook of these regions neuromodulation.

We included all original studies in English from the PubMed, Cochrane, and Scopus databases (PROSPERO ID - CRD42020141289). All studies were divided into two subgroups: (1) only healthy volunteers, (2) including patients. The following data were extracted from each study: sample characteristics, function investigated, rTMS parameters, the way of TMS coil targeting, and the primary outcome.

The final review sample consisted of 129 studies; a similar amount of studies was performed in healthy (68 studies) and clinical (61 studies) populations. There were substantially more articles dedicated to SMA-proper, compared to pre-SMA stimulation, both in the healthy (44 vs 19) and clinical subgroup (53 vs 12). In the healthy subgroup, SMA-proper target was used primarily to modulate the motor function (65%), 25% of articles were dedicated to cognitive processes, 10% of articles reported only neurophysiological output such as functional connectivity. Interestingly, pre-SMA stimulation in healthy population was mostly done to modulate motor function (79%). At the same time, in the clinical population, SMA-proper target was primarily used for motor function modulation in neurological populations, in particular Parkinson's disease (>40%), while pre-SMA target was used predominantly in the psychiatric population of obsessive-compulsive disorder.

Our review supports some preliminary conclusions about SMA-proper/pre-SMA as a highly promising target for NIBS in a wide range of neuropsychiatric conditions. However, more research, including EF modeling is needed to define interhemispheric and SMA/pre-SMA functional differences.

#### Research Category and Technology and Methods

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

**Keywords:** SMA, pre-SMA, rTMS, non-invasive brain stimulation

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## P2.141

### EXPLORING SENSE OF AGENCY WITH NONINVASIVE BRAIN STIMULATION: AN RTMS/EEG STUDY

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#### Abstract

Sense of agency (SoA) is the feeling that one's action is the cause of an external sensory event. Previous neurostimulation and neuroimaging studies suggest that the inferior parietal lobe (IPL) acts as a key structure in comparing action representations with action outcomes. Particularly the right IPL has been identified as an area responsible for a sense of agency. In the present study, we explored the effect of rTMS neurostimulation on the sense of agency. Participants ( $n=16$ ) completed four visits in which they received a TMS protocol followed by a simple sensorimotor SoA task in which they controlled the movement of a cursor on a screen. They were asked to indicate whenever they experienced the movement as being externally perturbed.

Our goal is to evaluate whether the tendency to over-attribute own actions to others is linked to inhibitory or rather excitatory stimulation of right IPL and to explore how are these changes reflected in resting state EEG. To this end, the effect of the inhibitory 1 Hz protocol and excitatory 10 Hz and 20 Hz protocols applied over the right IPL is compared with the placebo (sham).