

with a spaced double rTMS protocol. These target areas are known to be involved in various functional domains and robustly emerge as core nodes of the default mode network. Accordingly, participants completed three pre- and post-stimulation resting-state and three multi-task fMRI sessions directly after stimulation (left IPL, right IPL, and sham rTMS on different days). Building on our previous research, tasks were chosen from three functional domains (attention, semantic processing, social cognition) to exemplify highly relevant cognitive domains that significantly recruit the IPL. TMS field simulations were conducted to quantify cortical field exposure. Across individuals, we expected field exposure to relate to stimulation-induced changes in brain function. Specifically, we hypothesized that rTMS would differentially affect network activity and connectivity in each cognitive domain: rTMS should have stronger modulatory effects in the semantic network when applied over the left IPL. In contrast, rTMS over the right IPL should strongly affect the attention task, while social cognition should be affected by rTMS over either hemisphere. Furthermore, we hypothesized that intrinsic functional connectivity is predictive of functional plasticity on the individual level. Preliminary results support these hypotheses, showing a high degree of subject specificity.

Keywords: TMS, inferior parietal lobe, plasticity, brain state

P1.079

CLINICAL EFFECTIVENESS OF 1 HZ/20 HZ BILATERAL RTMS TREATMENT IN ADOLESCENTS WITH MAJOR DEPRESSIVE DISORDER

Paul Croarkin¹, Victoria Middleton², Naima Monira², Joseph Kriske², Theodore Wiebold², Nancy Donachie², Jonathan Downar³. ¹Mayo Clinic Minnesota, Rochester, MN, USA; ²Saliency, USA; ³University of Toronto, Toronto, ON, Canada

Abstract

Background: Although rTMS is an effective and FDA approved intervention of treatment resistant depression in adults, there is presently less data available on its efficacy in the adolescent population.

Methods: This naturalistic study evaluated outcomes of adolescents with major depressive disorder (MDD) (N=201, $n_{\text{males}}=79$, $M_{\text{age}}=19.09$ years, $SD_{\text{age}}=2.23$ years) treated with bilateral rTMS. Further Patient age groups Further analysis compared patients aged 18 and younger ($n_{\text{older}}=121$, $M_{\text{age}}=20.55$, $SD_{\text{age}}=1.20$) and those 19-22 years old ($M_{\text{age}}=16.9$, $SD_{\text{age}}=1.48$; $\text{Age}_{\text{min}}=12$). Patients received at least 30 bilateral rTMS sessions (range 30-36), ($M=35.63$, $SD=1.26$) with 1 Hz delivered to the right dorsolateral prefrontal cortex (dlPFC) for 360 pulses, followed by left dlPFC stimulation at 20 Hz for 1200 pulses. PHQ-9 and GAD-7 were administered before and after an acute course of rTMS treatment.

Results: 43.3% of patients experienced remission in their depressive symptoms and 50.3% of patients in their anxiety symptoms (≤ 4 on PHQ-9 and GAD-7, respectively) after rTMS treatment. Overall, improvement was observed between pre-rTMS PHQ-9 ($M=16.00$, $SD=5.81$) and GAD-7 ($M=12.64$, $SD=5.49$) scores and post-rTMS PHQ-9 ($M=7.45$, $SD=6.35$), ($t(200)=18.99$, Cohen's $d_{\text{paired}}=1.40$) and GAD-7 ($M=6.05$, $SD=5.42$), ($t(200)=16.55$, $d_{\text{paired}}=1.21$) scores. There were significant reductions in the outcome measures across the entire sample. Despite age, similar effect was observed on the PHQ-9 and GAD-7, respectively, between those 19-22 years old ($d_{\text{paired}}=1.53$, 95% CI [7.94, 11.10]), ($d_{\text{paired}}=1.10$, 95% CI [5.66, 8.47]) and for those aged 18 and younger ($d_{\text{paired}}=1.22$, 95% CI [5.26, 8.89]), ($d_{\text{paired}}=1.28$, 95% CI [4.20, 7.52]).

Conclusions: Bilateral 1 Hz/20 Hz rTMS delivered in a naturalistic, clinical setting appeared to be well tolerated, safe, and effective in this sample of youth. Future efforts should consider control and comparison groups.

Keywords: rTMS, MDD, Adolescents, Naturalistic

P1.080

A COMPUTATIONAL MODEL TO GUIDE THE FUNCTIONAL DECOUPLING OF TWO BRAIN REGIONS WITH TRANSCRANIAL ALTERNATING CURRENT STIMULATION

Jesús Cabrera-Álvarez^{1,2}, Gianluca Susi^{1,2}, Jaime Sánchez-Claro³, Martín Carrasco², Alberto del Cerro², Fernando Maestú^{1,2}, Claudio

Mirasso³. ¹Complutense University of Madrid, Madrid, Spain; ²Polytechnic University of Madrid Center for Biomedical Technology, Madrid, Spain; ³Institute for Cross-Disciplinary Physics and Complex Systems, Palma de Mallorca, Spain

Abstract

Recent research has shown that cortical hyper-synchronization between frontoparietal areas in resting state could be an early biomarker of Alzheimer's disease (AD). It is expected that reducing this synchronization could slow down the development of AD typical symptoms. In this sense, non-invasive neurostimulation techniques are candidate tools to desynchronize distant regions of the brain. In specific, transcranial Alternating Current Stimulation (tACS) can influence the oscillatory dynamics of neuronal groups in the brain specially modifying signals' frequency and amplitude. Here we explore the possibility of using tACS to desynchronize frontoparietal brain regions: would this be possible? What frequencies would be the most suitable to minimize synchronization? Thus, we built ten personalized brain models in *The Virtual Brain* from magnetic resonance imaging and magnetoencephalography recordings. They are built of a structural connectivity network linking brain regions (from AAL2 atlas) and neural mass models per region to simulate electrophysiological dynamics. We applied tACS to stimulate those virtual brains areas on the parietal cortex (P3, P4 positions), using ROAST to calculate a current propagation model that determines how much electric field reaches each part of the brain. Our results show that it is possible to reduce cortical synchronization between two regions with tACS applying frequencies around the natural (i.e. in resting state) oscillation frequency of the stimulated region. These results could lead the experimental search of brain desynchronization with tACS on real subjects. Additionally, they strengthen the possibility of using that technique as an early intervention in Alzheimer's disease.

Keywords: Simulation, The virtual brain, Magnetoencephalography, tACS

P1.081

A DIGITAL TRANSCRANIAL MAGNETIC STIMULATOR FOR GENERATING ARBITRARY PULSE-SHAPES AND PATTERNS

Majid Memarian Sorkhabi¹, Karen Wendt², Jacinta O'Shea³, Timothy Denison^{2,4}. ¹MRC Brain Network Dynamics Unit, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; ²MRC Brain Network Dynamics Unit, Nuffield Department of Clinical Neurosciences, University of Oxford, UK; ³Wellcome Centre for Integrative Neuroimaging (WIN), Oxford Centre for Human Brain Activity (OHBA), University of Oxford Department of Psychiatry, Warneford Hospital, Warneford Lane, Oxford, UK; ⁴Department of Engineering Science, University of Oxford, UK

Abstract

Introduction: Transcranial magnetic stimulation (TMS) is a non-invasive and clinically effective therapeutic method to modulate the central nervous system. Current theoretical and experimental studies reveal that the temporal dynamics of the stimulus waveform affect recruiting neuronal targets and the neuromodulation dynamics. Despite three decades of research, the generation of bespoke magnetic stimuli is still a considerable challenge for TMS, which limits systematic investigations of stimuli waveform effects on neural behavior.

Objectives: We are introducing a second-generation modulation-based TMS device with advanced magnetic pulse shaping and patterns. As a special case, the implemented device imitates the conventional monophasic stimuli by the pulse-width modulation (PWM) method. In vivo experiments include the measurement of motor evoked potentials (MEPs) in response to conventional and modulation-based stimuli.

Methods: The proposed TMS pulse generator uses multiple modern power-electronic inverters. This modular topology enables flexibility, scalability and leads to the standardization of modules of the TMS solution. The PWM switching patterns permit maximum recovery of the energy transferred to the coil, which allows the generation of rapid arbitrary protocols.

Results: We present experimental measurements of different waveforms, such as monophasic, biphasic, and polyphasic shapes with peak coil current and the delivered energy of up to 6 kA and 250 J, respectively. The

modulation-based device enables the generation of arbitrary and individual stimulus waveforms in rapid repetitive protocols (up to 1 kHz) at the maximum device output. Previously conducted computational modelling, based on morphological neural models, indicates an equivalent effect on the human nervous system of our device as compared to conventional devices. Preliminary results of an in-human study examining this equivalence using MEPs are discussed.

Conclusion: A new TMS architecture enabling arbitrary pulse shapes and patterns for brain modulation will be made available to the research community.

Keywords: TMS, TMS pulse generator, Neurostimulator, Arbitrary Pulse-shape

P1.082

POLARITY DEPENDENT EPICRANIAL DIRECT CURRENT STIMULATION OVER THE CEREBELLUM SUPPRESSES HARMALINE TREMOR IN RATS

Ahmad Khatoun, Boateng Asamoah, Myles Mc Laughlin, KU Leuven, Leuven, Belgium

Abstract

Background: Essential tremor (ET) is a neurological movement disorder that manifest a tremor in different body parts, but mainly the hands, leading to movement disability and social withdrawal. It is the most prevalent movement disorder with more than half of the patients not achieving satisfactory tremor reduction using medication. Thus, deep brain stimulation (DBS) becomes a standard treatment. However, DBS is highly invasive with stimulation electrodes being implanted in deep brain regions. To overcome that, the motor and the cerebellar cortex have been suggested as an alternative, more superficial, targets for stimulation. While results from an epidural cortical stimulation study were promising, this technique remains highly invasive requiring a craniotomy to implant the electrodes. Recently, we proposed a novel minimally invasive neuromodulation technique, epicranial current stimulation (ECS), that can deliver strong cortical current through subcutaneous electrodes. Here, we used Harmaline ET model in rats to test the ability of direct current epicranial current stimulation (DC-ECT) in reducing tremor.

Methods: Rats were implanted with discrete epicranial electrodes placed over the motor cortices, the cerebellum and the frontal cortex. After surgery recovery, the rats were injected with Harmaline (15 mg/kg) to induce tremor which was measured using an accelerometer. Then DC-ECT was applied and different electrodes configurations were used to test the effects of stimulation on tremor suppression.

Results: Our results show that DC-ECT suppresses Harmaline tremor in rats. Cerebellar stimulation showed a significant decrease in tremor compared to no stimulation. This effect was polarity dependent with anodal stimulation showing tremor reduction but not cathodal one.

Conclusion: DC-ECT is a very promising neuromodulation technique that can suppress harmaline induced tremor in rats. Given its minimally invasive nature, it could be an alternative to DBS for ET patients.

Keywords: epicranial stimulation, Essential tremor, Harmaline, Direct current stimulation

P1.083

PROTOCOL OF TRANSCRANIAL MAGNETIC STIMULATION AND PHOTOBIOMODULATION INTEGRATION

Li-Da Huang^{1,2}, Kung-Bin Sung³. ¹University of Texas at Austin, USA; ²CytonSys Inc, USA; ³National Taiwan University, USA

Abstract

Transcranial magnetic stimulation (TMS) is a noninvasive procedure that uses magnetic fields to stimulate nerve cells in the brain to improve symptoms of depression and other disorders. TMS is typically used for

major depression and no other treatments have been effective. Some studies have shown promising results, but no conclusively positive results. The recent studies demonstrated that the positive outcomes of the TMS are much more consistent among the group of the participants with higher cognitive functions. If the cognitive functions of the participants are lower, then the TMS treatments will not be effective. Therefore, this research focuses on enhancing the cognitive functions of the brain before applying the TMS treatment. The PhotoBioModulation(PBM), or Low Level Light Therapy(LLLT), has been proven to be an effective and safe approach to enhance cognitive functions, especially when applied on the prefrontal cortex region. 810nm or 1064nm of near infrared light is mostly adopted for this purpose. In this study, a protocol integrating the PBM and the TMS is proposed. The power density, location, area, and exposure time of the PBM is clearly defined and easily deployed to be integrated with the existing TMS treatment protocols. After photons activate the prefrontal cortex, which dominates the cognitive functions, the TMS is applied on the dorsolateral prefrontal cortex region. The advantage of this integrated protocol is its safety and ease to be deployed in existing clinical settings. The pilot study demonstrated very promising results.

Keywords: Transcranial magnetic stimulation (TMS), Photo-BioModulation(PBM), Low Level Light Therapy(LLLT), Depression

P1.084

ORIENTATION-DEPENDENT EFFECTS OF TRANSCRANIAL ALTERNATING CURRENT STIMULATION (TACS) ON SPIKE TIMING IN AWAKE NON-HUMAN PRIMATES

Harry Tran, Ivan Alekseichuk, Sina Shirinpour, Blair Vail, David Maisson, Benjamin Voloh, Jan Zimmermann, Alexander Opitz. University of Minnesota, Minneapolis, MN, USA

Abstract

Transcranial alternating current stimulation (tACS) is a non-invasive method to modulate ongoing neural activity in the brain. Previous work shows that external oscillations entrain neural firing activity in a phase- and dose- dependent manner. Thus, tACS holds promise as a new treatment for people suffering from brain disorders. However, neural responses to oscillating electric fields exhibit variability and we hypothesize that they largely depend on the neocortical column orientations relative to the induced electric fields.

We first perform a computational study to investigate the relationship between tACS and neural entrainment in a set of 25 morphologically realistic neocortical neurons exhibiting ongoing spiking activity. The electric field was aligned with the somato-dendritic axis of the pyramidal cells and intensities were between 0.1 mV/mm and 3 mV/mm. We then computed the phase-locking value (PLV) of spikes times across neurons and field strengths. We found that 1) pyramidal neurons are more entrained than interneurons resulting in a higher phase-locked spiking to the applied oscillation (pyramidal cells $n=15$, 0.0788 ± 0.0821 and interneurons $n=10$, 0.0495 ± 0.0414 at 1mV/mm) and 2) pyramidal cells are more preferentially entrained when parallel to the electric field direction. Second, we perform in-vivo recordings of single-unit activity in awake non-human primates while applying tACS in 3 orientations (Anterior-Posterior, Left-Right and diagonal orientations) and 2 intensities for each of them (0.4mA and 0.8mA). We record neuronal activities using a 128-channel amplifier at 30 kHz sampling rate. Preliminary findings in one macaque (8 y.o., male) show that neurons ($N=159$) exhibit significant entrainment to tACS with strong orientation preference (Rayleigh test $p \leq 0.01$).

Overall, these findings advance our mechanistic understanding of tACS effects and highlight the importance of neuronal architecture on the susceptibility to the external electric fields. Highlighting neural directional sensitivity represents a milestone for understanding brain networks interactions.