

differences. This pilot study suggests that greater measures of local excitability on TMS-EEG are related to worse cognition.

**Keywords:** Transcranial Magnetic Stimulation, Electroencephalography, Alzheimer's disease, Biomarkers

## P2.095

### AN OPEN-SOURCE PLATFORM FOR ROBOTIZED TRANSCRANIAL MAGNETIC STIMULATION

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#### Abstract

Neuronavigation systems increase precision and accuracy in clinical and experimental procedures with transcranial magnetic stimulation (TMS). Small variations in the positioning of the stimulator evoke distinct responses in the brain. Collaborative robots (cobots) have been used to decrease variability and improve the reproducibility of the TMS coil positioning on the patient's scalp. However, TMS robotic positioning is not widely used due to low portability, high cost, and limited features due to closed-source development platforms. To increase the accuracy and reliability of TMS procedures, we aim to develop an open-source platform for the robotized positioning of brain stimulators, providing research centers with access to the latest technology in this scenario. Our group has developed the open-source neuronavigation system InVesalius Navigator, for navigated TMS, written in Python and compatible with multiple spatial tracking devices. InVesalius Navigator was selected as a suitable platform to develop the control of cobots. Two models of cobots have been integrated into the platform, the iiwa cobot (KUKA Robotics) and the Elfin cobot (HAN\*S Robots). The precision and accuracy of the cobot TMS position were recorded with the navigation system. The precision error was defined as the Euclidean distance between the coordinates measured in the image space during navigation and the real coordinate in the simulated image. The average precision error ( $\pm$  standard deviation) was  $1.05 \pm 0.49$  mm. The estimated error was smaller than those commonly reported for manual TMS placement.

The cobot-navigated open-source platform might improve the reproducibility and accuracy of the TMS experiments, creating an integrated development environment for new technologies on robotized TMS and allowing users to build their features on demand.

**Keywords:** Transcranial magnetic stimulation, Neuronavigation, Robotics, cobot-navigated

## P2.096

### A PILOT TRIAL APPLYING 18-SESSIONS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION TO THE DORSOLATERAL PREFRONTAL CORTEX OF PARTICIPANTS UNDERGOING ACUTE MEDICALLY-MANAGED WITHDRAWAL FROM OPIOIDS OVER THREE-DAYS

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#### Abstract

Opioid Use Disorder (OUD) is an impactful condition with only moderately effective treatments available and relapse especially common early in treatment. This project determined the feasibility of delivering an accelerated course of repetitive transcranial magnetic stimulation (rTMS) to participants with OUD during medically managed withdrawal. If feasible, delivering rTMS at this early stage of treatment may improve outcomes.

Participants included those with moderate or severe OUD who were undergoing medically-managed withdrawal using either buprenorphine or methadone. During the taper, eighteen-sessions of rTMS were applied over three days (6-sessions/day separated by 30-minutes, 10Hz, figure-of-eight-coil, EEG coordinate F3, 3000 pulses each, 120% rMT, delivered during opioid image presentation). The first participant underwent open-label study-treatment, while the final six were treated in a double-blind sham-controlled fashion. The primary outcome measures included provoked craving following a standardized cue paradigm, as well as subjective pain measures.

Four participants received active stimulation, three of which (27F, 27M, 31F) completed treatment at 120%rMT, and one (27M) withdrew due to symptoms of opioid withdrawal. Three participants received sham stimulation (30F, 27M, 51M) two of which completed treatment at 120%rMT and one other completing treatment at 100% rMT. The blind was effective and only one headache occurred as an adverse event. No statistics were run due to the small sample size, however the participants who received active stimulation reported that composite craving (want, resist, crave opioids) dropped numerically more in the active-group (mean decrease  $10.3 \pm 8.1$ ) then in the sham-group (mean decrease  $7.0 \pm 4.6$ ) following a standard opioid cue paradigm. Clinical pain was low at baseline and changed minimally following the intervention.

No firm conclusions can be drawn from this pilot trial, which was stopped early due to the COVID19 pandemic, however accelerated treatment with rTMS appears to be well tolerated by those undergoing medically managed withdrawal.

**Keywords:** opioid, craving, clinical trial, rTMS

## P2.097

### UNCERTAINTY QUANTIFICATION IN BRAIN STIMULATION USING UNCERTAINTSCI

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#### Abstract

Predicting the effects of brain stimulation with computer models presents many challenges, including estimating the possible error from the propagation of uncertain input parameters through the model. Quantification and control of these errors through uncertainty quantification (UQ) provide statistics on the likely impact of parameter variation on solution accuracy, including total variance and sensitivity associated to each parameter. While the need and importance of UQ in clinical modeling is generally accepted, tools for implementing UQ techniques remain limited or inaccessible for many researchers.

We have developed UncertainSCI as an open-source, flexible, and easy-to-use tool to make modern UQ techniques more accessible in biomedical simulation applications. Our goals in developing UncertainSCI were to provide numerical accuracy, a simple application programming interface (API), adaptability to many applications and methods, and an interface with diverse simulation software. UncertainSCI implements polynomial chaos expansion (PCE) to estimate uncertainty of a model non-invasively, allowing UQ with a vast array of modeling applications, and uses Python to create a simple API that can interface with many simulation packages.

To demonstrate the functionality and adaptability of UncertainSCI, we implemented UQ on three brain stimulation modeling pipelines: electrocorticography (ECoG) stimulation, transcranial current stimulation (tCS), and transcranial magnetic stimulation (TMS). We used UncertainSCI to predict the model uncertainty due to variations in tissue conductivities and electrode positions in simulations of ECoG, tCS, and TMS with realistic human head models solved in SCIRun. We compared the results between these modalities and with other UQ packages, which showed that UncertainSCI was equally accurate and more efficient. The UQ predicted by UncertainSCI allows researchers to gain insight into the behavior of these

three pipelines as a result of parameter variability and where researchers may focus efforts to improve model accuracy.

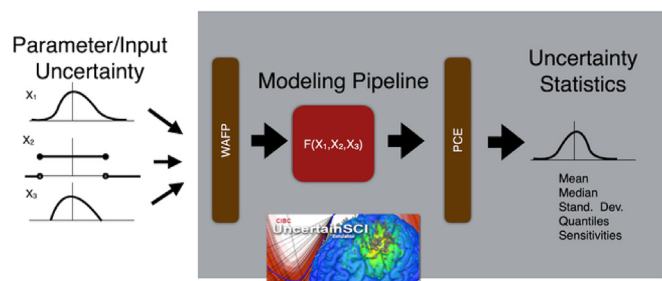


Figure 1: **UncertainSCI pipeline for non-invasive uncertainty quantification (UQ).** UQ is performed on a modeling pipeline with known input parameters distributions by first, sampling with Weighted Approximate Fekete Points (WAFP), running the modeling pipeline with each parameter sample set, and finally computing the output distributions using Polynomial Chaos Expansion (PCE) and calculating statistics of the model uncertainty.

**Keywords:** Uncertainty Quantification, Computer Modeling, Polynomial Chaos, Software Tools

## P2.098

### COVID-ENCEPHALOPATHY TREATMENT WITH TRANSCRANIAL NEAR INFRARED LASER STIMULATION

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#### Abstract

Many COVID-19 survivors experienced obvious cognitive function impairments, also known as “brain fog,” which includes confusion and forgetfulness. How COVID-19 damages the brain has recently become clearer. New evidence suggests that the coronavirus could attack certain brain cells directly, reduce blood flow to brain tissue, or trigger the production of immune molecules that can harm brain cells as an inflammation reaction. With these kinds of multipronged attacks, can an early intervention help prevent them from developing into long-term damage? Or reverse it? The Transcranial Near Infrared Laser Stimulation (TILS) based on the PhotoBioModulation (PBM) phenomenon has been proven to enhance cognitive functions by increasing the cerebral blood flow and upregulating the cytochrome c oxidase in the mitochondria. Many other studies also showed that the PBM could reduce inflammation. In our pilot study, the 1064 nm near-infrared laser with 4.5 cm aperture collimated beam was applied to the prefrontal cortex region with power density 250 mW/cm<sup>2</sup> and duration time 10 min. The tested results were very positive. The near-infrared stimulation is expanding to use 810nm LEDs with the same power density to cover the whole prefrontal cortex. The LEDs based light source makes the deployment of this therapy much more accessible and ready to integrate with all other therapeutic modalities. The Wisconsin Card Sorting Test is adopted to measure the improvement. The results demonstrate that the TILS on the prefrontal cortex is very effective, safe, and easy to deploy in a clinical setting or even home-based self-treatment.

**Keywords:** COVID-Encephalopathy Brain Fog, Transcranial Near Infrared Laser Stimulation(TILS), PhotoBioModulation(PBM), Cognitive functions

## P2.099

### THETA PHASE-LOCKED TMS MODULATES FUNCTIONAL CONNECTIVITY DURING WORKING MEMORY RECALL

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#### Abstract

**Background:** Synchronization of activity between brain regions has been demonstrated to play a role in working memory. TMS applied at specific oscillatory phases has been shown to modulate excitability and coherence in motor cortical regions. How phase-locked TMS affects functional connectivity during working memory processes requires further investigation. **Aim:** The objective of this study is to examine the effects of theta closed-loop TMS (applied at positive vs. negative theta phase) on functional connectivity during working memory encoding, maintenance, and recall. **Methods:** State-dependent electroencephalography-triggered repetitive transcranial magnetic stimulation (EEG-TMS) was applied to target the EEG negative vs. positive peak of medial prefrontal cortex (mPFC) theta oscillation in healthy subjects: 1200 triple pulses, 100 Hz ISI, 120% RMT. Working memory was accessed using the Sternberg working memory task. Functional connectivity was indexed by calculating the phase slope index (PSI) at theta during working memory encoding, maintenance, and recall. EEG preprocessing and sensor-level analyses were conducted utilizing the FieldTrip toolbox in MATLAB.

**Results:** Cluster permutation revealed significant ( $p < 0.05$ ) pre-post differences during recall after theta closed-loop TMS locked at the positive oscillatory peak. Clusters with significant decreases were between fronto-medial and parieto-occipital electrodes and clusters with significant increases were found between occipital and fronto-medial electrodes.

**Conclusions:** Theta-locked TMS at the mPFC modulates theta functional connectivity during working memory recall between fronto-medial and parieto-occipital brain regions.

**Keywords:** Closed-loop TMS, working memory, Functional connectivity, Phase-locked TMS

## P2.100

### CHANGES IN BRAIN FUNCTIONAL CONNECTIVITY FOLLOWING THETA BURST STIMULATION AUGMENTED WITH COGNITIVE TRAINING FOR THE TREATMENT OF YOUTH DEPRESSION

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#### Abstract

Recent studies have shown that repeated sessions of theta-burst stimulation (TBS) applied to the dorsolateral prefrontal cortex (DLPFC) and its combination with cognitive training may be an effective treatment for youth depression. Therapeutic response to various antidepressants has been linked to changes in brain functional connectivity. However, the association between response to TBS and brain functional connectivity in youth with depression has not yet been investigated. A deeper understanding of TBS-related neural mechanisms could lead to enhanced treatment efficacy and help to identify predictors of treatment response in the youth depression population.

Transcranial magnetic stimulation combined with electroencephalography (TMS-EEG) was used to examine potential changes in functional connectivity following 4 weeks of bilateral TBS augmented with cognitive training for the treatment of youth depression. In 26 youth with depression (aged 16 - 24 years old), single-pulse TMS was applied to bilateral DLPFC and intraparietal lobules (IPL), brain regions within the frontoparietal and default mode network, respectively, at baseline and after the treatment completion. The imaginary part of coherency (iCOH) was extracted from TMS evoked potentials to evaluate pre- and post-treatment brain network connectivity. Correlations between changes in iCOH and changes in Hamilton Rating Depression Scale – 17, Ruminative Response Scale, and Dimensional Anhedonia Rating Scale scores were also investigated.

Results showed a decrease in iCOH in the delta band frequency (2–4 Hz) following stimulation of the left DLPFC. Moreover, this reduction in connectivity was significantly associated with a reduction of depressive and