

electroencephalography (TMS-EEG), which can provide information on local and global functional reactivity. The current study used TMS-EEG to characterise the differences in neural plasticity responses, and its relation to cognitive performance in younger, older and MCI participants.

Methods: 20 healthy younger adults, 20 healthy older adults and 9 individuals with MCI participated in the study. All completed a neuropsychological battery, computerised cognitive tasks (n-back and Cogstate subtests) and TMS-EEG (50 single pulses, 110%RMT, 0.2Hz \pm 5% jitter), prior to delivery of transcranial direct current stimulation (tDCS). 20 minutes 1mA tDCS was administered to the left dorsolateral prefrontal cortex (DLPFC), with TMS-EEG and cognitive tasks repeated across multiple time-points post-tDCS.

Results: Preliminary analyses show a significant effect of time for TMS-Evoked Potentials (TEPs) in the N120 amplitude in the left frontal region ($p < .01$). Post-hoc analysis revealed a reduction in the T20 compared to Pre and T5 time points ($ps < .05$) in younger and older adults. Behavioural measures showed n-back performance improved over time. In older adults, the N120 amplitude at T20 positively correlated with reaction time on the n-back task post-tDCS ($p < .05$).

Discussion: Novel brain stimulation methods were used to characterise neurophysiological changes in aging and MCI. Preliminary results revealed reduction in N120, a marker of inhibition, post-tDCS in younger and older, but not MCI. Older adults who showed greater inhibition demonstrated faster reaction times on a working memory task. This suggests varied response and outcome to brain stimulation across the lifespan.

Keywords: TMS-EEG, Transcranial Direct Current Stimulation (tDCS), Cognitive Aging, Mild Cognitive Impairment (MCI)

[0390]

EFFECT OF SINGLE-SESSION TDCS ON COGNITION IN SCHIZOPHRENIA: A RANDOMIZED DOUBLE-BLIND CROSS-OVER STUDY

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Introduction: Cognitive impairment is an integral feature of schizophrenia and a major predictor of functional outcome. Combining cognitive retraining with transcranial direct current stimulation (tDCS) has been postulated to address these deficits. The effect of combining a neuropsychological/psychophysiological task with tDCS, called "online-tDCS" for cognitive enhancement in schizophrenia has not been rigorously evaluated yet. This proof-of-concept study aimed at evaluating the effect of a single session of "online-tDCS" on working-memory (WM) and other cognitive functions.

Methods: The effect of 20 minutes anodal stimulation of left dorsolateral prefrontal cortex and cathodal stimulation of left temporoparietal junction during Sternberg's task (a WM task) on the accuracies and reaction times of nBack test (measuring WM), digit symbol substitution test (DSST) (assessing attention and processing speed) and emotional matching and labeling test (E-MALT) (evaluating social/emotional cognition) were measured. Among the 23 schizophrenia patients with cognitive deficits, 19 completed the study; 9 patients were randomized to receive online-tDCS sessions and 10 to offline-tDCS sessions. All patients received one session each of true and sham tDCS, 2-7 days apart in a randomized counterbalanced double-blind cross-over design.

Results: Repeated measures ANOVA revealed a significant interaction effect between type of tDCS (Online vs Offline) and trueness of tDCS (true vs sham), such that the reaction time of nBack tests (0,1&2-Back) improved in offline-true and online-sham tDCS session only ($F=6.12, p<0.05$) ($F=5.01, p<0.05$) ($F=5.48, p<0.05$). No significant changes were noted in DSST and E-MALT.

Discussion: Better performance after offline-true tDCS session as well as online-sham tDCS session meant both tDCS and sternberg's task influenced in enhancing the WM performance across the session. Paradoxical failure of online-tDCS to enhance WM performance may be related to the aberrant plasticity in Schizophrenia which might attain a transitional ceiling on combining the two plasticity modulators. The transferability of improvement to other cognitive domains could not be appreciated.

Keywords: Online-tDCS, Cognitive deficits, Schizophrenia, Working memory

[0391]

PHASE OF BRAIN OSCILLATIONS DETERMINES THE DIRECTION OF INDUCED PLASTICITY IN REAL-TIME EEG-TRIGGERED TMS

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Introduction: Can the large intra- and inter-individual variability of the effects induced by different repetitive TMS protocols be explained by the dynamics of ongoing activity at the time of stimulation? This study examined the influence of endogenous sensorimotor 10 Hz alpha rhythm on corticospinal plasticity

Methods: A custom-built millisecond-accuracy real-time signal processing system was used to trigger repetitive TMS bursts according to the instantaneous phase of sensorimotor rhythm. Each burst was triggered either during the EEG surface positive peak or the surface negative peak of the local mu-rhythm. Single TMS pulses were applied before and after the intervention to assess the plasticity effect on corticospinal excitability.

Results: A sequence of 200 repetitive TMS bursts (triple pulses of 100 Hz) delivered over a period of ca. 200 seconds resulted in a long-term (>30 min) increase of corticospinal excitability if triggered consistently at the EEG surface negative peaks of the mu-alpha oscillation, whereas the same TMS bursts triggered at the positive peaks decreased corticospinal excitability.

Discussion: TMS triggered by a specific phase of an endogenous oscillation is a suitable tool to study the spatiotemporal properties of cortical dynamics and to induce reliable neuromodulatory effects in the human brain. In light of the results of this study, a realisation of the full therapeutic potential of brain stimulation in the treatment of brain network disorders will require a closed-loop approach that synchronises each stimulus with the individual patient's instantaneous brain state.

Keywords: real-time, closed-loop, neuromodulation

[0394]

MODULATION OF PHYSIOLOGIC ARTIFACTS DURING CONCURRENT TDCS AND EEG

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Introduction: The field of non-invasive brain stimulation (NIBS) has benefited from integration with imaging including magnetic resonance imaging (MRI) and electroencephalography (EEG). Several studies have reported on concurrent tDCS and EEG, and used signal processing of varying complexity (e.g. high-pass filtering to ICA) to remove "non-physiologic stimulation artifacts" - namely artifacts arising from non-ideal stimulation and recording amplifier performance. None has compressively addressed "physiologic artifacts" which are defined here as non-stationary changes in artifacts resulting from interactions between the stimulation induced voltage and body. We identified and systematically characterized a series of tDCS-induced physiologic and nonphysiologic artifacts during concurrent EEG and High Definition (HD)-tDCS with physiological monitoring, and adapted MRI-derived computational modeling to corroborate physiologic EEG findings.

Methods: Subjects underwent three main simulation routines including 1) repeated, randomized, brief stimulation intensities over varied montages; 2) single intensity, randomized stimulation devices over a single montage; and 3) single device stimulation over a long duration with varied montages. Dosages ranged from 0.5-2.0 mA over 0.5-10 mins.

Results: We identify and characterize three classes of artifacts including inherent stimulator artifacts, inherent physiologic artifacts, and non-inherent artifacts. Physiologic artifacts included 1) cardiac distortion; 2) ocular motor distortion; 3) movement (myogenic) distortion. The power and voltage distribution of these artifacts were modulated in a tDCS montage, intensity, and polarity specific manner.

Discussion: Contamination from these physiologic artifacts cannot be accounted for by typical control experiments (e.g. EEG changes that are dose specific). High-resolution finite element models explained artifact-based modulation of the tDCS voltage by artifact-specific impedance changes. Importantly a) physiologic artifacts are universal, they are nominally independent of device and so exist regardless of devices; b) the broadband nature of contamination may confound a range of experiments (e.g. oscillations, ERP); c) removal of artifacts requires recognition of their peculiar dynamic and individualized nature.

Keywords: tDCS, EEG, Physiological Artifacts, Computational FEMs

[0395]

ON CERTAIN POSSIBILITIES OF THE NECK NEURAL STRUCTURES NEURO-ELECTROSTIMULATION METHOD

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Introduction: We present a new non-invasive neuro-electrostimulation method of the central nervous system that affects neural structures of the neck by the field of spatially distributed current pulses.

Methods: The field of current pulses is generated in the "SIMPATOCOR-01" device and appears between its two multi-channel electrodes. The peculiarity of this field is the coordination of its amplitude-frequency characteristics with rates of excitation conduct in the myelinated and unmyelinated nerve fibers. Targets of the field are nerve structures located in the upper third of the neck. The usage of the cervical plexus as a target for the neuro-electrostimulation allows one to stimulate the reticular formation through the spinal afferent fibers. Reticular formation is involved in the sensory processing and motor controls. Impact on the branches of the vagus and glossopharyngeal nerves allows one to influence on the central nucleus of parasympathetic regulation through afferent pathways. Stimulation of the gray matter of the brain stem is able to be spread on the thalamic and striatal structures. This, in turn, will have an impact on cognitive processes, memory in particular. Stimulation of the sympathetic trunk cluster will allow to influence the sympathetic innervation of the cerebral arteries of small and medium caliber, as well as on the sympathetic spinal nucleus.

Results: The proposed system of neuro-electrostimulation is capable of modulating the autonomic processes, affecting motor control and cognitive function, activating the processes of neuroplasticity. Our previous experimental studies on laboratory rats have shown the ability to control segmental and suprasegmental levels of autonomic regulation. Subsequent clinical trials of the SPECT scans confirmed the functional and metabolic changes in brain tissues after stimulation for patients with epilepsy.

Discussion: For clarification of the neuro-electrostimulation mechanisms clinical effects it is necessary to conduct fundamental studies by means of neurovisualization methods (fMRI, PET).

Keywords: neuro-electrostimulation, neuroplasticity, spatially distributed current pulses field

[0398]

POWER NAP STIMULATION TO ENHANCE MEMORY CONSOLIDATION IN AGING AND NEURODEGENERATIVE DISEASE

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Sleep-related consolidation of declarative memories, as well as associated neurophysiological events such as slow oscillatory and spindle activity, deteriorate in the course of aging. This process is accelerated in neurodegenerative disease. Slow oscillatory transcranial direct current stimulation (slow tDCS) during sleep has been shown to enhance frontal slow delta, and frontal spindle activity and in parallel improve memory consolidation in young subjects [1]. Here, we investigated whether slow tDCS applied to older adults, and to patients with mild cognitive impairment (MCI), possibly a precursor of Alzheimer's disease, during an afternoon nap exerts similar effects.

Eighteen healthy older adults [2], and 13 patients with MCI [3], were assessed using visuo-spatial and verbal memory tasks before and after a 90-min nap either comprising weak so-tDCS at 0.75 Hz over fronto-central location or sham stimulation in a within-subject design. Electroencephalographic activity was recorded throughout the naps and immediate effects of stimulation on brain activity were evaluated. Here, spectral power within three frequency bands of interest were computed, i.e., slow oscillatory activity, slow spindle and fast spindle activity; in 1-min stimulation-free intervals following 5 stimulation blocks.

So-tDCS significantly increased frontal slow oscillatory activity as well as fast spindle activity in both groups, and improved picture memory retention after sleep. This effect was significant in the healthy older group, and trend-wise ($p = 0.062$) in MCI patients. No significant effect was noted for verbal memories.

These findings may indicate a novel strategy to counteract cognitive decline in aging in a convenient manner during brief daytime naps.

Keywords: aging, mild cognitive impairment, sleep-related memory consolidation, oscillatory tDCS

References

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[0399]

LONG-TERM PAIRED ASSOCIATIVE STIMULATION - A POTENTIAL THERAPY FOR SPINAL CORD INJURY PATIENTS

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Introduction: Therapeutic strategies for spinal cord injury (SCI) aim at the partial sparing or restoring of the corticospinal tract (CST) - thus, approaches that strengthen the weak CST are crucial. Transient plastic changes in CST can be induced through paired associative stimulation (PAS), the synchronization of transcranial magnetic stimulation (TMS) with electrical peripheral nerve stimulation (PNS). The TMS-PNS inter-stimulus interval (ISI) determines whether PAS leads to motor-evoked potential (MEP) potentiation or depression, and conventional PAS protocols require precise determination of ISIs.

It was previously unknown whether PAS can have clinically relevant effects after SCI. Long-term PAS might alter conduction of neural fibers over time, and determination of ISIs in patients may be challenging. We sought to design a PAS protocol effective at wide range of ISIs, and to apply it to SCI patients.

Methods: We tested PAS consisting of high-intensity TMS and high-frequency PNS in five subjects at five different ISIs. In addition, we recruited two pilot SCI patients with motor-incomplete chronic injuries. The patients received PAS for 20–24 weeks.

Results: Our protocol induced potentiation of MEP amplitudes in all subjects at all intervals. TMS and PNS alone did not result in MEP potentiation. The paraplegic patient, paralyzed below the knee level, regained plantar-flexion and dorsiflexion of the ankles of both legs. The tetraplegic patient regained grasping ability. The newly acquired movements could be performed by the patients for at least 1 month after the last session.

Our preliminary data in several additional chronic tetraplegic patients indicates that the method is effective, safe, and superior over PNS-only stimulation.

Discussion: This variant of PAS might be feasible as a rehabilitation of neurological patients. Further study is needed to confirm whether long-term PAS can be used in rehabilitation after SCI by itself and, possibly, in combination with other therapeutic strategies.

Keywords: paired associative stimulation, spinal cord injury, long-term potentiation