P1.002

OPTICAL IMAGING OF SUBCELLULAR RESPONSES TO ELECTRIC FIELD STIMULATION USING GENETICALLY ENCODED INDICATORS OF NEURAL ACTIVITY

Aman Aberra, Michael Hoppa. *Department of Biological Sciences, Dartmouth College, USA*

Abstract
Transcranial electric and magnetic stimulation techniques allow for noninvasive delivery of electric fields (E-fields) to the brain, providing powerful approaches to probe brain function and treat psychiatric and neurological disorders. However, developing effective neuromodulation protocols for specific applications is difficult given the massive stimulation parameter space and persistent questions about how E-fields affect neural activity at the cellular and subcellular level. Electrical recording techniques suffer from the stimulus artifact obscuring activity during the stimulus and have limited access to fine axonal and dendritic processes. To overcome these limitations, we used genetically encoded voltage (Archon2) and glutamate (GluSnFR3) indicators to measure membrane polarization, AP propagation, and modulation of synaptic transmission by spatially uniform E-fields in dissociated hippocampal neuron cultures. We used high-speed (1−2 kHz) voltage imaging and sub-frame interpolation to estimate spatial propagation of action potentials induced by pulsed, suprathreshold E-field stimulation. Varying the E-field direction altered the site of AP initiation and sensitivity to E-field direction varied between cells. Using subthreshold, dc pulses in the presence of TTX and TEA, we measured the distribution of steady-state membrane polarization. Neurons exhibited biphasic polarization distributions, with depolarization at the cathodal and hyperpolarization at the anodal side of the E-field, in line with theoretical predictions. Finally, we tested the effect of subthreshold, dc stimulation on glutamate release evoked by suprathreshold E-field pulses within individual presynaptic boutons. Subthreshold pulses acutely facilitated or suppressed the average magnitude of release in a subset of boutons as a function of intensity and polarity. These results demonstrate the utility of optical indicators of neural activity for studying the acute, subcellular effects of transcranial brain stimulation techniques, which, in combination with experimentally constrained computational models, can guide development of novel stimulation protocols.
Research Category and Technology and Methods
Basic Research: 10. Transcranial Magnetic Stimulation (TMS)
Keywords: Transcranial electric stimulation, Transcranial magnetic stimulation, Voltage imaging, Synaptic transmission

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Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

P1.003

QUANTITATIVE EEG (qEEG) IN PATIENTS WITH BIPOLAR PSYCHOTIC DEPRESSION AND UNIPOLAR PSYCHOTIC DEPRESSION UNDER ELECTROCONVULSIVE THERAPY (ECT)

Joana Bravo [1], Amílcar Silva dos Santos [2,1], António Melo [1], Miguel Sales [3], Pedro Mendonça [4], Zhanna Nagornova [5], Grigory Beljakov [5], Natalia Shemyakina [5], Mikhail Lebedev [6]. [1] *Hospital Vila Franca Xira, Portugal;* [2] *Hospital Cuf Tejo, Lisbon, Portugal;* [3] *Centro Hospitalar do Oeste, Portugal;* [4] *Faculdade de Ciências, Universidade de Lisboa, Portugal;* [5] *Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences, St. Petersburg, Russia;* [6] *Skolkovo Institute of Science and Technology Moscow, Russia*

Abstract
Introduction: In the last 21 years, there has been an increase in studies on quantitative electroencephalogram (qEEG) in psychiatry. Patients with unipolar and bipolar depression show different brain wave patterns. However, there is no consensus on the findings. In this study, we aimed to clarify some qEEG changes in patients with unipolar psychotic depression (UPD) and bipolar psychotic depression (BPD) during the ECT course.
Methods: 10 patients undergoing treatment with ECT were considered. Of the 128 total ECT sessions, 34 sessions from six patients included had valid EEG recordings (3 patients with UPD and 3 with BPD, some with catatonic features). They underwent bifrontal ECT on a Thymatron IV device. EEG data were digitally recorded from two frontal leads with a Thymatron device and the Genie software. Data were analyzed with WinEEG soft package. EEG activity was divided into 4 phases: 1) background (resting state); 2) anesthesia; 3) ECT-induced stimulation/seizure, and 4) recovery. Regression analysis was performed for each phase through the sessions. The following EEG power spectrums were analyzed: delta (1.5-3.75 Hz), theta (4-7.75 Hz), alpha1 (8-9.75 Hz), alpha2 (10-13 Hz), beta1 (13.25-18 Hz), and beta2 (18.25-30 Hz).
Results: Patients with psychotic unipolar depression showed an increase in the power spectrum of beta1 and/or beta2 in the resting phase over time ($p < 0.05$, linear regression). This increase was linked with clinical improvement. Patients with bipolar psychotic depression did not show this pattern.
Conclusion: Clinical improvement in patients with unipolar psychotic depression was linked to an increase in the beta power spectrum. The same does not occur in bipolar patients. One possible reason for this finding might be that some bipolar patients have an increased basal beta activity. However, more studies are needed to assess the significance of our findings.
Research Category and Technology and Methods
Clinical Research: 15. Electroencephalography (EEG)
Keywords: Quantitative electroencephalography, Electroconvulsive Therapy, Bipolar psychotic depression, Unipolar psychotic depression

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P1.004

SUDDEN AND TRANSIENT BLOCK OF LEFT BRAIN HEMISPHERE ACTIVITY IN CATATONIC PATIENTS UNDERGOING ELECTROCONVULSIVE THERAPY (ECT)

António Melo [1], Joana Bravo [1], Amílcar Silva dos Santos [2,1], Ricardo Gusmão [3], Elsa Lara [2]. [1] *Hospital Vila Franca de Xira, Portugal;* [2] *Hospital Cuf Tejo, Lisbon, Portugal;* [3] *EPI Unit, Public Health Institute, University of Porto, Porto, Portugal*

Abstract
Introduction: In the last 21 years, there has been an increase in studies on visual and quantitative EEG (qEEG). Although new findings have been reported, such as the extreme delta brush waves in anti-NMDA receptors encephalitis, there are still undocumented visual EEG alterations. In Psychiatry, these new findings are harder to detect because most patients do not undergo routine EEG. In this work, we report for the first time an EEG finding of a sudden and transient block of left brain hemisphere activity in two patients who underwent treatment with ECT.
Methods: The EEG activity of the two patients undergoing ECT treatment was recorded using a Thymatron System IV device. Patient number 1: 23 year-old man with severe major depressive disorder with psychotic features and catatonia. Patient number 2: 48 year-old woman with bipolar disorder with mixed features and catatonia.
Results and Discussion: The EEG recording of these two patients during their ECTs sessions showed a sudden and transient block (or arrest) of the left brain hemisphere activity. These findings are not attributed to background noise, electrode disconnection or device malfunction. Also, they were detected in two different patients. In patient 2 in two distinct admissions, two hospitals, utilizing two devices and by two different observers. After clinical improvement, these EEG alterations were not detected.
Conclusion: To our knowledge, this is the first report of a sudden and transient block of the left brain hemisphere activity in psychiatric patients. Although the exact meaning of this finding remains unknown, a comparison can be made between this transient bradypsychia/block (arrest) of brain activity and bradycardia events in cardiology. We acknowledge the need for further studies to better understand these findings, particularly studies addressing different EEG abnormalities and the clinical traits they are associated with.

Research Category and Technology and Methods
Clinical Research: 2. Electroconvulsive Therapy (ECT)
Keywords: sudden block of left hemisphere activity, electroconvulsive therapy, electroencephalography, catatonia

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P1.005

COMPARISON OF THRESHOLDING METHODS FOR TRANSCRANIAL MAGNETIC STIMULATION OF PRIMARY MOTOR CORTEX

Boshuo Wang [1], Angel Peterchev [1], Stefan Goetz [1,2]. [1] *Duke University, Durham, NC, USA;* [2] *University of Cambridge, Cambridge, UK*

Abstract
Transcranial magnetic stimulation (TMS) is a noninvasive brain stimulation method with research and clinical applications. However, determining TMS thresholds is a challenging procedure due to the high trial-to-trial variability of the stimulation responses. We examine existing methods and their variations, introduce new methods from other fields, and analyze their speed and accuracy for obtaining TMS motor thresholds.
Existing methods included relative-frequency approximation of the probability definition of motor threshold, for example the five-out-of-ten method, and adaptive threshold search using a probabilistic motor threshold model and maximum-likelihood estimation. We explored variations in the estimation and stepping procedure and incorporated population-level prior information to improve the performance of the latter. A Bayesian estimation method was introduced from psychophysics, which updated the threshold's probability density function iteratively using information from the TMS responses. We also adapted non-parametric stochastic root-finding methods with a range of stepping rules and convergence criteria. A virtual test bed was used to benchmark all methods to characterize their threshold estimation error.
The conventional relative-frequency methods had good accuracy on the population level but required a large number of stimuli and had wide error distributions for individual subjects. Thresholds were obtained much faster using parametric estimation methods, with accuracy depending on the specific estimation and stepping rules; including population-level prior information improved their performance significantly. Stochastic root-finding methods had speed and accuracy similar to adaptive estimation methods but their implementation was much simpler and not reliant on an underlying model.
Motor thresholding methods exhibit a wide range of performance, with two-parameter maximum-likelihood estimation, Bayesian estimation, and stochastic root-finding methods needing fewer TMS stimuli than established methods to determine thresholds accurately.
Research Category and Technology and Methods
Basic Research: 10. Transcranial Magnetic Stimulation (TMS)
Keywords: transcranial magnetic stimulation, threshold search, parametric estimation

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P1.006

HIGHLY FLEXIBLE ELECTRONICS FOR SELECTIVE NONINVASIVE STIMULATION THROUGH FREE PULSE SHAPING IN TRANSCRANIAL MAGNETIC STIMULATION AND MAGNETOGENETICS

Jinshui Zhang [1], Zhongxi Li [1], Boshuo Wang [1], Angel Peterchev [1], Stefan Goetz [1,2]. [1] *Duke University, Durham, NC, USA;* [2] *University of Cambridge, Cambridge, UK*

Abstract
Magnetic stimulation techniques get increasingly popular for noninvasive brain stimulation. Magnetic fields can easily permeate scalp and skull to non-invasively stimulate neurons in the brain. However, the magnetic stimulation has limited focality, which may be improved by magnetogenetics or pulse shaping in transcranial magnetic stimulation (TMS).
Magnetogenetic neural stimulation activates artificial magnetically-sensitive combinations of ion-channels with nanomagnetic elements and can be designed with different frequency sensitivity to switch between them [1]. Different shapes of TMS pulse were found to shift the activation balance between various neuron populations, introducing a level of selectivity. Therefore, TMS can improve stimulation functional focality through customized selective pulse shape.
To exploit these effects, both TMS and magnetogenetics need electronic devices with high power and wide bandwidth to replace previous oscillator-based designs to enable free high-quality control of the output waveform. However, conventional power electronics can hardly deal with the trade-off between bandwidth and power level. We address this challenge with the combination of highly flexible modular circuit topologies and wide-bandgap semiconductors [2, 3].
For multichannel magnetogenetics, we designed a system combining latest gallium-nitride transistors with a rapidly reconfigurable circuit topology, which features an unusually high spectral bandwidth (~5 MHz), considerably high output power (>10 kVA), and little distortion to avoid co-activation. The system can generate any output shape within the bandwidth without limitation to fixed frequencies and can concurrently mix several channels. To implement free pulsing shape for TMS, we applied silicon-carbide transistors to reach even higher instantaneous pulse output power (> 5 MVA) and still high bandwidth (>100 kHz). This modular pulse synthesizer TMS (MPS-TMS) device can synthesize all existing and diverse user-defined pulse shapes, as well as combine pulses with different strengths and shapes in pulse sequences. Unprecedented stimuli sequences will be present.
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Research Category and Technology and Methods
Translational Research: 10. Transcranial Magnetic Stimulation (TMS)
Keywords: transcranial magnetic stimulation, magnetogenetics, wide-bandgap power electronics, stimulator design

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P1.007

THERAPEUTIC USE OF CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) IN A SARDINIAN FAMILY AFFECTED BY SPINOCEREBELLAR ATAXIA 38 (SCA 38)

Angela Sanna [1], Massimiliano Pau [2], Giuseppina Pilia [1], Micaela Porta [2], Giulia Casu [2], Valentina Secci [1], Emanuele Cartella [1], Antonio Coiana [3], Alessandro Demattia [1], Stefano Firinu [1], Maurizio Urru [3], Antonio Milia [1], Eleonora Cocco [3], Paolo Tacconi [3]. [1] *Neurologia riabilitativa, ospedale SS Trinità, ASL 8, CAGLIARI, Italy;* [2] *Department of Mechanical, Chemical and Materials Engineering, University of Cagliari, Cagliari, Italy;* [3] *Centro Sclerosi Multipla ospedale Binaghi, ASL 8, Cagliari, Italy*

Abstract
Non-invasive brain stimulation (NIBS) has shown therapeutic potential for cerebellar ataxias. Cerebellar transcranial direct current stimulation (tDCS) was applied to 7 patients affected by Spinocerebellar Ataxia 38 (SCA38), a rare autosomal dominant disease caused by mutations in the ELOVL5 gene which encodes an enzyme involved in the synthesis of very long fatty acids, specifically expressed in cerebellar Purkinje cells. Only six families have been identified worldwide so far, one of which is of Sardinian descent. Seven affected members of the Sardinian family were exposed to 15 sessions of anodal cerebellar tDCS and clinical symptoms were evaluated before and after treatment by Modified International Cooperative Ataxia Rating Scale (MICARS). Robertson dysarthria profile was used to better evaluate the speech impairment and any possible improvement induced by tDCS. Moreover, we employed a single wearable inertial sensor located in the low back to objectively assess spatio-temporal parameters of