if stimulated at their intrinsic frequency and which may help optimize treatment outcome.
Keywords: TMS; EEG; individual alpha frequency; MDD

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NEUROPHYSIOLOGICAL MECHANISMS OF RTMS EFFICACY IN TREATMENT RESISTANT DEPRESSION

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Background: Little is known about the neurophysiological pathology of depression and how repetitive transcranial magnetic stimulation (rTMS) may affect neurophysiological markers such as cortical inhibition (CI) and cortical excitation (CE) in depression.
Methods: The TMS-Evoked Potential (TEP) waveform was assessed on 30 subjects with depression (21 subjects undergoing active rTMS treatment and 9 undergoing sham rTMS) through global mean field analysis (GMFA) and regional waveform analysis.
Results: Patients who received active rTMS demonstrated a significant decrease in N45 amplitude and a significant decrease in N100 amplitude whereas no change was seen with sham treatment. A decrease in N100 amplitude correlated with decreasing symptoms after active rTMS. Baseline TEP predicted presence or absence of suicidal ideation with 91.7% sensitivity.
Conclusions: Our results reinforce TMS-EEG measures of cortical inhibition as a potential biomarker of response to brain stimulation therapy in TRD. The most noteworthy changes occurred in the DLPFC, a region previously associated with the pathophysiology of depression.
Keywords: TMS evoked potentials; MDD; cortical inhibition and excitation; treatment outcome

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YOUTH TREATMENT RESISTANT DEPRESSION AND TMS-EEG: INSIGHT INTO NEUROPHYSIOLOGICAL ALTERATIONS OF INHIBITION, EXCITABILITY, AND CONNECTIVITY IN DEPRESSED YOUTH PRIOR TO RTMS THERAPY

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Introduction: Treatment resistant depression (TRD) in youth is a debilitating disorder in which many of conventional therapies, such as antidepressants and cognitive behavioral therapy, show suboptimal efficacy, creating the need for novel treatments. Repetitive transcranial magnetic stimulation (rTMS) has been shown to be efficacious in the treatment of depression in adults and youth. However, it is imperative to understand the neurophysiology of the developing brain as it relates to youth depression and its treatment, which may provide insight into the pathophysiology of youth TRD. Here, we investigated TMS-EEG measures of connectivity, inhibition, and excitability in a group of youth with TRD to healthy controls before they underwent rTMS therapy.
Methods: TMS-EEG data was collected from 30 TRD youth and 20 healthy controls, between the ages of 16-24. Single pulse TMS-EEG was recorded from: bilateral dorsolateral prefrontal cortex (DLPFC), bilateral motor cortex (MC), and bilateral inferior parietal lobule (IPL). Long interval cortical inhibition (LICI) was also recorded from the DLPFC, as well as the cortical silent period from the MC. TMS-EEG data was preprocessed using the open source TMSEEG application. Analyses included assessment of latency and amplitude of TMS-evoked potentials (TEPs), frequency analyses of said TEPs, as well as effective connectivity.
Results: Preliminary analyses revealed youth TRD to be associated with various alterations in neurophysiological properties, including alterations in the left and right DLPFC N100 and P200 TEPs responses to single pulse TMS-EEG, as well as in right DLPFC LICI measures of inhibition.
Discussion: For effective treatments of youth TRD to be developed, such as rTMS, it is critical that we also assess the neurophysiological properties of the developing brain in the context of depression. Our preliminary analyses suggest that youth TRD is associated with various neurophysiological alterations, findings which may provide insight into the development of targeted rTMS therapies.
Keywords: Youth, Depression, TMS-EEG, Neurophysiology

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10 HZ RTMS-INDUCED NEURAL RESPONSE OF GAMMA OSCILLATIONS IN SUBGENUAL ANTERIOR CINGULATE CORTEX (SGACC) IS ANTI-CORRELATED WITH LEFT DORSOLATERAL PREFRONTAL CORTEX (DLPFC) IN MAJOR DEPRESSIVE DISORDER

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Background: 10 Hz repetitive Transcranial Magnetic Stimulation (rTMS) administered to the left dorsolateral prefrontal cortex (DLPFC) is a highly effective treatment for depression. The mechanism of action of stimulation is thought to be related to transmission of local stimulation to other brain regions through brain networks. The neurophysiologic spread of this signal has not been well described.
Methods: 3000 pulses of 10 Hz repetitive rTMS was administered to left DLPFC during the initial treatment session in 113 adult patients with Major Depressive Disorder (MDD). Resting state high-density electroencephalographic (EEG) signals were recorded before and after rTMS treatment. A 12-tissue finite element head model and eLORETA method wereapplied to estimate 4,208 dipole sources for delta (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz) and gamma (30-45 Hz) bands pre- and post-treatment.
Results: 10 Hz rTMS to LDLPFC was associated with decreased delta oscillations and increased higher frequency neural activity, alpha and beta, in fronto-limbic circuits. Significant deactivation was found in the TPJ and pSTS, as the posterior part of the default mode network (DMN). Moreover, cross-subject correlation analysis showedthe TMS-induced gamma-band response in subgenual anterior cingulate cortex(sgACC) anti-correlated with the neural response in LDLPFC.
Conclusions: 10 Hz rTMS at 100% motor threshold over LDLPFC entrained neural oscillations in depressed patients. It showed leftover effects with the elevated high frequency neural activity and reduced low frequency oscillations in fronto-limbic neuronal circuits, as well as decreases beta-band activity in the DMN. Interestingly, the negative correlation between sgACC and LDLPFC we observed in EEG gamma band echoes previous fMRI studies showed TMS effects in sgACC, with antagonistic activity against LDLPFC. Our findings provided neural insight of the mechanism of 10 Hz rTMS antidepressant effects by tuning neural oscillations in fronto-limbic network andDMN.
Keywords: TMS; EEG source localization; gamma activity; subgenual anterior cingulate and DLPFC

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FOCUSED ULTRASOUND AS A POTENTIAL MEANS OF FACILITATED EXOSOME DELIVERY TO BRODMANN AREA 25 IN THE TREATMENT OF REFRACTORY DEPRESSION

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Emerging data has demonstrated that depression involves inflammatory processes in the brain. Exosome treatments are thought to have potential anti-inflammatory benefits. This study intended to provide clinical relief for patients with depression by increasing localized perfusion to Brodmann area 25 (BA25) in combination with intravenous exosome delivery. Here, we detail two case studies in which neuro-navigated ultrasound was used to aid exosomal delivery to the subgenual cingulate (SGC, BA25). The patients were both diagnosed with severe treatment-resistant Major Depressive Disorder (MDD) and had previously undergone transcranial magnetic stimulation (TMS) and intensive regimens of antidepressant medication with no symptom relief. Functional and structural imaging were used to navigate ultrasound application targets for the SGC. Safety and efficacy of focused ultrasound and exosomes were evaluated for both patients.

Two female patients (33, 51 years old) underwent a 30-minute targeted ultrasound session immediately prior to an intravenous exosome injection. The DWL Doppler Box^3 Ultrasound was delivered using a 2 MHz probe at a power of 510 mW/cm^2. Using functional and structural neuroimaging, the SGC was navigated and targeted for each patient. Outcome measures, including the Global Rating Scale (GRC) and Beck's Depression Inventory (BDI-II), were administered before and after treatment.

Both patients were able to tolerate treatment without notable side effects. Both patients reported clinically meaningful improvement in their symptoms and had improved BDI scores after treatment ($M\Delta = 10$, $SD = 8.49$). No adverse events were reported.

This study provides preliminary evidence supporting the safety and efficacy of combined exosome and focused ultrasound treatment for patients with MDD. Although this study was not designed to specifically demonstrate the ability of exosomes to penetrate BA25, these case studies suggest that focused ultrasound may be a method for facilitating localized exosomal delivery with clinically meaningful results.

Keywords: Depression, Focused Ultrasound, Exosomes

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THE CORRELATION BETWEEN BASELINE PRESTIMULUS BRAIN ACTIVITY AND ANXIETY CHANGE IN SINGLE-SESSION TRANSCRANIAL DIRECT CURRENT STIMULATION

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Objectives: Transcranial Direct Current Stimulation (tDCS) on the left dorsolateral prefrontal cortex (LDLPFC) has been shown to moderate anxiety. However, the effect of tDCS has high variability, and it is considered that the effectiveness differs depending on the individual differences. The possibility of using tDCS would greatly benefit if we could predict the effect of tDCS for anxiety before stimulation.

Methods: Healthy right-handed volunteers were enrolled. Anodal stimulation was administered over the LDLPFC (F5, 10-10 EEG international electrode placement) or the midline Prefrontal Cortex (AFz), with the cathodal electrode placed on the left shoulder. Each participant received either AFz stimulation (n=8, mean age ± S.D. = 45.63 ± 17.16) or F5 stimulation (n=12, mean age ± S.D. = 50.83 ± 14.57). Resting state EEG recordings were taken before stimulation, followed by administration of one mA direct current tDCS.

STAI (State-Trait Anxiety Inventory), which consists of two subscales, STAI-SI for state anxiety and STAI-CA for trait anxiety, was assessed before and after tDCS, and the amount of change was examined.

Cortical activity before stimulation was computed with standardized Low Resolution Electromagnetic Tomography (sLORETA). Correlations between cortical theta band (4-8Hz) activity and the change in anxiety in each brain region were studied.

Results: For F5 stimulation, the change of STAI-SI scores (post tDCS minus pre tDCS) showed significant negative correlation with cortical theta activity in left lower parietal lobe (R=-0.705), whereas the change of STAI-CA scores had negative correlation with the brain activity in the left inferior temporal lobe (R=-0.706), and in the precuneus (R=-0.545).

Discussion: LDLPFC stimulation induced changes in STA-SI and STAI-CA, which can be predicted from prestimulus cortical activity in different regions. These results suggest that stimulation site for tDCS should be considered depending on the anxiety symptoms.

Keywords: eeg, LORETA, Anxiety, tDCS, prediction

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CASE STUDY: COGNITIVE AND MOOD IMPROVEMENT IN A PATIENT WITH PARKINSON'S DISEASE AND TREATMENT-RESISTANT DEPRESSION FOLLOWING ACCELERATED INTERMITTENT THETA BURST TRANSCRANIAL MAGNETIC STIMULATION TO THE LEFT DORSOLATERAL PREFRONTAL CORTEX

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Objective: To present the cognitive and mood outcomes of a patient with Parkinson's Disease (PD) who participated in neuropsychological testing and mood ratings during a larger study examining the effect of accelerated intermittent theta burst transcranial magnetic stimulation (aiTBS) on patients with treatment-resistant depression (TRD).

Background: Depression and cognitive impairments in PD are not uncommon. PD patients who have depression may be at greater risk for cognitive impairments than those without depression. Symptoms of PD compounded with depression and cognitive impairments can result in even greater impacts on function and quality of life than from PD alone. Results from prior studies suggest that there may be benefit from repetitive TMS to the left dorsolateral prefrontal cortex (dlPFC) in PD on multiple areas of function, however, no studies have examined the effect of aiTBS on cognition and mood in PD.

Methods: In this open-label study, we investigated the efficacy and safety of aiTBS to the left dlPFC in 10 sessions per day for five consecutive days. By the end of the treatment, the participant had received a total of 90,000 pulses of aiTBS. Assessment of clinical efficacy and safety included neuropsychological testing as well as mood outcomes, comparing post-treatment results to pre-treatment baseline measures. Neuropsychological testing included the domains of memory, attention, working memory, and executive functions. Mood outcome measures included the Hamilton Depression Rating Scale (21-item) and the Montgomery-Asberg Depression Rating Scale.

Results: The patient with PD demonstrated significant improvement in cognitive abilities, particularly in executive functions, and mood, comparing post-treatment to baseline scores. There were no reported adverse side effects from the treatment.

Conclusions: Results suggest further investigation of aiTBS in the treatment of patients with PD and depression may be warranted in order to determine whether there is potential for a new application of aiTBS.

Keywords: aiTBS, Parkinson's, depression, cognition

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NON-INVASIVE GALVANIC VESTIBULAR STIMULATION AUGMENTS BETA DESYNCHRONIZATION AND IMPROVES MOTOR PERFORMANCE IN PARKINSON'S DISEASE

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Parkinson's disease (PD) is a progressive neurological movement disorder characterized by degeneration of dopaminergic neurons and abnormal brain oscillations. While invasive deep brain stimulation (DBS) can result in immediate improvement in motor deficits by disrupting pathological oscillations, achieving comparable results with non-invasive brain stimulation (NIBS) remains elusive.

Here we investigated galvanic vestibular stimulation (GVS), a safe, potentially portable NIBS therapy for PD. Previously, we have independently demonstrated that GVS improves tracking performance, ameliorates deficient inter-hemispheric and pedunculopontine (PPN) connectivity, and is capable of modulating cortical oscillations in PD.