

dominant effect of the underlying brain state of the output M1 was noted in all conditions, reinforcing our previous observation that the excitability of the primary motor cortex depends on the prestimulus phase of  $\mu$ -oscillation. **Discussion:** In the present study, we demonstrate for the first time that the IHC at rest and the interplay between sIHl/sIHF are brain-state dependent, based on the phase of the underlying  $\mu$ -oscillation.

**[0599]**  
**THE NEURAL BASIS OF VISUAL SENSITIVITY INVESTIGATED WITH ANTERIOR PREFRONTAL TMS**

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The conscious experience is what links the subjective internal world to the external world. By manipulating the external world we can manipulate our subjective experience. Similarly, by manipulating the activity of certain brain areas we can change the subjective experience of the external world. The role of prefrontal areas in visual experience is still under debate and offline transcranial stimulation (TMS) has yet to show its engagement in visibility judgements. The aim of this study is to affect participants' judgements of visual experience. We use a computer task consisting of a discrimination task of visual stimuli and judgments of their visibility, coupled with theta burst stimulation (TBS). Within the first task we measure to what extent a participant is sensitive to visual information. Within the second approach, we analyse participants' ratings of their subjective availability of visual information. A quantitative measure of metacognitive sensitivity is the degree of association between behavioural accuracy and visibility ratings.

By changing the neural dynamics of the left anterior prefrontal cortex with TBS, we attempt to manipulate metacognitive ability of the participants. The study involves application of three different TBS protocols: intermittent, continuous, intermediate-sham on sessions separated by a week. The first is predicted to facilitate the metacognitive abilities, while we expect the second to lower the metacognitive sensitivity. All protocols are predicted to have no influence on the accuracy of stimulus discrimination. We analyse behavioural accuracy, changes in mean stimulus contrast and ratings frequency distribution. Metacognitive sensitivity is analysed with a mixed logistic model. The current study will test the role of the left anterior prefrontal cortex area that has been recently implicated in metacognition and provide a novel insight into the relationship between behaviour and visibility judgements. **Keywords:** conscious experience, metacognition, theta burst stimulation, anterior prefrontal cortex

**[0601]**  
**SYNERGISTIC EFFECTS OF KETAMINE AND THETA BURST STIMULATION IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER (MDD)**

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**Introduction:** Repetitive Transcranial Magnetic Stimulation (rTMS) applied to dorsolateral prefrontal cortex (DLPFC) causes acute changes in neuronal excitability in this region as well as changes in functional connectivity of brain circuitry involving DLPFC. Theta burst stimulation (TBS) has particularly strong effects on cortical excitability: intermittent pulsing of left DLPFC (iTBS) increases excitability, while continuous pulsing of the right DLPFC (cTBS) reduces excitability. TBS modulation of cortical excitability is known to be dependent upon glutamatergic neurotransmission through the N-Methyl-D-aspartate receptor (NMDAR).

**Methods:** We used the NMDAR antagonist ketamine (KET) to probe glutamatergic mediation of functional connectivity changes seen with TBS. Excitability in, and neurophysiologic connectivity of, DLPFC during iTBS and cTBS was monitored using TMS-compatible quantitative electroencephalography (qEEG). Subjects were pretreated with KET or placebo (PBO) prior to administration of TBS. Baseline functional magnetic resonance imaging (fMRI) and Diffusion Tensor Imaging (DTI) were performed to examine functional and structural connectivity measures, with follow-up scans to examine changes associated with treatment.

**Results:** Both TBS and KET had robust effects on cortical excitability. TBS was associated with local changes in excitability involving DLPFC, while

KET (but not placebo) was associated with more global changes in excitability. Pretreatment with KET modulated the excitability effects of iTBS in left DLPFC and the inhibitory effects of cTBS in right DLPFC. Changes in excitability were correlated with connectivity of DLPFC, anterior cingulate cortex, medial frontal cortex, and orbitofrontal cortex.

**Discussion:** Ketamine constitutes a useful neurochemical probe of the mechanisms underlying the physiologic effects of TBS on excitability, connectivity, and neuroplastic processes. Future studies should examine the potential clinical impact of combining these treatment modalities.

**Keywords:** Ketamine, TMS, EEG, fMRI and DTI

**[0603]**  
**THE RELATIONSHIP BETWEEN THE INDIVIDUAL ALPHA FREQUENCY (IAF) AND RESPONSE TO SYNCHRONIZED TRANSCRANIAL MAGNETIC STIMULATION (sTMS) FOR TREATMENT OF MAJOR DEPRESSIVE DISORDER (MDD)**

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**Introduction:** sTMS delivers low-field brain stimulation for the treatment of Major Depressive Disorder (MDD) using permanent magnets rotating at an individual's alpha frequency (IAF), determined from a pretreatment electroencephalogram (EEG). The sTMS theory posits that low intensity stimulation delivered at the IAF will be more effective than stimulation delivered at a different frequency. We examined the relationship between response to sTMS and the IAF in subjects enrolled in a double-blind sham-controlled six-week treatment trial, and compared response between subjects who were treated at their IAF and those treated at a different frequency.

**Methods:** 202 subjects comprised the intent-to-treat (ITT) sample; 120 subjects comprised the per-protocol (PP) sample. Fifteen subjects were inadvertently treated at the incorrect IAF because of EEG acquisition difficulties, and these were excluded from the PP sample. Clinical outcomes were compared between subjects treated at incorrect IAF and a propensity matched group of PP subjects. Propensity matching included demographics, treatment history, IAF, and depression severity using the 17-item Hamilton Depression Rating Scale (HamD<sub>17</sub>).

**Results:** There was no relationship in the PP population between mean IAF and change in HamD<sub>17</sub> score or response rate. Eleven subjects in the incorrect IAF group received active treatment, and these subjects were propensity matched with 41 PP subjects. There was a statistically significant greater improvement seen in subjects treated at the correct versus incorrect IAF ( $-8.45 \pm 5.95$  vs.  $-0.36 \pm 7.03$ , respectively,  $p = 0.004$ ). There was no significant difference in response rates, although subjects treated at the correct IAF had a higher numerical rate (29% vs. 18%, respectively,  $p = 0.491$ ).

**Discussion:** These findings are consistent with the theory that sTMS stimulation at the correct IAF is more effective than treatment delivered at a different frequency. Future studies should compare stimulation prospectively assigned at different frequencies to further test this theory.

**Keywords:** sTMS, individual alpha frequency, EEG

**[0604]**  
**CLINICAL EFFECTS OF INTERMITTENT THETA-BURST STIMULATION OF THE ANTERIOR TEMPORAL LOBE TO PROMOTE VISUAL MOTOR INTEGRATION AND PERCEPTUAL REASONING IN PEDIATRIC TRAUMATIC BRAIN INJURY: A CASE STUDY**

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**Introduction:** Left anterior temporal lobe (ATL) has a vital role in visual cognition via semantic aspect of object recognition. To date, the use of navigated transcranial intermittent theta-burst stimulation (iTBS) of left ATL to promote visual perception after traumatic brain injury (TBI) has not been reported. Here, we demonstrate that iTBS of left ATL combined with intensive occupational therapy contributes to recovery of visual motor integration and perceptual reasoning in pediatric TBI.