scores (CHRT-R) and PHQ-9 Item #9 scores (I#9) before and after a course of rTMS in a naturalistic, clinical setting.
Methods: Patients received 30 to 36 rTMS treatments ($M = 35.90$, $SD = .58$) either bilaterally (right dorsolateral prefrontal cortex (dlPFC) at 1 Hz for 360 pulses, then left dlPFC stimulation at 20 Hz for 1200 pulses ($n = 678$)) or unilaterally (left dlPFC at 10 Hz for 3000 pulses ($n = 323$)). PHQ-9, GAD-7, and CHRT scores were obtained before and after the treatment course.
Results: 47.75% of patients ($n_{MDD} = 1001$) achieved MDD remission ($\leq$4 on PHQ-9), 54.75% of patients ($n_{GAD} = 1001$) achieved GAD remission ($\leq$4 on GAD-7). Of the 40.8% of patients with SI ($n_{SI} = 408$) prior to treatment, 299 (73.28%) achieved remission (I#9 score = 0) by the end of treatment. Reductions in suicidality were statistically significant with a moderate effect size, on both the I#9 ($W = 4224$, Cohen's $d_{paired} = .57$, $p < .001$) and the CHRT-R subscale ($W = 15622$, $d_{paired} = .52$, $p < .001$). Comparing outcomes for unilateral vs. bilateral rTMS, there were no significant differences in the degree of improvement in suicidality on either the I#9 score or CHRT-R score ($p > 0.05$).
Conclusions: Both unilateral and bilateral rTMS achieved significant reductions in suicidality, with moderate effect sizes overall. The two types of intervention each showed similar effectiveness against suicidality, without significant differences in outcome.
Keywords: rTMS, MDD, GAD, Suicidal Ideation

P2.016

SYMMETRY OF MOTOR AND PREMOTOR TRANSCRANIAL MAGNETIC STIMULATION (TMS)-EVOKED POTENTIALS

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Abstract
Background: TMS coupled simultaneously with EEG is a non-invasive and tolerable tool for brain stimulation. TMS/EEG can effectively assess cortical excitability. Therefore, the resulting transcranial evoked potentials (TEPs) are potential biomarkers of cortical excitability in humans. The physiological symmetry of the human cortex may provide meaningful information for several cortical mechanisms at both physiological and pathophysiological levels. Here, we hypothesized that TEPs evoked in homologous contralateral cortical areas share similar, symmetric morphology, whilst ipsilateral TEPs from different cortical areas (CAs) diverge.
Objectives: To assess the physiological symmetry of the human cortex, and to collect a normative dataset of TEPs in healthy individuals.
Methods: We performed single pulse navigated monophasic TMS, and simultaneously recorded high-density EEG with active electrodes in ten healthy subjects. To test our hypothesis, we targeted 2 CAs bilaterally including premotor and motor cortexes. We compared (using Wilcoxon Signed Rank Test) frequency power bands and performed Pearson correlation coefficient (CC) among the responses evoked by TMS.
Results: We found no statistical difference when comparing the most powerful evoked frequency derived from homologous motor TEPs (p=0.6426), and homologous premotor TEPs (p=0.7871). Significant differences resulted in left ipsilateral (p=0.0195), and right ipsilateral (p=0.0488) comparisons. Specifically, we found a gradient of decreasing frequencies from anterior (mean=28.14 Hz) to posterior (mean=17.88 Hz) areas. Furthermore, post-stimulation voltages showed higher CC (R=0.71 ±0.13) for homologous TEPs and lower CC (R=0.13 ±0.39) for ipsilateral comparisons.
Conclusions: These novel findings indicate that TEPs may reflect the underlying cortical cytoarchitectonic and neurophysiological behaviour, therefore providing a unique fingerprint of the underlying brain functional architecture. Our data can be used as a normative dataset in TMS studies of brain disorders, such as epilepsy or brain structural injuries. We also show the reliability of a novel TMS methodology, i.e. navigated monophasic TMS combined with high-density active EEG.
Keywords: TMS/EEG, Symmetry, Neurophysiology, Cortical excitability

P2.017

DEFAULT MODE NETWORK CONNECTIVITY AND BRAIN DERIVED NEUROTROPHIC FACTOR IN BRAIN STIMULATION OF TRAUMATIC BRAIN INJURY PATIENTS

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Abstract
Brain derived neurotrophic factor (BDNF) is the best-known predictor of patient response to repetitive transcranial magnetic stimulation (rTMS) as a treatment for depression. BDNF is a protein encoded by the BDNF gene that plays a significant role in the growth and maintenance of neurons. RTMS is also used as a treatment for traumatic brain injury (TBI), but biological markers underlying treatment response for TBI have not been clearly identified. Here we examine the relationship between levels of BDNF and default mode network (DMN) connectivity in a double-blind randomized clinical trial using rTMS for Veterans with TBI.
Twenty-four Veterans (21 male; mean age: 44 yrs.) with TBI were enrolled in treatment (n = 11) or sham (n = 10) at VA Palo Alto. FDA approved parameters for depression were used (10 Hz stimulation at left dorsolateral prefrontal cortex). Blood samples and MRI scans were collected at baseline and post treatment (T20).
Treatment did not significantly affect BDNF levels (Active: -0.31±3.02; Sham: 0.25±3.10) or DMN connectivity (Active: -0.35±2.15; Sham: -1.64±1.46; p>0.1). BDNF change was significantly correlated with DMN connectivity (p< .0211). At T20 DMN was the outcome, there were no significant effects of treatment on BDNF levels, baseline DMN or treatment/sham (p> 0.1). There was an overall effect of age on post T20 DMN (p=.0496).
Results show a correlation between BDNF change and DMN connectivity with higher BDNF levels associated with lower DMN connectivity – this relationship being an indicator of improved brain function. This association is not driven by rTMS treatment. Although the sample size is small, biomarker targets for rTMS treatment in TBI are important to study as these patients suffer from numerous psychiatric problems.
Keywords: brain derived neurotrophic factor, transcranial magnetic stimulation, traumatic brain injury

P2.018

PROBING INTRAHEMISPHERIC PMD – M1 INTERACTIONS WITH A NOVEL DUAL-SITE TMS SETUP

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Abstract
The net output of the primary motor cortex (M1) is shaped by several (non-)motor brain regions including the dorsal premotor cortex (PMd) which is playing an important role in sensorimotor integration, response selection, bimanual motor control, and motor learning. Previous dual-site transcranial magnetic stimulation (dsTMS) setups mainly investigated the interhemispheric PMd – M1 interactions, as testing the intrahemispheric PMd – M1 interactions yield technical difficulties due to the vicinity of both regions.
A novel dsTMS setup was used in a sample of 23 young healthy right-handed adults to probe intrahemispheric left PMd – M1 interactions at rest. Biphasic stimuli were applied to M1 to elicit an MEP of at least 1 mV peak-to-peak amplitude (testing stimulus, TS) in the resting first dorsal interosseus (FDI). The conditioning stimulus (CS) was applied ~2 cm

anterior to M1 at an interstimulus interval (ISI) of 6 ms and an intensity of 75% of the resting motor threshold (rMT).
To physiologically test this setup, short-interval intra-cortical inhibition (SICI) was measured with the same coil arrangement, using two coils targeted at M1 (ISI = 3 ms, CS intensity = 75% rMT, TS intensity = 1 mV). First, SICI could robustly be elicited using the novel coil setup. Second, conditioning left PMd lead to a robust modulation of left M1 output when using a CS intensity of 75% rMT. This interaction was mostly found to be inhibitory. However, in some subjects (~15%) a facilitatory PMd − M1 interaction was seen.
This novel coil setup opens new opportunities to measure intrahemispheric PMd − M1 interactions at rest and in different task-related contexts without facing technical difficulties such as large stimulation distances due to coil size or coil heating (particularly in small coils).
Keywords: TMS, intrahemispheric, premotor cortex, connectivity

P2.019

DEVELOPMENT OF NOVEL TDCS STIMULATION CONDITION TO INVESTIGATE TDCS NEUROPHYSIOLOGICAL MECHANISMS

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Abstract
Transcranial direct current stimulation (tDCS) is a noninvasive neuromodulation method that aims to increase cortical excitability and plasticity by applying a small direct current over scalp electrodes. Over the last 20 years, thousands of studies have highlighted wide ranging physiological and behavioral tDCS effects. However, the neurophysiological mechanism behind tDCS is highly debated.
Until recently, it was generally accepted that tDCS establishes its neuromodulatory effect due to direct polarization of cortical neurons under the influence of an extracellular electric field. However, tDCS studies have revealed that the resulting electric field in the brain is relatively weak. Instead, most of the applied current is shunted by the scalp, where the electric field can reach levels high enough to trigger peripheral nerves. We have already shown peripheral nerve stimulation affects the brain indirectly during alternating current stimulation (tACS), a mode of action that has currently been overlooked in the context of tDCS.
While many researchers are investigating how the weak electric field in the brain can account for the observed tDCS effects, we want to find out to what extend peripheral nerve stimulation during tDCS can influence cortical excitability and plasticity indirectly. We developed a novel tDCS stimulation condition called transcranial-only-tDCS (TO-tDCS), in which we minimized peripheral input by applying topical anesthetics on the scalp under the stimulation electrodes.
We will use this novel stimulation condition to investigate tDCS neurophysiological mechanisms. More specifically, by comparing observed tDCS effects of TO-tDCS with standard tDCS and sham stimulation in a motor sequence learning paradigm, we will determine whether tDCS effects are mainly caused by 1) direct polarization of cortical neurons or 2) indirect peripheral nerve stimulation or a combination of both. The newly gained mechanistic knowledge will be used to develop more effective and robust tDCS methods that will significantly advance the neuromodulation field.
Keywords: Transcranial direct current stimulation (tDCS), Neurophysiological mechanisms, Novel neuromodulation technique, Motor sequence learning paradigm

P2.020

WAVEFORM SIMULATION AND PULSE-WIDTH-MODULATION APPROXIMATIONS WITH MULTI-LOCUS TMS

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Abstract
Multi-locus transcranial magnetic stimulation (mTMS) is based on the superposition of electric fields from several stimulation coils, and it provides a means of changing the profile of the induced field without physical coil movement. We recently designed and built a custom mTMS device and a transducer consisting of five separate coils. The stimulation device is based on H-bridge power electronics, and it can drive up to six independent coils simultaneously. Manipulating the induced electric field can require drastically different initial voltages for the pulse capacitors, introducing serious limitations for pulse trains, as the charging and discharging processes are quite slow (on the order of several seconds maximally). Pulse-width modulation (PWM) offers a way to approximate lower-voltage waveforms with the capacitor charged to a high voltage. By rapidly switching the power circuit topology between different states, the current through the stimulation coil follows that of a conventional pulse of lower voltage. The induced electric field will momentarily be higher than one induced by traditional methods, but neurons, which respond to an integral of the electric field, will not notice a difference between the two conditions. Thus, most of the charging and discharging processes can be eliminated by making approximations of lower-voltage pulses while still driving the system with maximum voltage. More precise approximations require more switching events for the H-bridge electronics; we noticed that this started to introduce distortions in the measured waveforms compared to predictions. This is caused by system non-idealities, such as parasitic inductance and resistance. By identifying these non-idealities, we were able to make an accurate model of the system to predict the resulting waveforms with the different possible circuit topologies. The next step is to validate the equivalence of the PWM-pulse approximations to conventional pulses.
Keywords: TMS, mTMS, H-bridge, PWM

P2.021

CLINICAL VIM TARGETING FOR DEEP BRAIN STIMULATION BASED ON AN AUGMENTED INTELLIGENCE. THE REBRAIN SOLUTION

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Abstract
Background: Targeting in deep brain stimulation procedures remains controversial, mainly because research into the relationship between patient condition improvement and electrode location requires correction for anatomical variations. If these corrections are not undertaken could lead to poorly controlled errors.
These corrections are particularly important in VIM targeting, which is not visible on MRI.
Material et Method: To take into account these anatomical variabilities, we applied the inverse problem method by correlating the position of the active stimulation contacts in a series of successfully operated patients with essential tremor and anatomical landmarks easily identifiable on a T1 MRI.
We constructed a learning data base from 15 patients (29 leads) who had undergone surgery with a median tremor improvement of 72% on the Fahn-Tolosa-Marin (FTM) scale. All the patients underwent pre- and post-operative imaging from which the coordinates of 18 anatomical landmarks per hemisphere and of the active contacts were extracted. We used regression and deep learning methods (Artificial Intelligence). We were able to develop a prediction meta-model that expresses the position of active and clinically effective contacts depending on the position of MRI landmarks. The models were statistically and anatomically validated according to a leave-one-out cross-validation and the mean distance to VIM structure on the DISTAL atlas in the MNI space respectively. The generated meta-model is exploited by the OptimDBS software developed by Rebrain® (Bordeaux, France, https://rebrain.eu/en/home/) and allowed us to predict the effective location of the active contacts by identifying MRI landmarks.
Results: We applied this method to a validation set of 9 patients with essential tremor where electrodes were directly inserted at the predicted