Abstract Book

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Keynotes

Keynote I

Mutual Benefits of Combining Neuroimaging with Neuromodulation.

Vincent P. Clark

In this talk, I will review our successes and failures in combining neuromodulation with neuroimaging. In previous work, brain imaging has made great strides in understanding the mechanisms of normal and abnormal human brain function. However, this research has been mostly observational, unable to prove causation, and has provided few real-world benefits for treating brain and mental illness. By contrast, brain stimulation offers the hope of developing new treatments, but has been plagued by failed replications, uncertainty regarding its mechanisms and the effects of individual variability, and makes a nearly infinite variety of protocols available, while offering few methods for selecting among them. While such problems are difficult to solve independently, the combination of neuuroimaging and neuromodulation may provide many mutual benefits. Several studies from our laboratory illustrate these advantages, including the use of fMRI to guide tDCS placement, producing large enhancements in visual learning and attention, using closed-loop EEG to guide tACS to improve sleep quality and memory consolidation, using MEPs, EEG, MEG or MRS to infer the mechanisms of action of stimulation, including the effects of tDCS on hallucinations in schizophrenia and transcranial ultrasound (TUS) effects on brain excitability, among others. Possible future directions for this combined research will be discussed.

Keynote II

Synaptic plasticity in rodent prefrontal cortex neurons.

Satoru Otani

It is thought that the main cellular substrate for long-term memory in the brain is a lasting increase/decrease of synaptic connectivity between neurons, referred to as “synaptic plasticity”. Synaptic plasticity has been rigorously studied in the hippocampus, a well-known structure for memory formation. We have focused on synaptic plasticity in the prefrontal cortex. The prefrontal cortex is responsible for the high-order cognitive function, and it enables our planned strategic and goal-directed behaviors. In this lecture, the function of prefrontal cortex will be briefly introduced. We then discuss how the prefrontal function relies on synaptic plasticity. We will further show our experimental data to explain how rodent prefrontal neurons support synaptic plasticity, with the special emphasis made on the critical neurotransmitter dopamine.

Keynote III

Transcranial direct current stimulation neural mechanisms to prevent and treat opioid-induced hyperalgesia.

Felipe Fregni

Opioid misuse leading to dependence is a major health issue. Recent evidence has pointed out that chronic use of opioids leads to central sensitization and can contribute

to the maintenance of pain. In this context, noninvasive brain stimulation can be used not only to treat opioid induced hyperalgesia, but also to prevent it. In this lecture, I will discuss the role of transcranial direct current stimulation (tDCS) in preventing and treating opioid-induced hyperalgesia pain and opioid dependence. Despite the limited number of studies, preliminary encouraging evidence regarding the analgesic role of tDCS and its effects on the descending inhibitory pain system supports additional testing.

Keynote IV

Leveraging neuroimaging, computational modeling and tDCS to remediate working memory decline in older adults.
Adam J. Woods

Session Talks

OS1-1

Title
New Technology for Transcranial Magnetic Stimulation: Advancements in Targeting, and Paradigms.

Chaired by Pantelis Lioumis

Abstract
During this session, presenters will discuss several novel ways to improve the accuracy, specificity and control of transcranial magnetic stimulation (TMS). The future will bring multi-locus TMS devices, the use of EEG to guide stimulation sequences in closed-loop TMS, silent stimulators, and new algorithms to integrate with TMS anatomical (MRI and MRI tractography) and electrophysiological (EEG) information.

Speakers

Risto Ilmoniemi (Aalto University)

Multi-locus TMS

By combining transcranial magnetic stimulation (TMS) and electroencephalography (EEG), one can produce a bidirectional coupling to the brain that can serve as the basis for closed-loop brain stimulation. A major obstacle in closed-loop stimulation has been the difficulty and slow speed of changing TMS targets, as this has required the physical movement of the stimulator coil. Our plan is to develop multi-locus TMS (mTMS) that will allow one to change the location and pattern of the stimulating electric field (E-field) arbitrarily quickly without physical movement of the coil. We will be able to connect to the brain noninvasively at the time scale of neuronal activity. We have already demonstrated new research paradigms with a simple mTMS device covering a small part of the cortex. Our technology with multiple coils in different layers appears to be superior to side-by-side coil architectures. We have also developed techniques for the recording of EEG and for separating EEG signals and artifacts from each other. We aim at extracting information about the state of the brain from EEG in real-time and to use this information to guide the TMS targeting sequence, for example, when scanning the brain or when performing therapy. We foresee current TMS treatment practices that usually target just one brain area to be replaced by multi-locus stimulus sequences that are automatically adjusted during the treatment based on brain responses and other measurable indicators of the evolving state of the patient's brain.

Pantelis Lioumis (Aalto University)

TMS and EEG

Thomas Picht (Charité Hospital)

Use of diffusion tractography with TMS

Lari Koponen (Duke University)

qTMS: developing transcranial magnetic stimulation device and coil with reduced acoustic noise

Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation method used in research, diagnostics, and treatment. A TMS device activates a targeted cortical location with focused magnetic field pulses that are generated by driving several thousand amperes through a TMS coil. In addition to desired neurostimulation, the current induces electromagnetic forces that excite mechanical vibrations of the TMS coil. This produces a brief but very loud clicking sound of up to 140 dB, which poses a risk for hearing damage and causes unwanted neural activation of the auditory brain circuits. The latter compromises the quality of simultaneous brain-activity recordings and potentially effects unintended neuromodulation. To mitigate these side effects of TMS, we aim to minimize the acoustic noise generated by TMS.
We aim to minimize the noise by developing (1) a quiet TMS (qTMS) device which pushes the dominant frequency of the TMS pulse to higher frequencies above the human hearing and (2) a qTMS coil that minimizes the conversion of electromagnetic energy to emitted acoustic energy. Either of the two can be combined with conventional TMS technology, or the two can be combined for maximum reduction of the acoustic noise. In this talk, key concepts behind the qTMS device and our latest qTMS coil designs will be presented; in addition, we will present data on the acoustic performance of our qTMS coils with a conventional TMS device.

Laura Marzetti (University of Chieti/Pescara)

Adaptive algorithms for real-time connectivity estimation

Christoph Zrenner (University of Tübingen)

Closed-loop stimulation

OS1-2

Title
New trends of clinical neurology: diagnosis and treatment of neurological diseases.

Chaired by Tetsuo Touge

Abstract
In this organized session, we will report on-going new approach according to advanced medical technology in various fields of clinical neurology including neurophysiology, genetics and neuroimaging, to diagnose and treat neurological diseases.

Speakers

Tetsuo Touge, Kentaro Sugawara, Kunihiko Tsutsui, Tadayuki Takada, Yohei Kokudo, Masaki Kamada, Tomokazu Doi, Kazushi Deguchi (Kagawa University)

Effects of transcranial magnetic stimulation with maximum voluntary muscle contraction (TSM with MVC) on chronic hand paresis caused by cerebral stroke.

Objectives: The present study aimed to evaluate the effects of TMS with MVC on chronic hand paresis caused by stroke using placebo-controlled crossover trial.
Subjects and Methods: Eleven subjects including seven males (65.5 + 11.0 years old, mean age + S.D.), consisting of 5 patients with cerebral infarction and 6 patients with cerebral bleeding, gave us informed consent to participate in this study. ´Brunnstrome stage in the patients was scored 5.3 + 0.8. This study was approved by the local ethical committee in our institution. Subjects sit down on a chair and relaxed their whole body muscles. According to the verbal cue by an operator, subjects were instructed to pinch a button-like strain-gauge transducer by their thumbs and index fingers in their paralyzed hands for 2 seconds with MVC as far as possible. In the test condition, double TMS with a interstimulus interval of 1.5 ms was delivered to the primary motor cortex for targeted hands using a 12 cm round coil 1 second after the onset of muscle contraction. The stimulus intensity was 110% of the active motor threshold of first dorsal interosseous muscle (FDI). Motor evoked potentials (MEPs) in FDI and the thenar muscle (Th) evoked by TMS were recorded. One session of MEP recording consisted of 4 TMS with MVC trials with interstimulus intervals of 10 seconds. In each subject, five sessions as a cool were repeated with intervals of 10 minutes, and three cools were undergone at every other day in the test or control condition. The experiments in the test and control conditions was randomly performed during serial weeks. In the control condition, sham TMS was delivered instead of real TMS during MVC as that the round coil was positioned tangentially and its lower edge was fixed on the vertex. Other experimental setting was the same as that for the test condition. The pressure for pinching the strain-gauge transducer was converted to electric signals (Voltage) by an amplifier (NEC San-ei, AS2603, Japan) and was simultaneously stored in a computer as a marker of pinching muscle force (PMF). The pegboard test was examined before and after the experiment in test or control condition.

Results: PMF was significantly stronger in the test condition than in the test condition ($F=5.557$, $P<0.05$). In Wilcoxon signed-rank test, PMF in the 4th session of the first cool significantly higher in the test condition than in the control condition. The MEP amplitudes or areas were tended to be higher in the test condition compared with the control condition. The score of pegboard test significantly improved after TMS with MVC in the test and control conditions ($F=3.620$, $P=0.024$).
Conclusion: The present study showed TMS with MVC significantly increased PMF in the test condition than in control condition. Since the effect started from the first day of TMS with MVC and lasted for five days, we think the frequency of TMS with MVC can be reduced once or twice a week to improve muscle force. This fact suggests that TMS with MVC using double TMS is a beneficial procedure for rehabilitation to the chronic hand paresis caused by stroke.

Masaki Kamada (Kagawa University)

MRI evaluation of Parkinson disease and Atypical Parkinsonisms

Background: In early stage, precise differential diagnosis of parkinsonism is challenging. Therefore, Various MRI parameters have been proposed to make an accurate diagnosis of parkinsonism.
Objective: We aimed to evaluate the brain magnetic resonance imaging (MRI) of Parkinson disease and atypical parkinsonisms.
Methods: 90 patients [mean age, 72.6±7.7 years; Parkinson disease (PD) (n=40), diffuse Lewy body disease (DLB) (n=6), progressive supranuclear Palsy (PSP) (n=18), corticobasal syndrome (CBS) (n=11), multiple system atrophy with predominant parkinsonism (MSA-P) (n=5), and multiple system atrophy with cerebellar features (MSA-C) (n=10)] who have undergone brain MRI were included in this study. MRI-derived parameters including midbrain area-to-pons area (M/P), magnetic resonance parkinsonism index (MRPI), and MRPI 2.0 were compared in patients with PD, DLB, PSP, CBS, MSA-P, and MSA-C. The cut-off value, sensitivity, specificity, positive predictive value, negative predictive value, receiver operating characteristic (ROC) of MRI-based characteristics were analyzed in different groups.
Result: The M/P, MRPI and MRPI 2.0 differentiated patients with PSP from those with PD, DLB, CBS, MSA-P and MSA-C. The MRPI 2.0 was the best method to distinguish between PSP and PD (cut-off value : 4.38 , sensitivity : 94.4% , specificity 92.5% , positive predictive value 85.0% , negative predictive value: 97.4%).
Discussion: Various MRI parameters are useful for differentiating PSP from PD, DLB, CBS, MSA-P and MSA-C. However, pathological confirmation is necessary for more accurate evaluation.

Tadayuki Takata, Yohei Kokudo, Masaki Kamada, Tomokazu Do, Kazushi Deguchi, Kunihiko Tsutsui, Tetsuo Touge (Kagawa University)

Comparison between effects of single and double transcranial magnetic stimulation with maximum voluntary muscle contraction on pinching muscle force and motor evoked potentials (MEPs)

Objectives: Effects of single and double transcranial magnetic stimulation with maximum voluntary muscle contraction on pinching muscle force and motor evoked potentials (MEPs) were compared in the present study.
Subjects and Methods: Seven healthy subjects including four males (36.5 + 12.5 years old, mean age + S.D.) gave us informed consent to participate in this study. This study was approved by the local ethical committee in our institution. Subjects sit down on a chair and relaxed their whole body muscles. According to the verbal cue by an operator, subjects were instructed to pinch a button-like strain-gauge transducer by their thumbs and index fingers in their paralyzed hands for 2 seconds with MVC as far as possible. Single TMS or double TMS with a interstimulus interval of 1.5 ms was delivered to the primary motor cortex for targeted hands using a 12 cm round coil 1 second after the onset of muscle contraction. The stimulus intensity was 110% of the active motor threshold of first dorsal interosseous muscle (FDI). Motor evoked potentials (MEPs) in FDI and the thenar muscle (TH) evoked by TMS were recorded. One session of MEP recording consisted of 4 TMS with MVC trials with interstimulus intervals of 10 seconds. In each subject, five sessions as a cool were repeated with intervals of 10 minutes. The experiments by single and double TMS were performed the intervals over a week.The pressure for pinching the strain-gauge transducer was converted to electric signals (Voltage) by an amplifier (NEC San-ei, AS2603, Japan) and was simultaneously stored in a computer as a marker of pinching muscle force (PMF).
Results: PMF was significantly decreased after a cool of TMS with MVC. There was no difference between changes of PMF by single and double TMS with MVC.
MEP amplitudes and areas in FDI or TH were significantly larger in double TMS then in single TMS. Although there were no significant differences of MEP amplitudes or areas between single and double TMS, MEP amplitudes or areas tended to be increased by double TMS and decreased by single TMS after a cool of TMS with MVC than before that.
Discussion and Conclusion: Maruyama studied differences between two groups: One group received a pair of TMS pulses superimposed on each MVC, and the other did not receive any stimulation as a control. As a result, training with superimposed TMS pulses increased pinch MVC more than in the control group.
In the present study, effects on PMF by TMS with MVC did not significantly differ between single and double TMS. However, there were different tendencies as that double TMS increased MEP amplitudes or areas, whereas single TMS decreased those. This result suggests that double TMS strongly facilitates motor neuron excitability compared with single TMS. We speculate that double TMS with MVC is useful method to applicate neurorehabilitation technique in patients with motor paresis.

Yusaku Nakamura (Kagawa University)

Non-invasive high frequency peripheral magnetic stimulation in focal hand dystonia

Objectives: Patients with focal hand dystonia (FHD) is one of the most common form of dystonia. FHD have task-specific uncontrolled muscle activity with simultaneous contractions of agonist and antagonist muscles. Muscle afferent block and sensory trick can reduce the symptom of FHD. A loss of inhibitory functions of somatosensory system in the central somatosensory system from muscle afferents might also account

for the sensory overflow and altered sensorimotor cortical excitability. Some studies reported that transcutaneous electrical nerve stimulation (TENS) may improve FHD and cervical dystonia. The new magnetic stimulator (Pathleader®, IFG corporation) is noble special type of non-invasive high frequency peripheral magnetic stimulation. Pathleader® can stimulate peripheral nerve and muscles at high frequency up to 50Hz. The induced current by pulsed magnetic field excites αmotor and proprioceptive nerve fibers in the deep tissues. The aim of this study is to evaluate the effectiveness of non-invasive high frequency peripheral magnetic stimulation in FHD. *Methods and Subjects:* Five patients of male were enrolled. They composed of four patients with FHD and one patient with essential tremor. Their age was 58.6year-old, their disease duration was 6.2 year. Peripheral magnetic stimulation was delivered to forearm flexor muscles by a Pathleader®. The intensity was 90% motor threshold, the frequency was 25Hz, the delivery lasted for 15minites. Patients were clinically evaluated before, after and 5minituets after the end of the therapy. Handwriting ability was assessed drawing and writing. The performance was video-recorded. *Results:* Improvement of hand writing was recoded in four patients with FHD. However, patient with essential tremor did not show improvement of hand writing. *Discussion and conclusion:* High frequency peripheral magnetic stimulation to forearm muscles can induce significant improvement of hand writing in FHD.

OS1-3

Title
Multi-modal approaches to study cognitive functions.

Chaired by Rafael Polania, Carmelo Vicario

Speakers

Rafael Polania (ETH Zürich)

Can we study brain function with tACS?

Carmelo Vicario (University of Messina)

Reward and punishment in the tongue motor neurons: some preliminary evidence

A challenge for modern Neuroscience is to provide conceptual tools and innovative methodologies to understand, predict and modell the influence of reinforcement on human behavior. Starting from evidence in non-human primates (e.g., Alipour et al., 2002) that neurons of the tongue representation in the primary motor cortex are connected to reward system, I discuss preliminary evidence in human models that this neural region might serve as cortical target, to detect physiological states along the reward/dislike continuum.

Shane Fresnoza (University of Graz)

Exploring and modulating reasoning ability via noninvasive brain stimulation

Higher cognitive functions such as creativity, decision making, numerical and language processing are subserved by functionally connected yet anatomically segregated brains networks. This structural and functional organization of the brain may impose a limitation on the effectiveness of noninvasive brain stimulation (NIBS) techniques that usually target specific brain areas. However, over the last years, there has been an increasing body of evidence demonstrating that localized stimulation can modulate complex and higher-order cognitive processes. In the present study, we aimed to identify and modulate brain areas that are causally involved in different types of reasoning ability. Specifically, we will test whether high-definition transcranial direct current stimulation (HD-tDCS) to different areas of the frontal lobe will influence inductive and deductive reasoning ability. In deductive reasoning, the validity of the conclusion can be inferred from the logical relationship between the premises (e.g. all humans are mortal, Socrates is human => Socrates is mortal), whereas a plausibility judgment is necessary for inductive reasoning (e.g. cats purr, a lion is a cat => lions purr). When anodal tDCS is applied to the brain area involved in deductive or inductive reasoning, performance should improve, whereas it should be impaired for cathodal tDCS. The findings of the study will contribute to a better understanding of the

reasoning processes which can be of use in designing NIBS intervention to improve our ability to reason and to decide.

Jessica Grundey (University of Göttingen):

Nicotinic effects on cognition are linked to cortical excitability/neuroplasticity in healthy smokers

Introduction: Former studies with nicotine have proposed enhancing effects of nicotine on various cognitive functions mainly in animal studies. Aim of our study was to assign these studies to healthy, smoking humans by testing different cognitive functions after administration of nicotine and link these results to nicotinic changes of cortical excitability and neuroplasticity.
Methods: Cognitive studies were performed on smokers after administration of nicotine patch/placebo patch respectively. For assessing different cognitive domains, we used the Stroop interference test (attention; 21 smokers), the n-back letter task (working memory; 16 smokers) and the serial reaction time task (SRTT, implicit motor learning; 20 smokers).Cortical excitability and neuroplasticity were measured with transcranial magnetic stimulation (TMS; 12 smokers), paired associative stimulation (PAS; 12 smokers) and transcranial direct stimulation (tDCS;12 smokers). All methods above are non-invasive brain stimulation techniques that are able to assess cortical excitability or induce neuroplasticity similar to long-term potentiation (LTP) or long-term depression (LTD).
Results: Nicotine in deprived smokers improved attentional deficits (error rates and reaction time), working memory performance (reaction time) and implicit motor learning (reaction time). On the neurophysiological basis, nicotine restitutes intracortical facilitation in deprived smokers as parameter of cortical excitability. In terms of LTP-like neuroplasticity, that seems to be connected to hippocampal learning, nicotine likewise re-established compromised tDCS- and PAS-induced excitatory aftereffects.
Discussion: Our study supports former animal studies by providing strong evidence of nicotinic effects on cognitive functions in deprived smokers. It is also the first study to allow conclusions about the neurophysiological mechanisms in healthy humans. On this basis, further experiments can focus on receptor-mechanisms, up- and downregulation and possible clinical application areas, p.e. in Alzheimer disease or schizophrenia.

OS2-1

Title
Non-invasive brain stimulation effects on human executive functions.

Chaired by Michal Lavidor

Abstract
Prior investigations employing transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) have shown that stimulation can elicit subsequent improvement on tests of various cognitive abilities. However, it is still unclear how consistent and replicable are these effects, and whether findings from laboratory studies with healthy subjects are applicable to clinical populations including at-home treatments. Here we gathered four leading experts of non-invasive brain stimulation studies of executive functions, and together we aim to discuss recent findings relevant to these questions. Prof. Agnes Flöel will present learning and memory in elderly populations, Prof. Anna Pecchinenda will present brain stimulation effects on attentional blink and flanker, Dr. Gorana Pobric will present language and memory findings and Prof. Michal Lavidor will present embodiment and decision making. Together we will give a thorough and timely review of the main executive functions changes following stimulation.

Speakers

Agnes Flöel (University Medicine of Greifswald)

Impact of non-invasive brain stimulation on learning, memory formation, and memory consolidation in older adults

Combination of cognitive training protocols with noninvasive transcranial brain stimulation (NIBS) techniques may constitute a promising means for cognitive enhancement in older adults (Perceval et al., 2016). Given decline of cognitive function even in healthy aging, modulation of brain plasticity with transcranial direct current stimulation (tDCS) concurrent to intense task practice over multiple days holds promise to induce sustained improvements of trained and untrained functions.
In this contribution, I will present own work on the impact on single-day and multiple-day training and constant current tDCS on learning and memory formation as well as functional networks in older adults with and without cognitive impairment (Antonenko et al, NBA 2018; Antonenko et al, Scientific Rep 2019; de Sousa et al, work in progress). Moreover, I will present recent work on slow oscillatory tDCS on sleep-related memory consolidation in these populations (Ladenbauer et al, J Neurosci 2016, 2017)
Finally, I will outline further future strategies to improve on this approach, with the ultimate goal to transfer this intervention into clinical practice.

Anna Pecchinenda, Francesca De Luca, Bianca Monachesi, Manuel Petrucci, & Michal Lavidor (La Sapienza Università di Roma)

Impact of tDCS on visual selective attention

A well-consolidated strategy for studying selective attention limitations consists of overloading the (visual) attentional system through the concurrent or very rapid presentation of multiple task-relevant visual events and assess how the presence and/or temporal proximity of task-irrelevant information modulates the probability that specific information is reported. For example, when visual events succeed one another rapidly in foveal vision, at a rate of about ten items per second (e.g., Rapid Serial Visual Presentation procedure; RSVP), our ability to report the second of two targets (T1 and T2) embedded among distractors is severely compromised when the T2 follows the T1 within a time window of 200-500 milliseconds (*Attentional Blink*, Broadbent & Broadbent, 1987; Raymond, et al., 1992). In this task, a good performance requires the correct identification of T1 and T2 but also the inhibition of irrelevant distractors.
Previous studies indicate that a broad network of frontal and parietal regions is implicated in selective attention, with ever increasing evidence pointing to a more prominent role of dorsolateral prefrontal (DLPFC) compared to parietal regions. However, studies assessing whether potentiating the activity of the DLPFC via tDCS improves selective attention, have often provided mixed findings (e.g., Imburgio & Orr, 2018).
In this contribution, I will present findings on the effects of anodal vs sham tDCS over the DLPFC and over the Posterior Parietal Cortex (PPC) to assess the contribution of top-down and bottom-up modulations on temporal selective attention. I will discuss this evidence and that of previous studies on the modulation of the *Attentional Blink* by tDCS over the DLPFC.

Gorana Pobric, Jason Taylor, Johan Hulleman, Shruti Garg (University of Manchester)

Cognitive training and transcranial direct current stimulation effects in neurofibromatosis type 1: pilot study

Background: Executive function and working memory (WM) impairments are core deficits of neurofibromatosis type 1 (NF1), a single-gene autosomal dominant neurodevelopmental disorder [1]. In animal models of NF1, an increase of synaptic GABAergic inhibition results in impaired Long Term Potentiation and synaptic plasticity linked to cognitive impairment [2]. Cognitive remediation interventions can improve cognitive function [3]. They may be combined with non-invasive brain stimulation techniques. The strong evidence of GABAergic abnormalities in NF1 suggests the use of anodal tDCS. We had two aims: **(1)** to examine the effectiveness of a WM-training paradigm in ameliorating cognitive impairments in NF1 and **(2)** to investigate feasibility and tolerability of tDCS in NF1.
Method: Design: Single-site double blinded, randomised controlled trial of active tDCS versus Sham tDCS. *Sample:* Sixteen children with NF1 (mean age 13.1,SD 1.65, 9 males), randomly assigned to either active or sham group and 16 controls (mean age 13.4, SD 1.62 9 males). *Intervention:* tDCS (anode over left dorsolateral prefrontal cortex-lDLPFC; cathode over vertex) was delivered in conjunction with cognitive

training using a working memory n-back task for three consecutive days for our NF1 participants. Stimulation lasted for 20 minutes (active) or 1 minute (sham) at 1mA current. Primary endpoint was Day 3, with a follow-up visit at 1 month for both trained (n- back) and transfer (Corsi block) tasks. EEG (64 channel BioSemi ActiveTwo) was recorded during a working memory task at baseline, day 3, and at follow-up. EEG data were analysed in both time (P300 component) and frequency domains (theta coherence 4-8 Hz).
Results: NF1 and control group were significantly different on all parent-reported measures (e.g. Conners, ABC), at both baseline and follow-up visit. At baseline, NF1 and control group showed significant differences on the n-back task and Corsi Blocks. But at follow-up these differences were no longer significant. The NF1 group had abnormally right-lateralised baseline EEG P300 responses (vs. left-lateralised in controls). By Day 3 this difference had diminished, to re-emerge at follow-up. *tDCS effects*: A mixed 2X3 (treatment x session) ANCOVA on mean n-back with ABC scores as covariate yielded a main effect of session, $F(2,26)=25.0$, $p<0.001$; $\eta p^2= .657$. Neither the main effect of treatment nor its interaction with session was significant: $F(1,13)=1.4$, $p=.257$; $\eta p^2=.098$ and $F(2,26) = 2.5$; $p=.106$; $\eta p^2=.159$, respectively. Planned interaction contrasts, comparing NF1 active and sham groups on working memory improvement from first to last tDCS session, found a larger learning gain for the treatment group [$t(14)=1.7$ $p=0.056$]. We tested transfer effects on the Corsi blocks task using a similar 2X3 ANCOVA on maximum memory span. There were main effects of session [$F(2,26)=8.0$, $p=.003$, $\eta p^2=.382$] and treatment [$F(1,13)=5.7$, $p=0.03$, $\eta p^2=.306$], but no interaction: $F(2,26)=1.6$, $p=.215$, $\eta p^2=.113$. For both Day 3 and FU, planned interactions found a larger improvement in memory span for the active group: Day 3 vs baseline $t(14)=1.9$, $p=.037$; and FU vs baseline $t(14)=2.0$, $p=.033$. Similar analyses of EEG P300s found no significant F-values. For coherence, at baseline, the lateral>medial pattern evident in controls was weaker in both NF1 groups. By follow-up, the coherence pattern of the active group was nearly identical to controls. But for the sham group it was again similar to their baseline.
Conclusions: While both active and sham group improved on mean n-back performance, anodal stimulation resulted in enhanced transfer effects on the non-trained visuospatial task. These findings suggest that repeated anodal tDCS over lDLPFC combined with a challenging WM task may be an effective method to enhance domain independent performance. EEG measures, particularly fronto-parietal coherence, showed some promising trends but were not reliable in this small sample. The results indicate the feasibility of safe tDCS intervention in children with NF1.
References: **[1]** Lehtonen et al. Behaviour in children with neurofibromatosis type 1: cognition, executive function, attention, emotion, and social competence. Dev Med Child Neurol. 2013;55(2):111-25. **[2]** Shilyansky et al. Neurofibromin regulates corticostriatal inhibitory networks during working memory performance. PNAS. 2010;107(29):13141-6. **[3]** Jaeggi et al. Short and long-term benefits of cognitive training. PNAS, 2011;108(25):10081-6.
Funding: The study was funded by the NewLife, The Charity for Disabled Children, UK

Katya Rubia, Samuel Westwood, Philip Asherson, Bruce Wexler, Joaquim Radua
(King's College London)

tDCS in ADHD: a meta-analysis and a tDCS study targeting right inferior frontal cortex

Introduction: Stimulants are effective in ADHD but have side effects and there is no evidence for longer-term efficacy. Non-invasive brain stimulation, such as transcranial

direct current stimulation (tDCS), can modulate cortical excitability, with potentially long-lasting neuroplastic effects leading to gains in the function of targeted brain regions. In ADHD, there have been some promising effects of tDCS on improving cognition and clinical symptoms. tDCS may therefore offer a side-effect free, brain-based, neuroplastic treatment alternative to psycho-stimulants. We present here a meta-analysis of published tDCS studies in ADHD and findings from our own multi-session tDCS study of right inferior frontal cortex (rIFC) combined with cognitive training in ADHD children.
Methods: (1) Meta-analysis of tDCS studies: search of PubMed, ScienceDirect, and Web of Science for single-/double-blind, randomised controlled trials (until January 2019) identified 12 tDCS studies (n range 9 to 60) targeting mainly dorsolateral prefrontal (DLPFC) regions. Due to heterogeneity in cognitive tasks, composite effect size estimates were generated for outcome measures clustered into 3 cognitive domains: Inhibition, Attention, and Speed of Response. (2) For the tDCS randomised controlled trial (RCT), 50 ADHD boys, aged 10-18 years, received either anodal sham (N = 25) or real tDCS of right inferior frontal cortex (rIFC) (N = 25) (cathode over the right eyebrow) in fifteen 20 min sessions across 3 weeks. Outcome measures included parent-rated ADHD symptoms, cognitive performance on an ADHD-relevant task battery of inhibition, attention and timing tasks and EEG measures.
Results: (1) For the tDCS meta-analysis, findings revealed that anodal tDCS of mostly left dorsolateral prefrontal cortex is associated with a trend-level significant improvement of Inhibition and Processing Speed with small effect sizes but no improvements of Attention. (2) For the RCT of tDCS of rIFC, findings will be presented at the conference.
Conclusions: The meta-analytic findings suggest that tDCS of mostly left DLPFC has limited effects with small trend-level improvements on inhibitory control and processing speed but no effects on attention. Overall, tDCS of DLPFC does not seem to be a promising novel neurotherapy for ADHD. Further studies targeting other regions, applying different stimulation protocols (i.e., intensity, duration, combination with different training games etc), or using other non-invasive brain stimulation techniques will be needed to further elucidate clinical and/or

OS2-2

Title
Reducing tACS artefact in electrophysiological data – status quo and future directions.

Chaired by Christoph S Herrmann, Ursula Voss

Abstract
Transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) have been widely used in an attempt to alter brain function, both in basic neuroscience research and, more recently, in clinical studies aiming at symptom relief in mostly psychiatric patients. Especially tACS has received much attention as it represents a frequency-specific method of brain stimulation. Theoretically, this holds the possibility of entraining neuronal oscillations in a task-specific way and thereby altering brain functioning. However, in spite of a multitude of intriguing observations and treatment results, the mechanism by which these effects are mediated remains unclear. This is partly due to the tremendous difficulties in removing the stimulation signal as well as various induced artefacts from the ongoing EEG/MEG recording. The majority of such spurious signals have been found to stem from interferences due to respiration, heart rate, and muscular artefacts. The proposed symposium will provide an overview on the current state of knowledge regarding such artefacts in EEG and MEG recordings, and it will focus on methodological strategies to reduce and/or remove them.

Speakers

Romain Holzmann (GSI Helmholtzzentrum für Schwerionenforschung
Investigating nuisance effects induced in EEG during tACS application)

Transcranial alternating current stimulation (tACS) in the frequency range of 1-100 Hz is nowadays commonly used in EEG studies of brain function via entrainment of neuronal oscillations. However, it turns out to be highly non-trivial to remove the stimulation signal including its harmonic and non-harmonic distortions, as well as various induced artefacts from an ongoing EEG recording. In my contribution I will discuss some of the problems encountered and methodological approaches aimed at overcoming them.

Asif Jamil (IfADo)

Novel methods of altering oscillatory brain activity by phase-synchronizing rTMS and tACS

Altering or restoring the rhythmic network activity associated with deficient cognitive functions in mental disorders remains a difficulty with current invasive and noninvasive neuromodulation techniques due to either insufficiently weak (e.g. tACS) and/or temporally non-specific alignment of the induced electromagnetic stimulation with the intrinsic properties of neural oscillatory rhythms (e.g. rTMS). In the following talk, we present a novel non-invasive brain stimulation protocol whereby synchronizing

suprathreshold pulsed magnetic stimulation (rTMS) with continuous subthreshold electrical alternating current stimulation (tACS) establishes and sustains local and network oscillatory activity specific to the induced frequency. This technique relies on both stimulation modalities, and is temporally specific with phase timing, suggesting that neural oscillations may also be sensitive to phasic properties of excitability.

Florian Kasten (Carl Ossietzky University Oldenburg)

Concurrent tACS-MEG - Recovering event-related oscillations in the presence of residual artifacts

Transcranial alternating current stimulation (tACS) receives growing popularity as a tool to modulate brain oscillations in a frequency specific manner and to study causal relations between these oscillations and cognition. However, so far mechanisms of tACS especially during stimulation are poorly understood as a strong electro-magnetic artifact is introduced to electrophysiological measurements. Recent work demonstrated that the application of LCMV beamforming leads to a strong, yet imperfect suppression of this tACS-artifact in MEG recordings. Such imperfect artifact suppression results in the presence of residual tACS-artifacts after beamforming, severely limiting the range of meaningful analyses that can be performed. Here, we propose an approach to analyze event-related oscillations in the presence of residual tACS artifacts and to perform control analysis tailored to disentangle stimulation effects from residual stimulation artifacts. Further, we will discuss major pitfalls of concurrent tACS-MEG/EEG measurements concerning experimental design, data analysis and interpretation of results.

Nima Noury (University of Tübingen)

Does tACS entrain neural oscillations?

Despite the widespread use of tACS for manipulating neuronal oscillations, it is still not clear whether this method is able to entrain neuronal oscillations. This is mainly because stimulation artifacts interfere with simultaneously recorded brain signals and make it hard to search for such possible entrainments. In my talk, I will first review our current knowledge about these artifacts and provide a mathematical model for them. Next, I present our recent results from an MEG experiment, in which we search for the echoes of tACS entrainment after stimulation offset.

OS2-3

Selected poster presentations

Chaired by Tetsuo Touge, Michael Nitsche

Sandor Markon (Kobe Institute of Computing, Graduate School of Information Technology):

Fusion of Touch and Vision with Floating Image Visualization

Lídia Mulet-Pons (Universitat de Barcelona)

tDCS-induced reconsolidation memory effects in Subjective Cognitive Decline (SCD) are related with structural brain integrity

Yasuko Maekawa (Kagawa University)

Comparison of acquired knowledge by nursing students for learning elderly dementia care between a digital learning and a text-book study

Carmen Weidler (RWTH Aachen University)

Consequences of prefrontal tDCS on inhibitory control and reactive aggression in alcohol dependent patients and tobacco users

OS3-1

Title
Roles of intrinsic and extrinsic neural oscillations in the brain.

Chaired by Shozo Tobimatsu

Abstract
Neural oscillations are rhythmic or repetitive patterns of neural activities in the brain. This session will introduce the attempt to clarify the mechanism of functional correlation in the brain by analyzing the oscillation using various methods.

Speakers

Shozo Tobimatsu (Kyushu University)

Neuromagnetic Oscillations in the Human Sensory Systems: A Magnetoencephalographic Study

Background: Oscillatory neuronal (electrical) activity in defined frequency ranges supports synchronous interactions between anatomically distinct regions of the human brain during cognitive tasks that require deliberate or automatic attention, memory, or visual processing. It is now widely accepted that defining network interactions is key to understanding normal cognition. In this organized session, I will review our previous studies that focused on the neuromagnetic oscillations in the sensory systems in response to the external stimuli in normal healthy subjects and neurological disorders.
Methods: Magnetoencephalography (MEG) was used to measure the magnetic fields generated by neuronal activity of the brain. We evaluated the induced oscillatory activity that appears with a jitter in latency from one trial to another, centered around a given latency. The time–frequency power of the signals by means of a complex Morlet's wavelet transform was applied to each single trial, followed by an averaging of the powers across trials. Thus, it becomes possible to identify non-phase-locked activity.
Results: From our studies, several interesting results were recognized. We have demonstrated that the oscillatory gamma synchronization binds the primary and secondary somatosensory areas (S1 and S2) in humans. This functional coupling is modulated by aging. We have found that neuronal synchronization plays an important role in distributed cortico-cortical processing during cognitive tasks that require purposeful attention, memory, or audio-visual processing. In people who stutter (PWS), functional and structural reorganization of the right auditory cortex appears to be a compensatory mechanism for impaired left auditory cortex function. This may be partly caused by increased right hemispheric local phase synchronization and increased inter-hemispheric phase synchronization. We have also found that the hippocampus modulates auditory processing differently under normal conditions and in patients with hippocampal sclerosis, which indicates that altered neural synchronization may provide useful information about possible functional deterioration in patients with unilateral mesial temporal lobe epilepsy.
Conclusion: It is apparent that neuronal synchronization plays an important role in distributed cortico-cortical processing. Thus, the induced oscillatory activities are

responsible for temporal binding of spatially distributed information processing in the human brain. Future studies will be necessary to facilitate our understanding of the roles of the neural oscillations in the network interactions.

Tsuyoshi Okamoto, Kaori Tamura, Sayaka Matsumoto, Yu Hsuan Tseng, Haruka Matsuo, Takayuki Kobayashi, Jun'ichi Miwa, Toyotaka Hirao, Seiji Hiramatsu (Kyushu University)

Neural oscillations in the brain under different airflow conditions

Indoor environmental quality is extremely important for occupant health and comfort. Huge number of studies have been conducted on the effects of visual, auditory,eural oscillations in the brain could help explain and understand the reasons behind this preference. To examine the neural oscillations in the brain under different airflow conditions, we compared the electroencephalograms (EEGs) recorded during direct and indirect under two different temperature conditions: cooling and heating in an air-conditioned test room. Beta (14-30 Hz) and gamma frequency bands (30–50 Hz) of EEGs were analyzed because it was reported that the amplitudes of the bands can change according to the change of mental state. For each of the temperature conditions, humidity levels were maintained at similar levels for both the direct and indirect airflow conditions. The EEGs were recorded using a wireless dry EEG headset, which supports the full 10-20 array (Quick-20 system, CGX, USA). Cooling experiments were performed on 19 healthy volunteers (8 females and 11 males; 19-27 years), and heating experiments were performed on 20 healthy indirect airflow conditions. The thermal environment in the test room was controlled using a commercially available airconditioner (Mitsubishi Heavy Industries Thermal Systems LTD., Japan), which can adjust the airflow by means of a special kind of flap. The experiments were approved by the local ethics committee of Kyushu University and performed in accordance with the approved guidelines. For the cooling experiment, the beta band amplitude at a left-frontal site, and the gamma band amplitudes at the left-frontal and midline-parietal sites were higher under the direct airflow condition than the indirect airflow condition. For the heating experiment, the beta and gamma amplitudes at the right-frontal and left-temporal sites were higher under the direct airflow condition than the indirect airflow condition. The higher beta and gamma amplitudes in the temporal association cortex underthe direct airflow condition in the heating experiment may reflect the participantsfeeling of unpleasantness or dislike. On the other hand, the higher beta and gamma amplitudes in the frontal area under the direct airflow condition in the heating and cooling experiments may reflect the airflow sensation directly. From an alternate perspective, these results can be interpreted to be biomarkers of airflow sensation. This study is expected to contribute to understanding the neuronal mechanism of airflow sensations.

Katsuya Ogata (School of Health Sciences at Fukuoka, International University of Health and Welfare)

Differential effects of 20 and 10 Hz-tACS on MEPs with intermittent Theta Burst Stimulation

Introduction: Transcranial alternating current stimulation (tACS) is shown to modulate the cortical excitability such as primary motor cortex (M1), which is supposed to entrain cortical oscillations. We have revealed the online effect of 20 Hz-tACS over M1 in a phase-dependent manner (PLoS ONE 2016) while the aftereffect was unremarkable. Nevertheless, it is possible to modulate the effect of patterned rTMS such as intermittent theta burst stimulation (iTBS). We hypothesized that 20 Hz tACS would enhance the effect of iTBS while 10 Hz tACS would not in a phase dependent manner. In this study, we studied the effect of 20Hz and 10 Hz-tACS on motor evoked potentials (MEPs) with iTBS.
Methods: Healthy adult subjects were recruited for 20 Hz or 10 Hz-tACS over the left M1 hot spot. TMS was also delivered over left M1 hot spot. In an iTBS protocol, bursts are delivered for 2 s, then repeated every 10 s. The time of the first pulse for each train of iTBS was controlled to match the peak or bottom phase of tACS. A sham condition of tACS was used as a control, in which tACS lasted first 20 seconds only. Thus, each subject was tested in the three conditions for each tACS frequency: peak and bottom of tACS phase and sham tACS. M1 excitability was evaluated by MEPs of right FDI using single-pulse TMS.
Results: 20 Hz tACS + iTBS suppressed MEP amplitudes compared with iTBS only irrespective of tACS phase. On the other hand, 10 Hz tACS + iTBS resulted in the tendency of suppression for 90° phase compared with 270° condition.
Discussion: The inhibitory effect of 20 Hz-tACS over iTBS might be induced by synchronizing both of the stimulations because 20 Hz-tACS did not influence iTBS in a previous study without matching the phase. 10 Hz-tACS might suppress iTBS in a phase dependent manner. The inhibitory effect 90° for 10 Hz tACS over iTBS would be compatible with our previous study that 10 Hz-tACS over M1 showed tendency to inhibit MEPs.

Takao Yamasaki, Toshihiko Aso, Yumiko Kaseda, Yasuyo Mimori, Hikaru Doi, Naoki Matsuoka, Naomi Takamiya, Tsuyoshi Torii, Tetsuya Takahashi, Tomohiko Ohshita, Hiroshi Yamashita, Hitoka Doi, Saeko Inamizu, Hiroshi Chatani, Shozo Tobimatsu (Minohara Hospital)

Altered oscillatory V1 activity to motion perception in patients with mild cognitive impairment: An fMRI study

Background: Motion perceptual deficits are common in Alzheimer's disease (AD) and can be observed even in the prodromal stage of AD (i.e., amnestic mild cognitive impairment, aMCI). Although the posterior parietal cortex (higher-level cortical area engaged in motion processing) is thought to play a critical role in these deficits, it is currently unclear whether the primary visual cortex (V1, the visual area involved in the first stage of visual cortical processing) contributes to these deficits in aMCI and AD.
Methods: To solve this issue, we investigated the oscillatory neural activity within V1 in 17 aMCI patients, 17 AD patients and 17 normal controls (NC) using functional magnetic resonance imaging (fMRI). fMRI was recorded under two conditions: visual motion stimulation and resting-state conditions. Both fMRI datasets with visual motion stimulation and resting-state conditions were analyzed by independent component analysis (ICA) to examine the difference of the stimulus-driven oscillatory neural activity within V1 among the three groups.

Results: In the NC group, the oscillatory neural activity within V1 extracted by ICA was significantly increased by a series of visual motion stimuli, compared with the resting-state condition. Conversely, the augmentation of V1 activity was not observed in either the aMCI or AD groups. In the between-groups comparison, stimulus-driven V1 activity was significantly higher in the NC group compared with the AD group. Thus, stimulus-driven V1 activity elicited by visual motion stimulation relative to the resting-state was attenuated in the patients.
Conclusion: The present fMRI results suggest the altered stimulus-driven oscillatory neural activity within V1 relative to the resting-state fluctuation, which may correspond to the previously reported motion perceptual deficits in aMCI and AD. Therefore, the decreased stimulus-driven V1 activity measured as the strength of the ICA component may provide a new disease biomarker for early detection of aMCI and AD.
Index Terms – Alzheimer's disease; amnestic mild cognitive impairment; functional magnetic resonance imaging; resting-state; motion perception; primary visual cortex

OS3-2

Title
How functional neuroimaging and neurophysiological data can help us to assess and improve cares of post-comatose patients with disorders of consciousness.

Chaired by Aurore Thibaut

Abstract
Patients with disorders of consciousness are by definition unable to communicate. This makes the evaluation of their state of consciousness a major challenge. To date, beside behavioral assessments, assisting technologies, such as high-density electroencephalography (hdEEG), functional magnetic resonance imaging (fMRI) or positron emission tomography (PET-scan) are more and more used to increase the accuracy of the patients' diagnosis. Novel therapeutic options, such as transcranial current stimulation – tCS) are also being developed aiming at improving the recovery of these patients who had suffered a severe brain injury.
With this symposium, we will bring scientists with an extensive expertise in dealing with intensive evaluation of the state of consciousness in patients sustaining severe brain injuries. Our aim is to illustrate how we can infer a clinical diagnosis by integrating different data from behavioral and brain function as measured with different technological modalities. We will also raise the challenges of these different tools given the specificity of the population. More precisely, we will discuss how electrophysiological (i.e., hdEEG) and neuroimaging data (fMRI and PET-scan) are acquired and analyzed and how they can help patients' diagnosis and management. We will show how each of these evaluations are performed in step-by-step manner. Each presenter will further illustrate the methodological challenges and pragmatic solutions towards the inference of valid conclusions.

Speakers

Federico Raimondo (*University of Liège)*

Automated Machine Learning-based diagnosis of impaired consciousness: cross-center and protocol generalization of EEG biomarkers.

Introduction: Patients suffering from disorders of consciousness (DOC) demonstrate that it is possible to be awake in the absence of behavioral evidence of consciousness. Among the DOC clinical, one distinguishes the Unresponsive Wakefulness Syndrome (UWS) Minimally Conscious State. MCS but not UWS patients show signs of awareness, while neither achieving functional communication nor object-use. It is nevertheless believed that these patients can have a partial and fluctuating awareness of themselves and their surroundings and are more likely to recover which emphasizes the importance of reliable diagnostic tools. Despite best efforts for consistency, current diagnostic procedures rely on human interaction and are, therefore, error-prone. To date, electroencephalography (EEG) and machine learning begin to assist the diagnostics of post-comatose conditions of impaired consciousness after severe brain injury.

Methods: We analyzed 327 EEG recordings from two clinical centers (Paris and Liege) and extracted 120 EEG-based markers as described in a previous work. The EEG recordings were divided into 3 sets, corresponding to the previously published data under an auditory paradigm4 (Paris 1, N=142), recordings obtained later in the same center and under the same recording conditions (Paris 2, N=107) and data obtained from an independent clinical center under a resting state condition (Resting State, N=78). We then trained a nonparametric classifier based on ensembles of decision trees and analyzed the performance across various EEG-configurations (different number of sensors and recording lengths), as well as generalization across data sets.
Results: Our classifier exhibited an average AUC of 0.75 when we analyzed the performance across different EEG configurations using the data from Paris 1. When training the classifier on the Set 1 dataset, and testing this algorithm on the Paris 2 dataset we observed significant classification performance with an AUC of 0.73. Likewise, when trained on all available data from Paris but ignoring the markers corresponding to the auditory task, the classifier scored an AUC of 0.78 on the Liège resting state data.
Conclusions: Our findings demonstrate that EEG signatures of consciousness can be reliably, economically and automatically identified with machine learning in various clinical and acquisition contexts. Furthermore, this signatures can be combined into coherent predictive models, encouraging future efforts in large-scale data-driven clinical neuroscience. Finally, these findings are now translated to a web server in which clinicians upload recordings and obtain an automated report with EEG markers and a prediction of the state of consciousness.

Stephen Larroque (University of Liège)

A clinical and research 3T MRI protocol under 30 minutes? Yes, it's possible!

In the past decades, non-invasive neuroimaging allowed significant progress in the understanding of all neuroscientific domains from neuroanatomy to neurofunctional connectomes. Magnetic resonance imagery (MRI) is an ubiquitous tool nowadays, being available in most hospitals, which allows a wide array of imaging contrasts, from structural anatomy and connectivity, to functional connectivity and blood flow imaging. Although MRI is widely used for both clinical and research purposes, the relative protocols are often very different, to fulfill different and seemingly irreconcilable needs: clinical pertinence and time efficiency in the clinical setting with a total acquisition time often strictly restricted below 30 minutes per patient slot, whereas research MRI has more flexibility and more cutting-edge needs, with total acquisition time reaching up to 2h for a single subject, allowing to acquire complex sequences like multi-shell DTI. Furthermore, the targeted populations are often fundamentally different: uncooperative or motor uncontrolling patients for clinical are quite common, inducing motion artifacts, patient discomfort or even panic if the acquisition is too long, whereas research often is done on healthy volunteers who well understand the study instructions and can remain still for a long period of time.
During this session, we will present a new 3T MRI protocol that can be used for both clinical and research purposes, and which has been successfully applied on uncollaborative and very motion prone patients with disorders of consciousness. This protocol is acquired in less than 30 minutes, and can thus be implemented on a clinical machine. The acquisition speed also reduces motion artifacts. We will demonstrate

how we implemented and cursorily analyzed the sequences of this protocol, including multi-shell DTI for structural connectivity without T1 constraints, FLAWS MP2RAGE for physiologically segmented grey and white matter without computional approximations and sub-second EPI BOLD for dynamic functional connectivity analyses, as well as SWI MIP and FLAIR for clinical purposes or lesional studies. Furthermore, meta-protocol procedures will be described to support and enhance acquisitions in uncooperative patients, such as the use of innovative 3D axis motion reducing pillows like the Pearltec MultiPad and the importance of protocol programming such as sequence ordering and name changing on if-conditions. We hope this state-of-the-art protocol will allow clinicians and researchers alike to consider new opportunities in the optimization of MRI protocols as a mean to push beyond this seeming dichotomy.

Yorgos Antonopoulos (University of Liège)

Applying Machine Lerning in PET scans of brain lesioned patients for characterizing the level of consciousness

Positron Emission Tomography is a commonly used modality of functional neuroimaging, which can capture the glucose metabolic activity of the brain. It provides a quantified spatial representation of this activity and remains unaffected by magnetic properties of the human tissues. PET is not prone to motion artifacts since we can sedate the patient during the acquisition without affecting the data. Additionally, there is no noise during scanning and thus it does not distract the subject. Machine Learning algorithms can unveil patterns of data and undercover interactions of brain regions, using data-driven approaches. Further, they provide tools that can ensure success in predicting unseen data.
We applied Machine Learning techniques in PET to diagnose the level of consciousness for brain lesioned patients. Specifically we combined Support Vector Machine together with Extremely Randomized Trees to classify between patients in Minimally Conscious State and Unresponsive Wakefulness Syndrome. We built a model using 158 patients (106 MCS, 52 UWS) and validated it using an independent set of 53 patients (35 MCS, 18 UWS). We achieved a recall of 89%, a precision of 89% and an accuracy of 85%. Moreover, we defined the contribution of each brain region to the classification process.
The pipeline we developed for classifying the DOC patients will be presented in this session. The role of the algorithms that were used for the preparation of the PET scans, the development and the evaluation of the classification model will be explained. Finally, the performance of the models and the brain regional contribution will be discussed.

Aurore Thibaut (University of Liège)

Therapeutic challenges in non-communicative patients with disorders of consciousness

Neuromodulation techniques, aiming at normalizing the neurophysiologic disturbance of a brain lesion or deficit, have been studied for years trying to modulate brain activity

to treat several neurological diseases. The field of non-invasive brain stimulation offers a valuable alternative the improve the recovery of severely brain injured patients with disorders of consciousness (DOC), a population that lacks effective treatment options, especially at the chronic stage. In this presentation, we will describe non-invasive brain stimulation techniques, as therapeutic options for patients with DOC. The first studies using transcranial direct current stimulation (tDCS), targeting the left prefrontal cortex, have shown encouraging results, with significant behavioral improvements, in both acute and chronic patients. Beside behavioral improvements, mechanisms underlying the effects of these neuromodulation techniques need to be further investigated. A few studies using neuroimaging and electrophysiological data have tried to understand the neural mechanisms underlying a clinical response (ie., tDCS-responder). In this presentation we will also review how functional neuroimaging and neurophysiological data can help to better understand the neural correlates of responsiveness in order to optimize therapeutic strategies.

OS4-1

Title
New methods and experimental results for optimized multi-channel tES (I).

Chaired by Carsten Wolters, Till Schneider, Thomas Knösche

Abstract
Transcranial electric stimulation (tES) is a noninvasive method that delivers current through the scalp to enhance or suppress brain activity. The standard way of applying TES is by the use of two large rectangular sponge electrodes on the scalp. The resulting currents often stimulate a broad region of the brain distributed over brain networks. In order to address this issue, recently, multi-electrode TES with optimized montages has been proposed to stimulate brain regions of interest with improved trade-off between focality and intensity of the electrical current at the target brain region. Our session will emphasize the importance of individualized targeting (i.e., with regard to location and orientation of the target vectors) by electro- (EEG) and magneto-encephalography (MEG) source analysis and/or fMRI. In session part A, we will present new optimization and FEM forward modeling approaches, new stimulation hardware and neural mass modeling for modeling the whole brain stimulation process. In session part B, experimental results, in which individualized targeting methods were applied, will be presented.

Speakers

Marios Antonakakis (University of Münster)

Individual targeting effects and optimization of multi-channel transcranial electric stimulation of the human primary somatosensory cortex

Individually targeted multi-electrode transcranial Electric Stimulation (TES) has emerged as a promising approach for inducing inhibitory and excitatory effects in brain networks. Our sensitivity study investigates the influence of individualizing the targeting when different experimental conditions are employed in combined electro- and magneto- encephalography (EMEG) source analysis, so that the stimulation montage can then subsequently be optimized for multi-electrode TES. We focus on the P20/N20 component of combined somatosensory evoked potentials (SEP) and fields (SEF) data and use EMEG source analysis and calibrated realistic finite element method (FEM) head volume conductor models for targeting and optimization. SEP/SEF were acquired using the following stimulation types: (a) electric wrist stimulation of the median nerve, (b) electric, (c) Braille-tactile and (d) pneumato- tactile stimulation of the index finger. T1w, T2w, diffusion-weighted magnetic resonance images, and combined SEP/SEF data are exploited for modelling the individual skull-conductivity calibrated head volume conductors including six tissue compartments and white matter anisotropy. Differences in optimized TES montages and current densities due to individual targeting, differing especially in the source orientation components, are presented.

Guilherme Saturnino (Copenhagen University Hospital Hvidovre)

Efficient optimization of multichannel TES

Introduction: Transcranial electric current stimulation (TES) modulates brain activity non-invasively using scalp electrodes. Due to the conductive properties of the human head, currents generated by TES are usually unfocal, and often misses the stimulation target. Recently, methods for optimizing electrode montage for TES have been proposed, but control of key parameters, such as the number of active electrodes, has not been tackled effectively. In this talk, we will present new methods for optimizing electric fields in TES which can in a few seconds give certified optimal electrodes montages.
Methods: We created a new formulation of the TES optimization problem, in which we minimize the total energy delivered to the brain while reaching a user-defined electric field in a target brain region and controlling the total current injected, the current injected per electrode and the number of active electrodes. Limiting the number of active electrodes makes the optimization problem combinatorial, and therefore it cannot be solved effectively using conventional methods for convex optimization. To tackle this problem, we designed a new Branch-and-Bound algorithm.
Results: The new algorithm can find optimal electrode current configurations in under 10 seconds in all cases tested. The solutions are certified, meaning that they are known to be close to the global minimum. We used this new optimization method to map where in the cortex TES can be applied focally.
Discussion and Conclusion: We introduced a new method for optimizing TES electrode montages. It is highly efficient in controlling the number of active electrodes and offers certified solutions.

Thomas Knösche (Max Planck Institute for Human Cognitive and Brain Sciences)

Identifying the location of the effects of transcranial brain stimulation using the congruence factor approach

Mathematical modeling can substantially improve the reliability, predictability, and scientific interpretability of the effect of transcranial brain stimulation (TBS). The complete modeling chain includes descriptions of the induced electric field within the brain, of the mechanism by which this field influences neural cells, of how the altered behavior of the neurons influences the dynamics of neural circuits, and of how these dynamical changes give rise to the observed physiological, cognitive, or behavioral effects. Here I will present a novel method, the congruence factor approach, that allows for the identification of correlational (and potentially causal) relationships between the induced electric field in particular brain areas and the observable peripheral effects of brain stimulation. This way, we are able to precisely localize the neural populations that are responsible for the observed experimental effects, irrespective of the fact that much wider regions are potentially influenced by the stimulation process. I will demonstrate the performance of the method at the example of the causal relationship between the predicted electric field in TMS over the motor cortex and the observed muscle activity (Weise et al., under review). I will discuss the

potential extension of this method to other paradigms and its utilizability for brain mapping in clinical and research applications.

Reference:
K. Weise, O. Numssen, A. Thielscher, G. Hartwigsen, T.R. Knösche: A novel approach to localize cortical TMS effects, under review.

Jens Haueisen, Alexander Hunold (TU Ilmenau)

Bifunctional cap for simultaneous EEG and tES

We introduce a bifunctional flexible textile cap for simultaneous TES-EEG applications with novel electrode materials, textile stimulation electrodes and dry EEG electrodes. We verified the functionality of this cap in a study on ten volunteers, analyzing the stimulation effect of TES on visual evoked potentials (VEPs). In accordance to previously reported stimulation effects, the amplitude of the N75 component was modulated post stimulation. Further, we report for the first time a significant reduction of the P100 component in VEPs measured simultaneously during TES. The novel bifunctional cap overcomes limitations of conventional equipment for simultaneous TES-EEG studies.

OS4-2

Title
Non-invasive and invasive transcranial brain stimulation for motor and mood systems.

Chaired by Jui-Cheng Chen

Abstract
In the past decades, several techniques have been developed to stimulate conscious human's brain through intact scalp. Mostly, the techniques generate currents in the brain by placing either electrodes over the scalp to inject currents (e.g. tDCS: transcranial direct current stimulation) or a coil closed to the head producing changing magnetic field to induce eddy current (e.g. TMS: transcranial magnetic stimulation). More recently, focused ultrasound that is capable of generating mechanical force or thermal effects has drawn people's attention, and been used for transcranial brain stimulation. In this session, the application of these techniques for understanding neurophysiology and for therapeutic purposes for movement, e.g. Parkinson's disease, and mood disorders, e.g. depression, will be presented and discussed. The audience will be able to learn about these transcranial brain stimulation techniques and their applications in research and clinical practice

Speakers

Chi-Hung Juan, Chong-Chih Tsai, Yi-Chun Tsai, Jia-Rong Yeh, Norden E. Huang , Wei-Kuang Liang, Cheng-Ta Li (National Central University)

The effects and mechanisms of repetitive TMS (rTMS) and theta burst stimulation (iTBS) in Treatment-Resistant Depressed patients revealed with brain oscillations

A variety of studies have investigated the efficacy of repetitive TMS (rTMS) and intermittent TBS (iTBS) in treating treatment-resistant depression (TRD). However, the mechanisms of variant outcome of TMS treatment revealed by the brain oscillations are still unclear. This study was conducted to investigate the diversity of the brain oscillations during resting state in TRD patients and the variability between responder and non-responder to rTMS or iTBS treatment. We have preliminary recruited 37 TRD patients who were randomly distributed to iTBS group, 10 Hz rTMS group, or sham TMS group with a double blind design. Each participant was involved in ten sessions treatment phase and the resting state electroencephalography (EEG) was recorded before and after the treatment phase. The efficacy of TMS was evaluated by the 17-item Hamilton depression rating scales (HDRS-17) and Clinical Global Impression-severity (CGI-S) which were held by psychiatry doctors from Veterans General Hospital of Taipei at the beginning of the TMS treatment, at the 5th session and at the 12th week after the treatment. The non-linear analytical method, namely Holo-Hilbert spectral analysis (HHSA; Huang et al., 2016), was applied to the resting-state EEG data. This analytical method provides not only the carrier frequency information but also the amplitude modulation which can fully represent the complex nonlinear information in the EEG. The preliminary results have shown the effect after iTBS that the brain activities increased over the right hemisphere in the range from 4 Hz to 8 Hz (theta frequency band) and increased over central part in the range from 16 Hz to 64

Hz (beta and low gamma frequency band) in the responders. Nevertheless, the brain activities decreased in the range from 4 Hz to 32 Hz in non-responders. Regarding the effect after rTMS, responders showed overall increased brain activities from 4 Hz to 128 Hz, in contrast, nonresponders showed decreased brain oscillations from 32 Hz to 64 Hz. These results have indicated different mechanisms of rTMS and iTBS on TRD patients. Individual difference was also revealed by diversity of the treatment effect in TRD patients. Given these patterns of results, we aim to gradually derive reliable EEG predictors for determining the optimal TMS treatment in TRD patients.

Ming-Kuei Lu (China Medical University)

Paired electroacupuncture and transcranial magnetic stimulation

Paired associative stimulation (PAS) is one of the non-invasive brain stimulation techniques following the Hebbian principle of neural plasticity. It consists of pairs of electric stimulation at wrist median nerve and transcranial magnetic stimulation (TMS) at motor cortex (M1). Since electroacupuncture (EA) is an established medical technique in the eastern countries, we investigated whether EA paired with TMS induces M1 motor plasticity as observed in the conventional PAS protocol. In total 225 pairs of EA at acupoint “Neiguan”, 2 decimeters proximal from the wrist wrinkle, and TMS at M1 were applied with two interstimulus intervals. One interstimulus interval is shorter than the individual somatosensory evoked potential (SSEP) and the other is longer than that. The shorter and the longer intervals are supposed to induce suppressive and facilitatory M1 excitability, respectively. Motor-evoked potential (MEP) recruitment curve, short-interval intracortical inhibition (SICI), intracortical facilitation (ICF) and cerebellar inhibition (CBI) were compared before and after the 0.25 Hz EA-TMS at M1. SSEP and H-reflex were also measured. EA paired with sham TMS was designed as a control. We found that repetitive low frequency EA-TMS did not induce spike-timing dependent motor plasticity in M1. Complex sensory afferents with dispersed time locked to the sensorimotor cortical area may hamper instead of enhancing the motor plasticity in M1.

Tsung-Hsun Hsieh, Yu-Ting Huang, Xiao-Jun Feng, Ying-Zu Huang (Chang Gung University)

Therapeutic effects of transcranial direct current stimulation (tDCS) in motor and cognitive impairments in Parkinsonian rat model

Parkinson's disease (PD) is the second most common age-related neurodegenerative disease which affects an estimated 7-10 million people worldwide. The pathologic hallmark of PD is the loss of nigrostriatal dopaminergic neurons, leading to functional motor and cognitive disabilities. Transcranial direct current stimulation (tDCS) is one of the popular non-invasive brain stimulation approaches. It has been developed for modulating cortical excitability and is considered having therapeutic potential in PD. However, the therapeutic value of such an approach for PD is still unclear. By applying the PD animal model, it may be useful to clarify the existence of treatment effect and explore an effective therapeutic strategy using tDCS protocol. The neurotoxic PD rats induced by 6-hydroxydopamine (6-OHDA), was applied to identify the therapeutic

effects of tDCS in motor and cognitive behaviors following long-term tDCS treatment, as an early step toward possible eventual clinical.
After 24 h 6-OHDA injection, neurotoxic PD rats received daily sham or real tDCS (300μ anodal tDCS, 20 min) under the awake condition for 5 consecutive days/week for 4 weeks. The detailed functional behavioral tests including apomorphine-induced rotational behavior, anxiety, depression, akinesia, open field locomotor activity, and detailed gait analysis were assessed every week and up to 4 weeks. Under tDCS intervention over the course in the early stage of PD rats, we found that four-week tDCS intervention significantly ameliorated the 6-OHDA induced motor and cognitive deficits in open field locomotor activity gait pattern, akinesia, anxiety, apomorphine-induced rotation, and depression behavior. Immunohistochemically, tyrosine hydroxylase (TH)-positive neurons and fibers in the substantia nigra and striatum were significantly preserved following 4 weeks of tDCS treatment. These results suggest that early and daily long-term tDCS could reduce the aggravation of PD symptoms induced by 6-OHDA and exert the neuroprotective effect in a PD rat model. Furthermore, our results highlight the potential therapeutic effects of tDCS and could serve as a translational platform bridging human and animal studies in the development of therapeutic tDCS application for PD or other neurological disorders.

Ying-Zu Huang (Chang Gung University)

Fatigue and motor plasticity in human's motor cortex

The majority of motor learning comes from repetitive practice. During great efforts of motor practice, muscle fatigue is inevitable. It therefore brings up a great interest in how fatigue influences on motor learning. By understanding such interactions, it will be helpful to know how the system copes with fatigue and further improve the efficiency of learning. Such knowledge can then be applied for developing strategy for motor learning, e.g. sport training. While thinking of tiring and even exhausting brought by fatigue, the first impression of the influence of fatigue on learning would be negative. Indeed, there have been quite a few reports suggest that fatigue could slow down learning processes. However, to practice hard enough to a level bringing fatigue in is usually required for a breakthrough in learning. It is even truer in physical practice for motor skills. Hence, it is reasonable to speculate that fatigue may not be always bad for learning. Indeed, it has been reported that the performance of practiced exercise can be better in the fatigued group than in the non-fatigue group. Furthermore, it has been suggested that light, but not moderate or heavy, fatigue may optimize the performance of skill requiring sport. The diverged opinions and results attract our attention and deserve further evaluation to clarify the controversy. In this study, the effects of different, central and peripheral, types of fatigue on motor plasticity were tested in the hand muscles. Motor plasticity was induced by theta burst form of repetitive transcranial magnetic stimulation applied to the hand motor area and was measured by the changes in the size of motor evoked potentials recorded from the hand muscle. In the experiments, a task for fatigue induction was first performed by the hand, and then motor plasticity was measured. Different tasks were tested in different sessions that were at least one week apart from each other. As a result, indeed, we found that motor plasticity was modulated by preceding fatigue. The modulation effects were different between tasks.

OS4-3

Title
New video analysis methods ranging from entertainment to clinical applications.

Chaired by Nicolai Spicher, Prof. Markus Kukuk

Abstract

In recent years, the contact-free acquisition of physiological parameters, which have been measured by contact-based methods before, has received much scientific attention. One example method is photoplethysmography imaging, which allows to measure blood volume changes with the help of a video camera instead of a pulse oximetry probe in direct contact with human tissue. Another example is thermal imaging which measures variations in temperature from human skin and has been used successfully for estimating emotional states.
Additionally, the increase in computer processing power paved the way for novel video processing algorithms, e.g. “magnification algorithms” that allow to amplify subtle motions in videos to a level that they become visible for a human observer. This can be used for visualizing the flow of blood or motions of blood vessels. Another example are algorithms that allow to track humans in videos which have been refined in the past years due to the advent of machine learning to full 3D kinematic human pose estimation in real-time.

Speakers

Andreas Harrer (University of Applied Sciences and Arts Dortmund)

New video analysis methods - an application for the adaptive movie format M(e)y(e) Cinema

In our talk we will present the project M(e)y(e) Cinema that uses multiple types of sensors data to adapt a movie to the subconscious reactions of the indiviual viewer.
One of these sensor inputs - among our main information via eye-tracking - is the measurement of blood volume using Photoplethysmography imaging (PPGi), i.e. camera pictures and analysis of colour variation. This serves to measure the level of arousal and excitement of the viewer and thus informs our algorithm in selecting the appropriate continuation of the movie among the pre-fabricated different story branches and genres.

Christopher Bruman (University of Applied Sciences and Arts Dortmund)

New video analysis methods ranging from entertainment to clinical applications

Detection, identification and tracking of athletes using computer vision are techniques, that are already used for entertainment and match analysis purposes these days. For example in football, various metrics as ball possession, distances run in a period of time or the overall field domination are well-known. However, modern hardware

development and the resulting increase in computing power lead to new types of machine learning algorithms / architectures. Beside tracking athletes, they also provide the ability to perform human pose estimation, allowing a kinematic representation of the humans motion, based on a video signal, without placing any markers on the athlete. We like to present our work, which deals with motion analysis of squash players. We use a single, static camera located behind the court which also serves as a calibration pattern for on-court position estimation. While player detection is done by background subtraction using a Gaussian mixture model, identification is based on dominant color regions (player garments). Our goal is to measure and analyze stress and performance parameters in order to support the athletes training and exercises.

Nicolai Spicher (University of Applied Sciences and Arts Dortmund)

New video analysis methods ranging from entertainment to clinical applications

In recent years, the contact-free acquisition of physiological parameters, which have been measured by contact-based methods before, has received much scientific attention. One example method is photoplethysmography imaging, which allows to measure blood volume changes with the help of a video camera instead of a pulse oximetry probe in direct contact with human tissue. Another example is thermal imaging which measures variations in temperature from human skin and has been used successfully for estimating emotional states.
Additionally, the increase in computer processing power paved the way for novel video processing algorithms, e.g. "magnification algorithms" that allow to amplify subtle motions in videos to a level that they become visible for a human observer. This can be used for visualizing the flow of blood or motions of blood vessels. Another example are algorithms that allow to track humans in videos which have been refined in the past years due to the advent of machine learning to full 3D kinematic human pose estimation in real-time.
In this workshop, the speakers will present recent methods for processing videos of human subjects and their applications. The scope of application ranges from entertainment purposes (emotional state measurement), to sports medicine (motion analysis of squash players), to medical imaging applications (gating of magnetic resonance imaging scanners by photoplethysmography imaging), and clinical applications (magnification of subtle muscle activities for biofeedback).

Anke Schlüter (University Hospital Essen)

New video analysis methods ranging from entertainment to clinical applications

Objective: The quality of life (QoL) of patients with facial paralysis is significantly impaired. If no obvious irreversible nerve damage is apparent, an intensive training of the facial muscles is recommended, in addition to drug therapy with cortisone. In order to improve the training, we have developed a digital biofeedback mirror for motion magnification to influence the vegetative nervous system indirectly through self-control and associated training. The aim of this study was to evaluate the reliability of the biofeedback program compared to clinical examinations.

Methods: The described biofeedback system is similar to a mirror with the additional advantage of increasing the patient's self-control. However, it does not only reflect the patient's image, but also potentiates movement through video processing and a magnifying function. For this purpose, the patient's facial movements are filmed and amplified in real-time. Thus, even the smallest movements can be made visible and measured so that patients receive feedback on nerve regeneration.
Results: In the present study, we were able to demonstrate that the measurement of the facial movements showed reliable concordance with the clinical classification according to the House-Brackmann scale. Restriction of QoL could be evaluated and objectivized with FaCE and FDI questionnaires. A significant improvement of the measured values of the facial movements as well as quality of life of patients after 3 months could be demonstrated.
Conclusion: The biofeedback system is a reliable support during the regeneration phase for patients with facial paralysis leading to major improvement of their QoL.

OS5-1

Title
New methods and experimental results for optimized multi-channel tES (II).

Chaired by Carsten Wolters, Till Schneider, Thomas Knösche

Abstract
Transcranial electric stimulation (TES) is a noninvasive method that delivers current through the scalp to enhance or suppress brain activity. The standard way of applying TES is by the use of two large rectangular sponge electrodes on the scalp. The resulting currents often stimulate a broad region of the brain distributed over brain networks. In order to address this issue, recently, multi-electrode TES with optimized montages has been proposed to stimulate brain regions of interest with improved trade-off between focality and intensity of the electrical current at the target brain region. Our session will emphasize the importance of individualized targeting (i.e., with regard to location and orientation of the target vectors) by electro- (EEG) and magneto-encephalography (MEG) source analysis and/or fMRI. In session part A, we will present new optimization and FEM forward modeling approaches, new stimulation hardware and neural mass modeling for modeling the whole brain stimulation process. In session part B, experimental results, in which individualized targeting methods were applied, will be presented.

Speakers

Axel Thielscher, Oula Puonti (Copenhagen University Hospital Hvidovre)

Validation and application of individualized head models for transcranial brain stimulation

Electric field (E-field) simulations are increasingly used to inform researchers about the spatial distribution of the stimulation effects in the brain and to optimize spatial targeting. Individualized simulations are based on head models that are created from MR images, and the accuracy of the simulations depend on the accuracy of the segmentation procedure. In my talk, I will outline our recent work on a new automatic segmentation procedure that achieves highly accurate head models which include the neck region. I will give examples demonstrating the relevance of individualized simulations by comparing E-fields calculated with individualized models versus a “standard” head model for the same electrode montage.
Validations of the simulated E-fields by comparisons against in-vivo recordings is important to ensure that the simulated E-fields correspond to those induced in reality. In the last part of my talk, I will present our recent comparison of four different automated pipelines against intracranial voltage recordings in an existing dataset of 14 epilepsy patients. I will highlight the importance of accounting for noise in both the measurements and simulations to reach unbiased and robust conclusions about the fit between both.

Asad Khan (University of Münster)

Constrained maximum intensity optimized multi-electrode tDCS targeting of human somatosensory network

The conventional way for tDCS is to apply current to a two patch electrode montage with one electrode over the primary motor cortex (anode) and the other electrode over supraorbital area (cathode). However, as the currents are broadly distributed resulting in the stimulation of non-ROI's (Region Of Interest), targeting a specific ROI, like the underlying sources of the somatosensory P20/N20 components of the somatosensory evoked responses might profit from more focality and directionality. Recently multi-electrode tDCS optimization methods have gained interest in order to achieve an efficient trade-off between focality, directionality and intensity of the stimulation current parallel to the target. However, most of the multi-electrode optimization approaches, when modeling a specific brain region, only consider the location and do not consider individual target orientation differences between subjects. Here, we explore different current facilities and intensities achieved among subjects in a somatosensory experiment and simulation study using combined electroencephalography (EEG) and magneto-encephalography (MEG) source analysis in finite element method (FEM) based skull-conductivity calibrated realistic head models first to calculate the target location and orientation and then using four optimization methods with different goal functions, from which one, constrained maximum intensity (CMI), is a new approach. The new CMI approach better distributes the currents over multiple electrodes, therefore leading to less tingling and burning sensations at the skin, and thus allows an easier realization of the sham condition without significantly reducing the current intensity parallel to the target.

Jan-Ole Radecke (University Medical Center Hamburg-Eppendorf)

Individualized optimization of lateralized transcranial electric stimulation (tES) for experimental application

Although widely used, the modulation of neural activity by use of transcranial electric stimulation (tES) has revealed heterogeneous results. At the same time, variability across individual anatomies can be observed, affecting the spatial extent and intensity of electric fields induced by tES. Personalized tES in principle allows to control for this variability by optimizing targeted modulation of neuronal activity. In the present study, simulation of current densities induced by tES were computed for twenty-one subjects using MRI-derived six compartment finite-element method head models. A simulated target in the right parietal cortex was defined with three orthogonal target orientations. Current densities and spatial extent of the respective electric fields derived from a standard montage were compared to stimulation montages, which were individually optimized either for intensity or for focality. Simulation results are reported speaking in favor of the application of current flow optimization approaches for the individual brain in order to understand the underlying effects of tES. Specifically, the presented processing pipeline emphasizes the advantages of personalized tES for ad-hoc optimization of the stimulation and post-hoc evaluation of simulated fields.

Andrea Antal (Universitätsmedizin Göttingen)

Multichannel TES in the treatment of neurological and psychiatric disorders

The modulation of cortical excitability and resultant activity; a central mechanism of 'induced neuroplasticity', has been investigated using several low intensity transcranial electrical stimulation methods (TES) such as transcranial direct current (tDCS), alternating current (tACS) and random noise (tRNS). The most frequently used method is tDCS; this method is interventional use in research and of potential therapeutic use in neurorehabilitation, chronic pain and depression. Despite applications of tDCS in research, the precise physiological mechanisms by which stimulation influences brain function are only partly understood. Combining TES with concurrent functional magnetic resonance imaging (fMRI) and electroencephalogram (EEG) has recently opened a new research era because they have the advantage of measuring neuronal activity both under the stimulating electrodes and in remote brain regions.
By using tACS, alternating current is assumed to entrain endogenous neural oscillations possibly by modulating the power of oscillations or the phase-locking index between the driving and endogenous oscillations. In order to establish a causal relationship between oscillations and these functions as well as to try to restore disturbed oscillations that can be observed in several neurological and psychiatric disorders, it is desirable to develop new protocols. With regard to tRNS, it is so far not clear if this stimulation may interfere with ongoing network oscillations or with homeostatic mechanisms. The possible clinical application of tACS and tRNS is in its beginnings. A high number of stimulation paradigms will have to be tested and condensed to those with highest physiological relevance in order to introduce these methods in the clinical practice.

OS5-2

Title
Update on NIBS Technology in Brain Disorders.

Chaired by Giulio Ruffini, Ferdinand Binkofski

Speakers

Giulio Ruffini (StarLab)

Realistic modeling of tCS/tES: from research to clinical applications

The brain is a network of networks that can be studied at multiple scales. In this talk, I will first provide a brief overview of multichannel transcranial current stimulation (tCS or tES) technology and the biophysics of its interaction with the human brain, and explain how it can be seen to interact with such networks. I will review how it can be used to target specific restricted regions of the cortex or to target cortical networks using a method for optimization of multichannel montages (Stimweaver). In particular, the importance and challenges of defining appropriate targeting strategies for multichannel tDCS and tACS, and the tradeoffs that are needed in optimization due to the inherent physics underlying this intervention will be emphasized. I will then provide clinically relevant examples of montage optimization for more focal stimulation, e.g., of the motor cortex, the dorsolateral PFC or in cortical focal epilepsy, for the stimulation of networks derived from neuroimaging, or, finally, for “active” sham stimulation, a new sham approach designed for optimal double-blinding and for disentangling the CNS and PNS effects in tCS. Finally, I will discuss the use of realistic modeling for exploring basic research questions such as the role of ephaptic interactions in the cortex, and the need for more advanced modeling approaches that bring together physics and physiology.

Ferdinand Binkofski (University of Aachen)

Modulation of the front-striatal connectivity by theta-burst stimulation. A perspective at clinical application.

Background: The fronto-striatal network is involved in various motor, cognitive and emotional processes, such as spatial attention, working memory, decision-making and emotion regulation. Intermittent theta burst transcranial magnetic stimulation (iTBS) has been shown to modulate functional connectivity of brain networks. Long stimulation intervals, as well as high stimulation intensities are typically applied in transcranial magnetic stimulation therapy for mood disorders. The role of stimulation intensity on network function and homeostasis has not been explored in the fronto-striatal network systematically yet.
Objective: In our studies, we aimed to modulate fronto-striatal connectivity by applying iTBS at different intensities to the left dorso-lateral prefrontal cortex (DLPFC). We measured individual and group changes by comparing resting state functional magnetic resonance imaging (rsfMRI) pre-iTBS und post iTBS. Differential effects of

individual sub- versus supra-resting motor-threshold stimulation intensities were assessed. The results of the rsfMRI/iTBS study informed a [18F]Fallipride-PET study heading at measurement of modulation of basal ganglia activity by iTBS to the left prefrontal cortex.
Methods: In the rsfMRI/iTBS study sixteen healthy subjects underwent excitatory iTBS at two intensities (90 % and 120 % of individual resting motor threshold) on separate days. 600 pulses (2 s trains, 8 s pauses, duration of 3 minutes, 20 seconds) were applied over the left DLPFC. Directly before and 7 min after stimulation, task-free rsfMRI sessions, lasting 10 min each, were conducted. Individual seed-to-seed functional connectivity changes were calculated for ten fronto-striatal and amygdala regions of interest with the SPM toolbox DPABI.
In the PET/iTBS study twenty two healthy subjects underwent two hour measurements of [18F]Fallipride (a postsynaptic D2 receptor antagonist) induced activity in the basal ganglia. During this measurements the subjects got either four iTBS stimulations to the left DLPFC at 90% intensity or four sham stimulations every 30 minutes during the 2 hours measurement time. The binding capacity of the D2 receptors was assessed using SPM12 and other dedicated software packages.
Results: In the rsfMRI/iTBS study sub-threshold-iTBS increased functional connectivity directly between the left DLPFC and the left and right caudate, respectively. Supra-threshold stimulation did not change fronto-striatal functional connectivity, but increased functional connectivity between the right amygdala and the right caudate. In the PET/iTBS study verum stimulation, as compared to the sham stimulation, resulted in significant reduction of receptor bindings caused by the competitive increase of dopamine in the synaptic gap. This result indicate an increase of fronto-striatal connectivity especially in the caudate and the putamen bilaterally.
Conclusion: A short iTBS protocol applied at sub-threshold intensities was not only sufficient, but favourable in order to increase bilateral fronto-striatal functional connectivity, while minimising side effects. This result was achieved using two independent methods (rsfMRI and Fallipride-PET). Decreased functional connectivity after supra-threshold stimulation was possibly caused by network homeostatic effects. These results provide an important piece of information for the design of therapeutic stimulation protocols, like for treatment of depression.

Armin Kibele (University of Kassel)

Two studies on leg stabilizer strength in older adults

Introduction: The decline of muscle strength is a well-known effect observed in aging adults. However, little is known about differences between the skeletal muscles when gradually loosing strength during the aging process. In this paper, we summarize two studies A) on the assessment of strength differences in leg stabilizer muscles versus leg primary movers between four female age groups (10- to 13-year old girls (N=31), 19- to 29-year old sport science students (N=30), 41- to 55-year old females (N=27), and 63- to 79-year old females (N=33)) and B) on the effects of three different leg strength training modes (leg extensor machine-based strength training on stable platforms, hip adductor and hip abductor strength training in isolation on stable platforms, and metastability leg strength training with free weights on unstable platforms) in older adults between 65- and 80-years of age. Study B was motivated by the results of a previous study (Eckardt, 2016) and by a systematic review on emg

activation differences in stabilizer and primary mover muscles when exerting maximal forces on stable and on unstable platforms (Kibele, 2017). Hence, we aimed to find out about differences between training the leg stabilizer muscles in isolation on stable platforms and a metastability leg strength training on unstable platforms (see Kibele et al., 2015 for the specifics of a strength training in metastable states of equilibrium). Additionally, subjects exercising a leg extensor machine-based strength training on stable platforms were used as an active control group.
Methods: For study A, maximal isometric forces were measured in 121 female subjects in a random order with a hand-held force measurement device (Manual Muscle Testing System, Type 01165, Lafayette Instrument Company, Lafayette, IN, USA). Force values were converted to normalized maximal isometric torques with respect to body weight and thigh length. For study B, 68 male and female older adults randomly assigned to the three training groups participated in a 10-week training program. Measures of leg strength and power, literature based measures to indicate a risk of falls, and executive functions (e.g., Digital Memory Test) were compared before to after training. In particular, the model of Uncontrolled Manifolds was used to analyze mediolateral gait stability as a risk of falls indicator (Krishnan et al., 2013).
Results: The results of study A show that ratios between hip abductor (and hip adductor strength) to knee extensor strength values decrease from 1.01±0.21 (0.94±0.17) in the young female adults to 0.91±0.21(0.82±0.12) in the middle-aged females to 0.86±0.15 (0.78±0.12) in the elderly females. The ratio between between hip abductor (and hip adductor strength) to knee extensor strength values for the girls was 0.83±0.14 (0.80±0.10). Statistically significant differences were detected in the Oneway Anova with large effect sizes (hip abductor to knee extensor torques: $F = 8.24$, $p < 0.01$; $\omega^2 = 0.15$ and hip adductor to knee extensor torques: $F = 8.01$, $p < 0.01$; $\omega^2 = 0.15$). In study B, significant interaction effects time x group were found for the maximal isometric force in a leg extension task ($F = 12.0$, $p < 0.01$; $eta^2 = 0.27$ (large effect)), the mediolateral gait stability on uneven surfaces ($F = 4.11$, $p < 0.05$; with Cohen's $d = 0.71$ (medium effect)), and for the Digit Memory Test ($F = 6.0$, $p < 0.05$; $eta^2 = 0.16$ (large effect)). For these test values, metastability resistance training with squatting movements using free weights on unstable platforms showed superior effects as compared to the other strength training modes. No statistically significant interaction effect of time x group was found in the strength measures of the hip adductors and the hip abductors. In fact, a tendency was detected indicating the metastability resistance training to be slightly more effective for increasing hip adductor and hip abductor strength than training both muscle groups in isolation.
Discussion and Conclusion: The detected results of study A indicate that the extent of strength decline found in aging adults may vary from muscle to muscle and may depend on the use resp. the function of the muscles at age. Moreover, these results suggest out a more pronounced strength decline in the leg stabilizer muscles as compared to the leg primary movers in the course of the adult aging process. Possibly, the ratio of leg stabilizer strength to primary mover strength could be used as a valuable indicator for the risk of falls. The results of study B indicate that metastability resistance training with free weights on unstable platforms could be a valuable tool to improve leg extension strength and leg stabilizer strength. In addition, this training mode poses large attentional demands when lifting loads on unstable platforms while maintaining balance. Previously, such tasks have been shown to increase the Dopamin level in the body (Düzel et al., 2010). Hence, increased attentional demands and increased Dopamin, both promoting executive functions, and in particular memory performance, may benefit from metastability resistance training.

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Ester Miyuki Nakamura Palacios (Federal University of Espírito Santo)

Drug-cue reactivity as a potential neural target in the development of a neurofeedback system for cognitive training in substance use disorders.

Background: Interventions exploring modulation of the prefrontal cortex activity using non-invasive brain stimulation techniques in drug addiction are currently growing. In the later years we observed that the transcranial direct current stimulation (tDCS) applied bilaterally over the Dorsolateral Prefrontal Cortex (DLPFC) showed promising clinical effects, reducing craving and relapse to alcohol and crack-cocaine use in severely dependent patients. In addition to these clinical evidences, we observed that this bilateral prefrontal tDCS changed the drug cue-reactivity in the medial prefrontal region visualized by LORETA performed over Event Related Potentials (ERPs) responses to drug-related or neutral visual cues, especially in subjects with favourable clinical responses to the tDCS. Our following question is whether these potential changes in the medial prefrontal activation would constitute neural targets for a cognitive training strategy through neurofeedback that could reinforce the cognitive and inhibitory control over the compulsive behaviour. Here we will be focusing on these electrophysiological evidences and the challenge to input them into a computer (machine) that should identify and select these brain signals, process them and synchronize them (machine learning) and convert them into visual signs to be returned to the subjects as indicators of performance (neurofeedback), enabling the cognitive training.
Methods: The drug cue-reactivity in the P3 time window (250-400 ms for crack-cocaine use disorder – CUD - and 300-450 ms for alcohol use disorder - AUD) was measured with Event Related Potentials (ERPs) in response to drug-related (alcohol or crack-cocaine as target images) or neutral visual cues (non-target images). Neural current source density (CSD) analysis and localizations of the difference between target and non-target cues were performed offline with LORETA (BrainVision Analyzer 2.1) focusing on changes from baseline to 5 or 10 tDCS sessions (once a day, every other day) of bilateral (left cathodal/right anodal) tDCS (20 min, 2 mA, 35 cm2) or sham-tDCS over the Dorsolateral Prefrontal Cortex (DLPFC) applied in AUD and CUD patients.
Results: The Event Related Potentials were differently modulated by group (active vs. sham tDCS) and number of sessions (5 vs.10 tDCS sessions). LORETA processing has shown that the brain region with the greatest P3 drug cue-reactivity after 5 or 10

sessions is the medial portion of the prefrontal cortex (ventral medial prefrontal cortex or orbitofrontal cortex), especially in subjects receiving active tDCS who maintain abstinence for longer period in contrast to those treated with sham-tDCS or even those who had received active tDCS but had relapsed to the drug use. The CSD analysis, however, showed different directions of changes depending on the number of sessions of sham-tDCS or active tDCS. Here we will focus on the ventral medial prefrontal cortex area analysis. After 5 sessions, the CSD in this brain area increased from baseline in CUD subjects from the active tDCS group who maintained abstinence for at least 90 days by approximately 320% and much less, by only about 27%, in the sham-tDCS group who had relapsed to the drug use. In AUD subjects, the CSD in this brain area increased from baseline in about 230% in subjects from the active tDCS group who had maintained abstinence for 6 months, whereas the CSD decreased by about 12% in those subjects from the active tDCS group who had relapsed to the drug use and it was also decreased from baseline by about 53% in subjects from sham-tDCS group who had relapsed to the alcohol use. However, this effect was not linear as after 10 sessions, the CSD of this brain area decreased from the baseline by about 9% or 60% in CUD subjects from the active tDCS group maintaining abstinence for at least 60 days or relapsing to the crack-cocaine use, respectively, and by about 38% in AUD subjects who had not relapsed to alcohol use for at least 90 days, whereas subjects from both sham-tDCS groups, which had mostly relapsed to the drug use, showed CSD increases from baseline in approximately 65% in the CUD and 88% in the AUD.
Conclusion: The tDCS application over the bilateral DLPFC can impact drug cue-related activity of medial regions of the prefrontal cortex in CUD and AUD subjects, but the direction of changes may depend on the number of tDCS sessions, abstinence vs. relapse status, and the type of analyses conducted. The better understanding of these CSD changes imposes a great challenge that will impact the cognitive training setup over drug use in a virtual drug-related environment from a neurofeedback system currently in development by our research group.

Teodiano Freire Bastos Filho (Federal University of Espírito Santo)

A New Methodology for Neuro-Rehabilitation System of Post-Stroke Patients Using Brain-Computer Interface Based on tDCS, Motor Imagery, Virtual Reality and Robotic Devices

The objective of this work is to propose a new methodology for neuro-rehabilitation of post-stroke patients through an online Brain-Computer Interface (BCI) based on Motor Imagery (MI) and Virtual Reality (VR) (to improve MI) to cognitively rehearse physical skills in a safe, repetitive manner, in order to promote the neuroplasticity of these patients through exercises with robotic exoskeleton (for knee flexion/extension movements and gait assistance) and robotic monocycle (for pedaling). Previously, the patients will use tDCS (Transcranial Direct Current Stimulation), in order to improve their cortical excitability and neuro-plasticity, and thus accelerate their movement recovery.
Once the post-stroke patients have been submitted to a transcranial DC Stimulation (tDCS) at the cortical region related to the lower limb from ipsilateral hemisphere and the supplementary motor area more frontally, an EEG quantitative analysis will be carried out, aiming to conduct a positive motor rehabilitation therapy of those patients.

Additionally, the functional and effective connectivity will be studied, session by session, to know the effectiveness of the proposed method for neuro-rehabilitation, in order to increase neuroplasticity of the patients, and thus to prove that our neurorehabilitation system is able to accelerate the patients' movement recovery. In addition, at the end of the set of sessions, all participants of this research will be asked to answer a questionnaire (QUEST form), which measures the satisfaction index of use of that assistive technology using the robotic exoskeleton and robotic monocycle. The sessions will be progressed to try gradually improving amplitude, force (extension and flexion) and speed of knee and gait movements. All participants of this research will be submitted to a clinical and functional assessment, according to the following parameters: Barthel scale (for evaluation of activities of daily living); visual analogue scale (for quantication of perceived pain in the lower limb); knee injury and Osteoarthritis Outcome Score - KOOS (for evaluation of the domains pain, symptoms, daily function, function in the sport and quality of life relative to their knee). All the qualitative variables of the parameters of this research will be compared before and after the application of the protocol, using the Student's T-test to matched samples, with an adjusted level of significance to 0.05.

OS6-1

Title
Modulating sensory, motor, and cognitive Functions by training interventions and non-invasive brain stimulations: Results from the TRAINSTIM project.

Chaired by Stefan Getzmann

Abstract
Cognitive and sensory-motor functions usually decline with increasing age. In this session we will report approaches in which respective functions and neuroplasticity are modulated by non-invasive brain stimulation (NIBS) in combination with long-term cognitive training protocols.

Speakers

Pablo Maceiraelvira (Swiss Federal Institute of Technology)

Ensieh Ghasemian Sh/ Leila Farnad (IfADo)

Age dependency of neuroplasticity induced by transcranial direct current stimulation

Friederike Thams (University of Greifswald)

Effects of brain stimulation and cognitive training on age-associated cognitive decline

Many studies have found non-invasive brain stimulation techniques to be effective for enhancing various cognitive functions. Specifically, transcranial direct current stimulation (tDCS) was found to impact behavioural performance. However, most studies have been conducted in young adults. Only few studies have been published in older adults, with partially conflicting results, so more systematic studies in older adults are needed, with detailed analyses of mechanisms underlying improvements. In my contribution, I will address these open issues, embedding recent work from our group on tDCS effects and cognitive performance in aging into the context of modulating age-related alterations of neural plasticity and connectivity. Particularly, I will introduce a randomized controlled trial, assessing a multi-day intensive cognitive training intervention combined with tDCS in healthy older adults. Cross-sectional data of baseline behavioural performance in training tasks and MRI will be discussed together with the effects of the intervention. Our goal is to learn about the effectiveness of the intervention and to identify possible factors predicting efficiency of combined training and tDCS interventions in healthy aging. An improved understanding of tDCS effects on cognitive training performance and underlying neural correlates may additionally help to develop novel approaches for cognitive decline in healthy and pathological aging.

Kathleen Kang, Annika Dix, Luca Spliethoff, Susanne Passow, Shu-Chen Li (Technical University Dresden)

Effects of transcranial direct current stimulation (tDCS) on attentional control and decision making.

Attentional control and decision making are complex cognitive processes which are essential for our daily functioning. Both processes implicate the prefrontal cortex (PFC); hence, any age-related decline in the PFC might attenuate these two domains of functions. Nevertheless, these processes can be potentially modulated by regulating neuronal excitability using tDCS. However, there is limited research regarding the mechanisms underlying tDCS effects as well as the effects of different tDCS protocols. In this talk, two separate studies investigating the effects of prefrontal anodal tDCS on auditory attentional control and decision making will be presented. The first study investigated the effects of anodal tDCS in regulating attentional control during a dichotic listening task, as well as the underlying neurophysiological processes as measured by EEG. Thirty-two healthy young adults underwent offline anodal and sham stimulation using a within-participant cross-over design. The neurophysiological findings revealed that tDCS results in higher theta power during high attentional-perceptual conflict as compared to low conflict conditions. The effect was specific to the response selection phase. The second study explored the effects of offline and online tDCS on decision making (using the Markov's decision making task) in healthy older adults. In the first part of the study, 10 older adults underwent offline tDCS while another 10 underwent sham stimulation; whereas in the second part of this study, 9 older adults underwent online tDCS while another 10 underwent sham stimulation. The behavioural findings showed that only older adults who underwent online tDCS showed an earlier change point in the delayed condition, as compared to sham condition. This effect was, however, not apparent in older adults who underwent offline tDCS. Taken together, the findings from these two studies demonstrate the potential of both online and offline tDCS in regulating neuronal excitability and modulating cognitive functioning, thus, elucidating the potential of tDCS as a therapeutic intervention, e.g. for populations with constrained attention and decision-making functions. The effects of tDCS, however, depend on several factors like, for instance, the specific protocol applied (online vs. offline).

Stephan Getzmann (IfADo)

Influences of non-invasive brain stimulation and short-term training on auditory spatial attention

Speech perception in complex acoustic environments usually declines with increasing age. This decline is based – at least in part – on difficulties in detecting and localizing a relevant target speaker among concurrent sound, indicating deficits in selective auditory spatial attention. Our project aims at improving localization of speakers of interest under simulated "cocktail-party" conditions in younger and older human subjects using non-invasive brain stimulation (transcranial direct current stimulation, tDCS) and short-term training. Based on findings of beneficial effects of anodal tDCS on "cocktail-party" speaker-localization performance in younger adults (Lewald, 2019, Exp. Brain Res. 237: 1539-1549), we investigated cortical correlates of improved

sound localization using ERP recording. An increased N2 ERP component, indicating enhanced attentional processing, occurred after anodal, but not cathodal, tDCS and for targets presented on the side contralateral, but not ipsilateral, to the hemisphere stimulated by tDCS. Electrical imaging indicated specific modulation of activity in right posterior parietal cortex at the time of the N2, reflecting modulation of attentional control. In a second approach, two types of short-term training were applied using either synchronized auditory targets and visual stimuli presented at congruent locations or auditory spatial feedback about the correct location of the target. Here, an increased N2 was observed after audiovisual congruency training, as well as an enhancement of electrical activity in right dorsolateral prefrontal cortex. Taken together, the present results demonstrated brain correlates of tDCS- and training-induced short-term plasticity of processes involved in selective auditory spatial attention.

OS6-2

Title
Restoration of disturbed neuroplasticity – a technical solution to mental disorders?

Chaired by Lukas Frase

Abstract
Pathological changes of excitability and plasticity of neural systems and the resulting imbalance represent fundamental pathophysiological characteristics of various mental disorders. Novel non-invasive brain stimulation devices offer the opportunity to modulate neural excitability and plasticity beyond the stimulation period and, hence, potentially restore normal brain function. Concentrating on mood, vigilance, attentiveness and sleep as behavioural outcomes, data from healthy subjects as well as clinical applications in depression and sleep disorders will be presented, along with basic mechanisms obtained from animal models and computer simulations

Speakers

Claus Normann (University Medical Center Freiburg)

Disturbed neuroplasticity in depression – what we know and what we need to know

Changes in synaptic plasticity - a basic mechanism of adaption in neural networks and thereby human behavior - are considered fundamental pathomechanisms of mental disorders such as major depressive disorder (MDD). Recent findings of disturbed synaptic plasticity in animal models of MDD as well as patients with MDD are summarized. Modulation of synaptic plasticity is demonstrated as a potential mechanism underlying several known treatment options for MDD. From this background, potential future treatment approaches are introduced.

Lukas Frase (University Medical Center Freiburg)

Non-invasive electrical modulation of vigilance, attentiveness and sleep

Disturbances of vigilance, attentiveness and sleep comprise highly relevant symptoms of various neurological and psychiatric disorders. While the clinical burden for patients is often high, treatment options are very limited. Non-invasive electrical modulation with devices like transcranial direct current stimulators is a promising new pathway to modulate various aspects of vigilance and sleep. Improvements in this area of symptoms could potentially drive general improvement in the underlying disorder, e.g. major depressive disorder (MDD). On a side note, there also is a demand for improvements of vigilance and sleep in healthy subject with ethical implications. The talk summarizes the state of science regarding modulation of vigilance of sleep and proposes a model for such changes as important factors of usage as a treatment tool for MDD.

Frank Padberg (University of Munich)

Non-invasive electrical stimulation in mood disorders: A case for precision medicine

Mood disorders including major depressive disorders (MDD) are highly heterogeneous and constitute a particular challenge for precision medicine. Non-invasive brain stimulation (NIBS), e.g. transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are not only promising interventions for therapy, but also valuable tools for disentangling mood disorders in terms of their neurocircuit pathophysiology. Several approaches are currently considered in order to further develop tDCS for precision medicine: 1) Defining "dosage" at brain level: Computational modeling of tDCS induced electrical fields (efields) based on the individual MRI is an example of this strategy and first efield studies show considerable inter-individual differences as well as differences between health and disease states. 2) Identifying key regions based on multimodal MRI data which mediate therapeutic effects (Bulubas et al. 2019). Theoretically, the response to a given tDCS protocol may provide information whether this region is involved in the individual pathophysiology. Ideally, efficacy for connectivity based targets and multidimensional cluster analyses may identify such disease entities and/or endophenotypes in MDD. 3) Finally, tDCS effects may be functionally focused using behavioral tasks or TMS. This is related to the putative dependence of tDCS mediated effect on brain states. The goal of proofing target involvement by NIBS is challenging. Closed-loop approaches focus on this idea, however, accuracy in connectivity and timing are difficult to achieve at the same time (Bergmann et al. 2016).

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Andreas Vlachos (University of Freiburg)

TMS-based Restorative Neuromodulation – activate, modulate, treat

The ability of the brain to respond to specific stimuli with structural, functional and molecular adaptations is fundamental for physiological brain function and complex behaviour. While work from the past 40 years has attributed this remarkable property of neural tissue to plastic changes at excitatory and inhibitory synapses, the precise role of synaptic excitation/inhibition balance in physiological and pathological brain states is still a matter of debate. At the same time non-invasive brain stimulation techniques, such as transcranial magnetic stimulation (TMS), have been developed aiming at modulating and restoring brain function under pathological conditions. My presentation focuses on recent experimental evidence in animal models demonstrating that TMS modulates synaptic excitation/inhibition balance and thus the ability of neurons to express plasticity. I will present our current strategy to bridge biological scales using computational approaches in order to obtain a profound

mechanistic understanding on how TMS affects neural tissue and how these changes may modulate complex brain function and behaviour.

Han Lu (Bernstein Center Freiburg)

Network remodeling induced by transcranial brain stimulation: A computational model of tDCS-triggered cell assembly formation

Transcranial direct current stimulation (tDCS) is a variant of non-invasive neuromodulation, which promises treatment for brain diseases like major depressive disorder. In experiments, long-lasting aftereffects were observed, suggesting that persistent plastic changes are induced. The mechanism underlying the emergence of lasting aftereffects, however, remains elusive. Here we propose a model, which assumes that tDCS triggers a homeostatic response of the network involving growth and decay of synapses. The cortical tissue exposed to tDCS is conceived as a recurrent network of excitatory and inhibitory neurons, with synapses subject to homeostatically regulated structural plasticity. We systematically tested various aspects of stimulation, including electrode size and montage, as well as stimulation intensity and duration. Our results suggest that transcranial stimulation perturbs the homeostatic equilibrium and leads to a pronounced growth response of the network. The stimulated population eventually eliminates excitatory synapses with the unstimulated population, and new synapses among stimulated neurons are grown to form a cell assembly. Strong focal stimulation tends to enhance the connectivity within new cell assemblies, and repetitive stimulation with well-chosen duty cycles can increase the impact of stimulation even further. One long-term goal of our work is to help optimizing the use of tDCS in clinical applications.

OS6-3

Title
Modulating Cognitive Control with transcranial direct current stimulation (tDCS).

Chaired by Christian Plewnia, Martin Herrmann

Speakers

Martin J. Herrmann (Universitätsklinikum Würzburg)

Transcranial direct current stimulation (tDCS) of the right inferior frontal cortex (rIFC) improves emotional control

Although anxiety disorders can be treated very well with cognitive behavioral therapy, but there are a number of anxiety patients who are not responding adequately to the therapy (Gloster et al., 2012). Therefore, non-invasive brain stimulation methods have been successfully studied as an add-on to psychotherapy (for review Herrmann et al., 2019ab) showing increased efficacy. But there are also a large amount of patients who are refusing exposure therapy (Garcia-Palacios, 2007) with the consequence that these patients do not receive adequate therapy. This avoidance behavior might be influenced by anticipatory anxiety, which is a core symptom of different anxiety disorders. Studies have shown that downregulation of emotional responses to threat is strongly associated with frontal cortex functions. Therefore we tested in two studies the effects of transcranial direct current stimulation (tDCS) over the right inferior frontal cortex (rIFC) on the subjects' psychophysiological responses as measured by skin conductance reaction (SCR) during a anticipatory anxiety paradigm. We found in both studies a significant interaction effect of condition x tDCS for SCR during the anticipatory anxiety condition. Posthoc tests revealed a significant reduction in SCR during anticipatory anxiety in verum compared to sham stimulated group. The results confirm that tDCS of the rIFC attenuates anticipatory anxiety and might help patients to reduce their avoidance behavior.

Jessica Peter (Universitätsklinik für Alterspsychiatrie und Psychotherapie)

Targeting episodic memory with transcranial direct current stimulation: Is cognitive control the modulating factor?

Affect can directly influence memory storage and retrieval, which offers the opportunity to improve memory performance by changing affective responses. A promising target is the left dorsolateral prefrontal cortex (dlPFC), as it is functionally involved in both affect and memory. In different studies, we explored whether transcranial direct current stimulation (tDCS) to the left dlPFC modulates affective responses and thereby improves episodic memory retrieval.
In both young and elderly individuals, we applied either sham or anodal tDCS during encoding of a verbal episodic memory task. Participants completed two questionnaires assessing affective states pre- and post-stimulation. They had to recall items unexpectedly 20 minutes after encoding and to name which feelings were associated

with this free recall. We applied mediation models to explore the relation between tDCS, change in affect, and memory retrieval.
In young participants, the reduction of negative affect via anodal tDCS fully mediated the increase in memory retrieval: tDCS led to lower task-related negative affect, less negative feelings associated with the unexpected retrieval, and, consecutively, better memory performance. We did not observe these effects in the elderly. Our study provides a further link between affect and memory: As increased activity in the dlPFC is crucial for successfully coping with affective interference, anodal tDCS seems to help preventing irrelevant negative thoughts, thus foster attention allocation. We will discuss our results in light of the role of affect in cognitive control, which controls attention resources according to goals and situational requirements.

Philipp A. Schroeder (University of Tübingen)

Cathodal and anodal tDCS effects and the cognitive control network influence one another

Behavioral decisions in demanding situations draw on neural activations in cognitive control networks to disentangle relevant and irrelevant information and to initialize or inhibit the (in-)appropriate responses. Polarity-specific transcranial direct current stimulation (tDCS) is supposed to modulate cortical activity and can be used to modulate different aspects of cognitive control. Due to the different demands on cognitive processing imposed by a task, a behavioral observation of the tDCS intervention will reflect interactions between neurophysiological and neurocognitive effects, arising from manipulations of direct current flow and of the task requirements, respectively. Systematic variations of task parameters next to cathodal or anodal tDCS will reveal underlying differences in the recruitment of neurocognitive resource. I present results from experimental studies that used different task and stimulation parameters to inform about mutual influences between tDCS polarity and task-induced activity. Cognitive processes arising from task instructions must be considered as a manipulated or controlled factor for brain state-dependent stimulation.

Simone Weller, Christian Plewnia (University of Tübingen)

Enhancement of cognitive control training with tDCS: Effects of stimulation polarity, intensity and laterality.

Introduction: Cognitive control (CC) is an important prerequisite for goal-directed behaviour and effective information processing. Impaired CC is associated with reduced activity within the prefrontal cortex (PFC). By altering PFC activity through transcranial direct current stimulation (tDCS) it is possible to ameliorate CC. However, success of the intervention depends highly on the form of its application, and hard to compare study designs lead to inconclusive outcomes, sparking points of debate about tDCS's efficacy in current research. In this study, we took an organised, hierarchical approach to determine optimal stimulation parameters that help supporting CC.
Methods: We systematically modified tDCS parameters in 162 healthy subjects. Subjects were first grouped by polarity (anodal/cathodal), then subdivided by intensity

(1 mA/2 mA), and lastly laterality (F3/F4 plus extracephalic reference), ultimately resulting in eight stimulation groups and one placebo control. Additional to tDCS, each subject underwent two weeks of computerised training challenging CC (adaptive *paced auditory serial addition task*). Stimulation effects on performance gain and positive and negative affect were measured and compared to placebo treatment during the training as well as in follow-up sessions up to three months later.
Results: Due to the hierarchical setup of the study, we were able to determine that on the first analysis level anodal stimulation showed to significantly boost performance gain in the CC task. Division of the anodal group showed that this effect was carried by (and significant only for) the subsample stimulated with an intensity of 1 mA. Distinguishing the resulting sample further by laterality, treatment of the left PFC was shown to be most effective.
Conclusion: Involving a large number of healthy subjects, our results confirm the beneficial effect of anodal tDCS on adaptive neuroplasticity reflected in the enhancement of CC-training gains. In addition, they underline the non-linear influence of stimulation-intensity. These data will inform future clinical studies combining tDCS and cognitive training to ameliorate biased information processing in psychiatric disorders.

OS7-1

Title
Possibilities of multimodal MR imaging and translation to clinical tDCS application.

Chaired by Daniel Keeser

Abstract
For almost two decades, transcranial direct current stimulation has influenced neuroscience. Since then, important insights have been gained for basic science in various domains of investigation. The procedure has led to great interest in its application to psychiatric and neurological diseases, but the results have been mixed so far and there is still a lack of clear evidence of clinical application. Based on multimodal MRI-based pilot studies, this symposium will present and discuss mechanistic results from our studies. The focus of our studies is the bilateral stimulation of the dorsolateral prefrontal cortex (DLPFC). Eva Mezger shows the modulation of online tDCS on MR-based metabolites such as glutamate in healthy volunteers and patients with schizophrenia and major depression. Lucia Bulubas presents data suggesting the relationship between baseline MRI-based characteristics, such as gray matter volume and successful response in patients with major depression of ELECT trials (Brunoni et al., N Engl J Med 2017). Shun Takahashi will talk about the individual variability of simulated frontal transcranial direct current stimulation in healthy volunteers, schizophrenic and depressed patients based on the structural MRI of the volunteers and the importance of individualization of tDCS. Daniel Keeser will discuss about the challenges of multimodal Neuroimaging for prefrontal Non-Invasive Brain Stimulation. Frank Padberg will introduce the multicenter depression DC trial (DDC)(Padberg et al., EAPCN 2017) and discuss how it can be applied to the MRI data of the DDC trial based on the mechanistic pilot results obtained so far.

Speakers

Lucia Bulubas (University Hospital LMU)

Factors associated with antidepressant effects of tDCS: insights derived from multimodal baseline imaging from the ELECT-TDCS trial

ELECT-TDCS (Brunoni et al., N Engl J Med 2017) was the so far largest RCT (n=245) investigating the efficacy of a 10-week prefrontal tDCS treatment in depressed patients. This non-inferiority trial showed that tDCS treatment was not non-inferior to escitalopram, but escitalopram and tDCS were both superior to placebo. Based on baseline multimodal imaging collected from a subsample of ELECT-TDCS patients, we will discuss published (Bulubas & Padberg et al., Brain Stimulation 2019) and novel findings suggesting that brain morphological factors are associated with the antidepressant response to tDCS, thus shedding light upon biological mechanisms behind tDCS effects. Furthermore, we will discuss how this, and other exploratory evidence might have the potential to develop neurobiological predictors of clinical response to tDCS.

Eva Mezger (University Hospital LMU)

Effects of prefrontal cathodal tDCS on glutamate and resting state connectivity: Combining tDCS, electrical field modeling and multimodal MRI

Can a low non-invasive brain stimulation such as transcranial direct current stimulation (tDCS) really affect the brain as much as to improve symptoms of a psychiatric disease? What is really behind it and what is happening in the brain? In my talk, I will present data of a multimodal brain imaging study using MR spectroscopy and resting-state functional connectivity MRI (rsfcMRI) in combination with computational modeling of electrical fields to investigate effects of bifrontal tDCS stimulation on the brain, actually showing an impact of tDCS on brain metabolite concentration and functional connectivity. We further discuss findings of computational modeling for further systematically developing tDCS of frontal brain regions towards an innovative therapeutic intervention in the framework of precision medicine.

Daniel Keeser (University Hospital LMU)

Challenges of multimodal MR imaging for non-invasive brain stimulation

This presentation will reflect on the current state of “Imaging-Stimulation” literature and address the challenges of multimodal MR imaging, such as individual variability, reproducibility and open science. A special focus will be on consistent results of past studies, individual-based approaches and future perspectives.
Possibilities of multimodal MR imaging and translation to clinical tDCS application
For almost two decades, transcranial direct current stimulation has influenced neuroscience. Since then, important insights have been gained for basic science in various domains of investigation. The procedure has led to great interest in its application to psychiatric and neurological diseases, but the results have been mixed so far and there is still a lack of clear evidence of clinical application. Based on multimodal MRI-based pilot studies, this symposium will present and discuss mechanistic results from our studies. The focus of our studies is the bilateral stimulation of the dorsolateral prefrontal cortex (DLPFC). Eva Mezger shows the modulation of online tDCS on MR-based metabolites such as glutamate in healthy volunteers and patients with schizophrenia and major depression. Lucia Bulubas presents data suggesting the relationship between baseline MRI-based characteristics, such as gray matter volume and successful response in patients with major depression of ELECT trials (Brunoni et al., N Engl J Med 2017). Shun Takahashi will talk about the individual variability of simulated frontal transcranial direct current stimulation in healthy volunteers, schizophrenic and depressed patients based on the structural MRI of the volunteers and the importance of individualization of tDCS. Daniel Keeser will discuss about the challenges of multimodal Neuroimaging for prefrontal Non-Invasive Brain Stimulation. Frank Padberg will introduce the multicenter depression DC trial (DDC)(Padberg et al., EAPCN 2017) and discuss how it can be applied to the MRI data of the DDC trial based on the mechanistic pilot results obtained so far.

Shun Takahashi (Wakayama Medical University)

Reduction of simulated e-fields in schizophrenia and major depression during prefrontal tDCS

This presentation will show differences of simulated electric field distributions during prefrontal tDCS among patients with depression, schizophrenia and healthy controls. Using two cohorts which included the same blinded data set that were analyzed by two independent raters, this study showed suitable inter-rater variability of SimNIBS analysis and reduced simulated electric fields after simulated prefrontal tDCS in the MDD and SCZ groups compared to the HC group. Our results further suggest that brain structural pathology directly influences electric field spatial extent and intensity induced by prefrontal tDCS in patients with depression and schizophrenia.

OS7-2

Title
Advances in NIBS research of human brain physiology.

Chaired by Vera Moliadze, Giorgi Batsikadze

Speakers

Hwee-Ling Lee (University of Bonn)

Unravelling the functions of hippocampal subfields using ultra-high field MRI

Memories of past experience are crucial for future behavior. They are represented via activity of specific brain regions, especially within the hippocampal circuit. Each of the hippocampal subfields play a distinct role in memory processing, yet, previous neuroimaging studies are not able to dissociate the functional contributions of each hippocampal subfields. In this talk, I will present work that seeks to investigate the functions of hippocampal subfields using ultra-high field MRI technique, and whether transcranial direct current stimulation can be used to modulate the functional activity of the hippocampal subfields and influence memory processing.

Giorgi Batsikadze (University of Essen)

Effects of cerebellar transcranial direct current stimulation (ctDCS) on cerebellar-brain inhibition in humans

Background: Recently, ctDCS emerged as a popular method to non-invasively modulate cerebellar excitability and plasticity in healthy subjects and various patient populations and help us broaden our understanding of cerebellar functions and introduce new therapeutic applications. Despite its popularity, its parameters, such as current polarity, stimulation intensity and electrode positions to induce specific effects are poorly standardized. In this study we aimed to test the effects of ctDCS with different electrode montages (see below) on cerebellar-brain inhibition (CBI). In the first experiment, physiological after-effects of ctDCS were compared based on cerebellar-brain inhibition (CBI). In the second experiment, CBI after-effects of ctDCS were assessed using different transcranial magnetic stimulation (TMS) intensities (CBI recruitment curve). Additionally, an anatomically accurate head model was built based on a single MR image to compare the distribution of the induced electric field within the cerebellum between these electrode montages.
Methods: 15 and 14 young and healthy participants took part in Experiments 1 and 2, respectively. In all experiments, the target ctDCS electrode was placed over the right cerebellar cortex. In Experiment 1, the return electrode was placed over one of the following three positions: the right buccinator muscle, the left supraorbital area or the right deltoid muscle and in Experiment 2, it was positioned over the right buccinator muscle. 2mA ctDCS was administered for 15 minutes. CBI was measured by double-TMS protocol, with the conditioning stimulus (CS) over the right cerebellum with an intensity of 5% below the brainstem motor threshold (BMT) followed by the test pulse

over the left primary motor cortex 5ms later. For CBI-RC, five different CS intensities were used (-5, -10, -15, -20, -25 below relative BMT). The after-effects of 2mA anodal or cathodal ctDCS on CBI or CBI-RC in Exp. 1 and 2, respectively, were measured before and for two hours after ctDCS. Additionally, anatomically accurate single head model was built from MR image to simulate the electric field distribution for each of the electrode montages.
Results: In Exp. 1, both ctDCS polarities significantly decreased CBI for at least two hours compared to both sham and pre-stimulation values. No significant differences between different return electrode positions were observed. In Exp. 2, CBI was significantly increased after anodal and was decreased after cathodal ctDCS with low CS intensities in a polarity-specific manner. ctDCS had also no effect on the single pulse-MEP amplitudes or brainstem motor threshold. Computational modelling of the electric field distribution revealed negligible differences between non-target electrode positions based on the effect size.
Conclusions: The return electrode positioning has no significant impact on both the ctDCS physiological after-effects and modeling results. The results of Experiment 2 show that the recruitment of the cerebellar-M1 connection varies depending on ctDCS polarity and cerebellar TMS intensity, possibly due to diverse effects on different cell populations in the cerebellar cortex. This may be one of the reasons why ctDCS effects on functional measures are difficult to predict.
Funding: Mercur Pr-2015-0010 and SFB1280 (TP A05 and A06)

Vera Moliadze (University of Kiel)

Transcranial electrical stimulation in pediatric brain

Since the developing brain shows a greater capacity of brain plasticity, transcranial electrical brain stimulation(tES) might induce benefits in children. So far, applications of tES in the pediatric studies are not well developed. The Talk will give an overview how age and individual differences impact tES effects in healthy children and adolescents. Additionally, the research consortium STIPED (stimulation in pediatrics, European Union's Horizon 2020, grant agreement No 731827) will be introduced which aims (1) to characterize interaction between brain development and effects of transcranial direct current stimulation (tDCS) on neuropsychological function and (2) to apply individual head modeling and electrical current estimation to guide individualized treatment with tDCS in different stages of development

Roser Sanchez-Todo (StarLab)

Model-driven optimization of multichannel transcranial current stimulation

Personalization is becoming standard practice in medical diagnosis and treatment. Recent work has highlighted the importance of physical modeling of the electric field in brain stimulation research and clinical practice. We present two different approaches to personalize transcranial stimulation based on realistic biophysical and physiological models of the human brain. The first, already used with success in clinical pilots, relies on MRI-driven finite element modeling of the electric field produced by multichannel transcranial current stimulation, using a genetic algorithm

to optimize the number, current intensity and location of the electrodes based on a specific target. The second, more advanced, is based on modeling the brain as a network of neural masses embedded in a realistic physical matrix, representing both measurable electrical brain activity and electric interactions.

OS7-3

Title
Neuroimaging guided non-invasive brain stimulation in health and disease.

Chaired by Anirban Dutta

Abstract
Neuroimaging techniques can not only be used in computational modeling and optimization of non-invasive brain stimulation (NIBS) for rational dosing but also in monitoring NIBS-evoked response of the neurovascular brain tissue to estimate the dose-response online. Here, the dose-response may depend on the state of the neurovascular unit (NVU) that consists of the endothelium, glia, neurons, pericytes, and the basal lamina. Recent works suggest NVU as an integrated system working in concert using feedback mechanisms to enable proper brain homeostasis and function where the challenge remains in modeling these mostly nonlinear spatiotemporal interactions in health and disease. Therefore, it is postulated that neuroimaging-guided static volume conductor head models cannot account for the spatiotemporal interactions underlying dose-response that may be estimated using portable neuroimaging in conjunction with NIBS in health and disease.

Speakers

Shubh Mohan Singh (Postgraduate Institute of Medical Education and Research, India)

Repetitive transcranial magnetic stimulation in psychiatry – a case series at the PGIMER Chandigarh, India

Zeynab Rezaee, Sue Ann Sisto, Anirban Dutta (University at Buffalo)

Cerebellar Lobules Optimal Stimulation (CLOS) during gait and balance training in healthy and stroke survivors

Cerebellar transcranial direct current stimulation (ctDCS) is challenging due to the complexity of the cerebellar structure which is reflected by the well-known variability in ctDCS effects. Therefore, our objective is to present a freely available computational modeling pipeline for cerebellar lobules' optimal stimulation (CLOS).

Yashika Arora, Roy Chowdhury (Indian Institute of Technology, Mandi)

Assessing the role of electrodes for high-definition transcranial direct current stimulation configurations on cortical excitability in a computational framework

The paper presents a study on the effect of high definition transcranial direct current stimulation (HDtDCS) on cortical excitability using various types of electrodes. HD-tDCS utilizes small-sized electrodes on scalp to deliver weak amount of direct current

in various neuro-rehabilitation methods. For a bipolar configuration, the basic configuration of HD-tDCS has an electrode pair (anode and cathode). For m x n configurations, m is the number of return electrodes and n is the number of main electrodes. In our study, m x n HD-tDCS montages with disc, ring, and pad electrodes has been analyzed where m ranges from 1 to 4 and n is 1. The study assesses the electric field and voltage distribution by considering subject's specific anatomy in an open-source computational pipeline. The configurations presented in this study compare the effect of various m x n HD-tDCS on standard Montreal Neurological Institute (MNI152) head model which is a T1 MRI volume obtained by averaging 152 individuals at 1 mm3 resolution. The approximate surface area for each electrode in HD-tDCS application considered is 113 mm2. The voltage generated with ring electrodes was higher and of pad electrodes were lower in all m x n configurations as obtained in computational results. The affected region due to various configurations is calculated by considering a threshold value of voltage
and electric field as obtained from the computational results. This computational model approach is useful in fixing various parameters of current stimulation: intensity, type and arrangement of electrodes and target region by using structural MRI data of an individual prior to the real stimulation in clinical trials.

Anirban Dutta (University at Buffalo)

Simultaneous electroencephalography (EEG) and near-infrared spectroscopy (NIRS) under non-invasive brain stimulation in acute brain injury

Posters

1. Effect of toluene on cortical excitability, neuroplasticity, and cognitive functions in humans

Fatemeh Yavari
Department Psychology and Neurosciences, Leibniz Research Centre for Working Environment and Human Factors, Dortmund, Germany

Toluene is a well-known neurotoxic organic solvent and a major component of many industrial and commercial products such as adhesives, paint thinners and gasoline. Many workers are regularly exposed to toluene in their working environment and occupational exposure limits (OELs) have been set to avoid adverse health effects. These OELs or short-term exposure limits vary from 14 to 300 ppm across countries partly due to heterogeneity of the findings from animal and human studies about its neurotoxic effects and the evaluation of the adversity of the underlying mechanisms. Furthermore, its acute neurophysiological effects remain poorly understood in humans. The purpose of this study was to investigate the effects of acute exposure to toluene on cortical excitability, plasticity, and implicit motor learning in healthy volunteers. Seventeen subjects were assessed with different transcranial magnetic stimulation measurements: motor thresholds, short-latency intracortical inhibition, and intracortical facilitation, and short-interval afferent inhibition before and after clean air or toluene (single peak of 200 ppm) administration. Furthermore, we evaluated long-term potentiation-like neuroplasticity induced by anodal transcranial direct current stimulation (tDCS) over the motor cortex, and the participants conducted a motor sequence learning task, the serial reaction time task. Our findings revealed that toluene abolished the plasticity induced by anodal tDCS, attenuated intracortical facilitation, and increased inhibition in the short-latency afferent inhibition measure, while cortico-spinal excitability and intracortical inhibition were not affected. On the behavioral level, toluene did not alter the performance of the motor learning task. These results suggest that toluene might act by modulating NMDA receptor activity, as well as cortical glutamatergic and cholinergic neurotransmission in the human brain. This study encourages further research to obtain more knowledge about mechanisms of action and effects of toluene on both naïve and chronically exposed populations.

2. Probing the relevance of repeated cathodal tDCS over the primary motor cortex for prolongation of after-effects

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Transcranial direct current stimulation (tDCS) has promising results in pilot studies as therapeutic intervention in neurological disorders, more sustained effects are however required for clinical application. To address this issue, one possible solution is the use of repeated stimulation protocols. Previous studies indicated the capability of extending single session cathodal tDCS after-effects with repetitive tDCS protocols with a superiority of relatively short intervals. In this study, we thus investigated the effects of repeated stimulation protocols with short, and long intervals for a standard and a newly developed optimized tDCS protocol. In 16 healthy participants, we compared single session protocols of 1mA with 15min and 3mA with 20min, with repeated application of these protocols with intervals of 20min and 24 hours, and a sham tDCS session. tDCS-induced neuroplastic after-effects were then monitored with TMS-induced motor evoked potentials (MEP) until the next day evening after stimulation. Our results revealed that the duration of after-effects of single session of 1mA with 15min cathodal tDCS were doubled by the 3mA 20min protocol. Compared with single session protocols, 1mA repeated stimulation with 20min, and 24h intervals did not alter respective after-effects, but after-effects were shortened and reduced in amplitude with the 3mA stimulation intensity. Importantly, late-phase plasticity could not be induced by a single repetition of stimulation in this study, but repetition reduced the efficacy of stimulation protocols with higher intensities. This study provides further insights on the dependency of tDCS-induced neuroplasticity from the stimulation parameters, and therefore delivers crucial information for future tDCS applications.

3. Exploring and modulating consciousness-related oscillatory brain activity

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Neural oscillations are associated with many cognitive functions, including consciousness-related processes such as sleep. Developing novel non-invasive brain stimulation techniques that can modulate specific oscillatory activity may be a viable approach for understanding functional causality of oscillatory rhythms in cognition, and developing novel treatment strategies for patients with disorders of consciousness. Among existing state-of-the-art techniques, repetitive transcranial magnetic stimulation (rTMS) induces frequency-specific but relatively short-lasting neuronal oscillations, whereas transcranial alternating current stimulation (tACS) primarily entrains endogenous oscillatory activity. In this study, we investigate whether phase-synchronizing these two techniques may be a viable method in order to induce and entrain non-endogenous oscillatory rhythms in the human cortex. After assembling a control circuit that could precisely synchronize rTMS pulses with the phase of the tACS, we investigated whether combined alpha (10 Hz) rTMS and tACS to the prefrontal cortex (PFC) could induce sustained resting state PFC-alpha activity. 25 healthy participants took part in a single-blind, within-subject design. Resting state EEG was recorded at baseline before, immediately after, and 15 and 30 min after an 8 min stimulation block, in both eyes-open (EO) and eyes-closed (EC) conditions. 10 Hz tACS at 1 mA was applied through four bilateral electrodes over PFC and mastoid regions (EEG positions F3/F4, and TP9/TP10). 10 Hz rTMS at 70% AMT was delivered over positions F3/F4 with pulses aligned to the positive peaks of the tACS waveform. This combined protocol was compared to five control protocols: rTMS alone, tACS alone, sham rTMS combined w/sham tACS, combined rTMS+tACS during EC, and finally rTMS pulsed at the negative tACS peak. No effects were observed with sham rTMS+sham tACS. During both EO and EC states, PFC-alpha power increased the greatest (~30%) with the combined rTMS+tACS protocol (both during EO and EC) compared to the sham, with effects lasting up to 30 min. Slightly lesser increases were observed with the combined rTMS+tACS at the negative tACS peak, as well as short-duration effects of rTMS alone, while the weakest effects were observed for tACS alone. Our work demonstrates for the first time the feasibility of combined rTMS and tACS for enhancing non-endogenous oscillations. Further investigations are needed to unravel the mechanisms underlying these findings. Our study points towards the promising potential of integrating these protocols for functionally-relevant research and clinical applications.

4. Effects of caffeine on cognitive functions (attention processes, and working memory capacity) in humans

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Caffeine is a widely used psychostimulant drug and has increasingly drawn attention due to its effects in reducing drowsiness and fatigue, thereby possibly improving cognitive performance and behavior. However, conflicting results regarding the effects of caffeine in healthy subjects and patients, as well as physiological findings both in animal and human studies have aroused questions whether caffeine could indeed improve specific cognitive functions and performance in healthy subjects.
The aim of our study was to investigate if caffeine modulates cognitive functions such as attention processes, and working memory capacity. Fourteen (6 males) healthy young volunteers were recruited. The study was conducted in a placebo-controlled, double- blind, and crossover design. The Stroop task was employed to evaluate attention processes, and the 3-back letter task was performed to assess working memory function.
The results showed that Caffeine improved attentional processes by reducing interference effects and error counts, and improved working memory function by increasing the number of correct hits and reducing the number of missed hits.
The suggested beneficial effects of caffeine on cognitive functions in healthy humans encourage more investigations regarding its effects on other cognitive functions and also in patients with cognitive deficiency.

5. Prolongation of late-phase LTP-like plasticity in the primary motor cortex with repeated anodal transcranial direct current stimulation

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Background: Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique which can induce neuroplastic changes in the brain. After-effects of a single session of anodal tDCS induce LTP-like plasticity which last for about one hour, while repetition of stimulation within a time interval of 30 minutes results in late-phase effects lasting for at least 24 hours with standard stimulation protocols. Prolonging the duration of neuroplasticity induced by tDCS is desirable in clinical applications.
Objective: In this study, we explored if the after-effects of a recently developed optimized single session stimulation protocol can be relevantly prolonged in the motor cortex by repetition of the intervention.
Methods: 16 healthy right-handed subjects participated in this study. The effects of anodal tDCS of 3mA for 20 minutes and a 'standard protocol' – 1mA for 15 minutes with repetition intervals of 20 minutes and 3 hours were compared with the effects of respective single session tDCS (3mA-20min, 1mA-15min, and Sham). Cortical excitability alterations were monitored by single-pulse TMS-elicited MEPs, which were obtained for up to 32 hours after intervention.
Results: Compared to sham, both single session tDCS protocols (1mA-15min, and 3mA-20min) showed cortical excitability alterations lasting for about 30 minutes after stimulation. Repetition with an interval of 20 minutes resulted in prolongation of after-effects for the 1mA-15 min protocol, which lasted for more than 24 hours after stimulation. For the 3mA-20 min stimulation protocol, this repetition interval only prolonged the after-effects for 90 mins after stimulation. The 3-hour repetition interval resulted in no excitability changes post-tDCS for the 3mA-20min, and slightly reduced excitability enhancements for the 1mA-15min stimulation condition.
Conclusion: The results show that late-phase plasticity can be induced by specific tDCS protocols but suggest also a complex non-linear mechanism.

6. Ca2+ channel dynamics explain the nonlinear neuroplasticity induction by cathodal transcranial direct current stimulation over the primary motor cortex

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Background: Transcranial direct current stimulation (tDCS) induces polarity- dependent neuroplasticity: with conventional protocols, anodal tDCS results in excitability enhancement while cathodal stimulation reduces excitability. However, partially non-linear responses are observed with increased stimulation intensity and/or duration. Cathodal tDCS with 2mA for 20min reverses the excitability- diminishing plasticity induced by stimulation with 1mA into excitation, while cathodal tDCS with 3mA again results in excitability diminution. Since tDCS generates NMDA receptor-dependent neuroplasticity, such non-linearity could be explained by different levels of calcium concentration changes, which have been demonstrated in animal models to control for the directionality of plasticity.
Methods: In this study, we tested the calcium dependency of non-linear cortical plasticity induced by cathodal tDCS in human subjects in a placebo controlled, double-blind and randomized design. The calcium channel blocker flunarizine was applied in low (2.5 mg), medium (5 mg) or high (10 mg) dosages before 20min cathodal motor cortex tDCS with 3mA in 12 young healthy subjects. After-effects of stimulation were monitored with TMS-induced motor evoked potentials (MEPs) until 2 hours after stimulation.
Results: The results show that motor cortical excitability-diminishing after-effects of stimulation were unchanged, diminished, or converted to a late-phase excitability enhancement with low, medium and high dosages of flunarizine.
Conclusions: These results suggest a calcium-dependency of the directionality of tDCS-induced neuroplasticity, which may have relevant implications for future basic and clinical research.

7. Modulating task-related motor cortex excitability by transcranial electrical stimulation: probing neurorehabilitation strategies

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Introduction: Neurorehabilitation includes diverse multidisciplinary rehabilitation methods, aimed to improve neuroplasticity and functional skills after neurological injury [1]. Action observation treatment and transcranial electrical stimulation play an essential role in the development of new treatment approaches in the field of neurorehabilitation. These techniques can modulate the activity of the central nervous system, induce neuroplasticity, and hereby increase the acquisition and retention of motor skills, improve motor performance and generate sustained therapeutic benefits [2,3]. We explored whether combinations of these novel stimulation techniques and approaches can be used as potential physical therapy methods for symptom reduction after neurological injury.
Methods: The two main research questions were addressed by multi-modal experimental methods. The first study aimed to investigate the effect of movement observation coupled with real or sham transcranial random noise stimulation (tRNS) on subsequent movement execution-related motor cortex excitability. Sham or real tRNS over the left primary motor cortex (M1) was delivered 10 minutes with a current intensity of 1 mA during movement observation. The main experiments explored the effect of sham or real tRNS over M1, while participants observed a video showing a task which required repeated button pressing in response to a cue, including either the right hand (Experiment 1) or a mirror-reversal video (Experiment 2, Figure 1), and then movement execution of the right hand. In control experiments 1 to 3, real tRNS was applied while participants watched a perceptual sequence, a landscape image, or a video showing left hand buttons presses (the cue sequence was identical to Experiment 1), followed by movement execution with the right hand. In the fourth control experiment, participants performed the protocol of experiment 1, except for movement execution. Motor evoked potentials (MEPs) in the right first dorsal interosseous (FDI) muscle were recorded before and immediately after movement observation, observation of the perceptual sequence or presentation of a landscape image coupled with sham or real tRNS, and subsequent after movement execution or an interval of 6 minutes rest. The second study aimed to investigate the impact of sham or real cathodal transcranial direct current stimulation (tDCS) over the left M1 during movement observation on subsequent movement execution-dependent motor cortex excitability alterations. The experimental protocol was identical to that of experiment 1 in the first study except participants received sham or real cathodal tDCS (1 mA) 10 minutes during movement observation. MEPs in the FDI muscle were recorded prior to sham or real cathodal tDCS combined with movement observation, immediately after observation of actions and after movement execution.
Results: The main results of the studies show that (a) tRNS coupled with mirror-matching movement observation promotes observation-dependent motor cortex excitability, and this effect subsequently facilitates execution-related motor cortex excitability; (b) cathodal tDCS during movement observation inhibits motor cortex excitability, and it subsequently inhibits motor execution-dependent cortical excitability.

Discussion: These findings indicate that tRNS and cathodal tDCS combined with movement observation result in an alteration of task-related motor cortex excitability, which could be beneficial to counteract pathological alterations in neurological diseases [4]. These findings suggest that transcranial electrical stimulation combined with task-related activity could develop into physical therapy strategies in neurorehabilitation.

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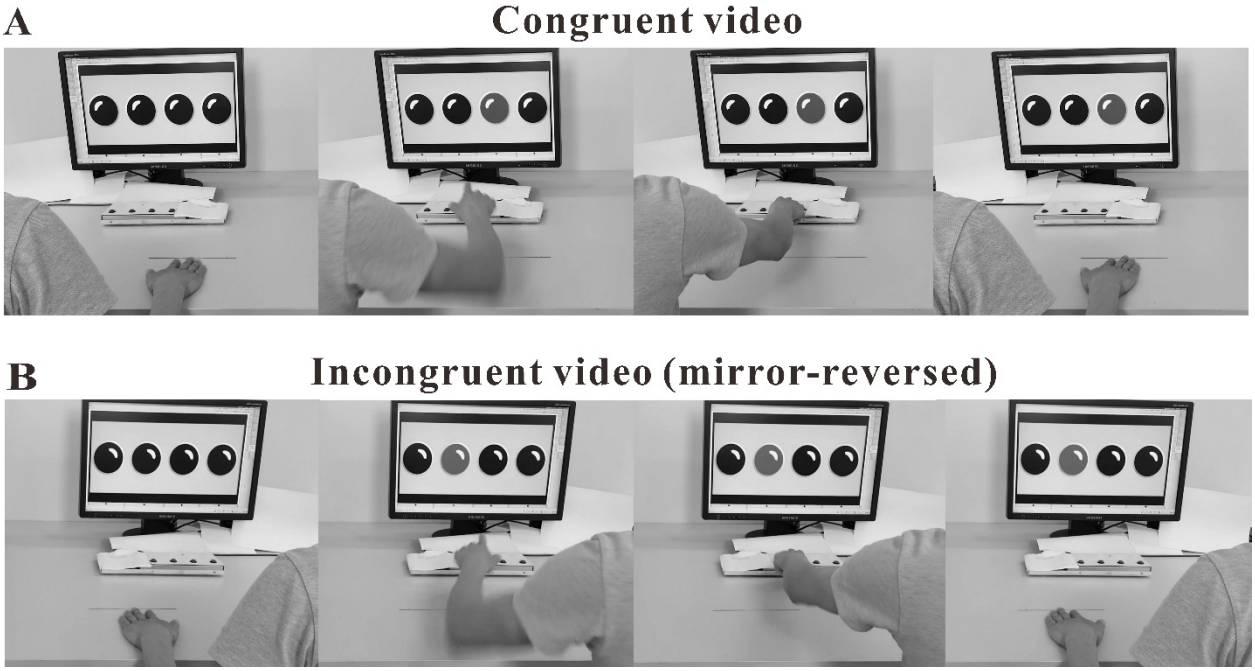

Fig. 1. Action observation videos. **(A)** The video displayed right-hand button presses (congruent video). **(B)** This video displayed the mirror-reversed of the congruent video.

8. Evaluation of pH changes and skin redness in direct current stimulation to the forearm

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Transcranial direct current stimulation (tDCS) is applied via electrodes contacting the skin via saline solution soaked sponges or electrolyte gel. Applied in clinical and research studies, tDCS demonstrated promising effects e.g. for treating neuro- psychiatric disorders. In rare occasions participants reported adverse effects including skin irritation [Antal et al., 2017]. The weak currents of a few mA applied over several minutes lead to oxidation and reduction processes across the electrode – electrolyte interfaces [Merrill et al., 2005]. Resulting changes in pH might contribute to skin irritation due to skin contact with acid/base products. Previously, pH value changes due to direct current stimulation have been evaluated at agar phantoms [Minhas et al., 2010].
Here we evaluate pH value and skin redness in relation to direct current stimulation intensity and application time at the forearm.
We included ten participants (four females, six male) in the range from 25 years to 50 years in age without known skin diseases. Two rubber electrodes (5 cm x 7 cm) in 0.9% saline soaked sponges were fixated with rubber bands along the left forearm (anode 2 cm above the wrist, cathode with 4 cm distance to the anode). Stimulation intensities of 500 µA, 750 µA and 1000 µA and sham stimulation were applied for 30 min in separate sessions with at least one intermediate day without stimulation. In a five minutes' interval, we tested the pH value of the saline solution in the sponge. After stimulation, the skin redness was evaluated according to the Draize dermal irritation scoring system [Draize, 1959]. Measurement data were grouped according to stimulation intensities and separated in classes corresponding to the seven measurement time points (0, 5, 10, .. 30 min).
Initially, saline solutions provided pH values around 6 which changed during the stimulation time to acidic and alkaline values at the anode and cathode. For the stimulation intensity of 500 µA, the pH values decreased to 5.3 at the cathode and increased to 6.7 at the anode over the time course of 30 min. For the stimulation intensity of 750 µA, the pH values decreased to 5.4 at the cathode and increased to 7.1 at the anode over the time course of 30 min. For the stimulation intensity of 1000 µA, the pH values decreased to 5.1 at the cathode and increased to 7.2 at the anode over the time course of 30 min. In accordance, higher Draize scores occurred more frequently after stimulation with increasing current strength. For the stimulation intensity of 500 µA, scores of 0 and 1 occurred 4 and 6 (2 and 8) times below the anode (cathode). For the stimulation intensity of 750 µA, scores of 0 and 1 occurred 3 and 7 times below the anode and scores of 1 and 2 occurred 7 and 3 times below the cathode. For the stimulation intensity of 1000 µA, scores of 1 and 2 occurred 8 and 2 times below the anode and scores of 0, 1 and 2 occurred 1, 6 and 3 times below the cathode.
The Draize scores were higher underneath the cathode. This can be explained by the stronger deviation of the pH values at the cathode from the normal condition of the skin with a pH value of 4–6 [Ali and Yosipovitch, 2013]. The pH value changes due to direct current stimulation presented here are in line with the data reported by Minhas and colleagues [2010]. However, our end values are smaller, which is likely due to the lower stimulation intensities and the different electrode configuration.
Our results indicate a connection between pH value changes in the electrolyte layer and the level of skin redness. Stronger skin irritation connected to higher pH value changes might be expected for stimulation intensities exceeding 1 mA.
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9. Different online and post-stimulation effects of prefrontal tDCS and tACS on working memory-related neural activity and functional connectivity: an exploratory study

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Background: Transcranial direct and alternating current stimulation (tDCS and tACS, respectively) have acquired a relevant role in the modulation of human brain dynamics and cognition. However, the comparability of these approaches regarding their underlying neurophysiological mechanisms has not been thoroughly investigated, particularly the one related to the modulation of large-scale functional networks.
Methods: In this study, 44 subjects were randomly assigned to receive anodal tDCS (N = 15), theta tACS (N = 14) or sham (N = 15). The anode was positioned over the left dorsolateral prefrontal cortex and the cathode was placed over the right supraorbital cortex. In the real stimulation groups, the current was supplied during 20 min. For the sham group, the current dosage finished after 30 s of stimulation. tDCS was delivered with a constant current of 2 mA. tACS was fixed to 2 mA (1 mA peak-to-peak) in a 6 Hz frequency and 0° phase. Stimulation was applied concurrently with functional magnetic resonance imaging (fMRI) acquisitions, both at rest and during a verbal working memory (WM) task. After stimulation, subjects repeated the fMRI WM task.
Results: At rest, tDCS increased functional connectivity, particularly within the default-mode network (DMN), while tACS decreased it (**Fig. 1**). During the online WM task, tACS reduced task-related DMN deactivations, mainly within posterior midline structures (**Fig. 2**). In contrast, during the post-stimulation WM task, tDCS enlarged DMN deactivations in medial frontal regions (**Fig. 3**). Further, greater reductions of brain activity in these areas after tDCS were associated with lower reaction time post-stimulation, possibly reflecting increased neural efficiency.
Conclusions: tDCS and tACS modulate fMRI-derived network dynamics differently. However, both effects seem to focus especially over regions linked to the DMN, both at rest and task. These findings are aligned with previous evidence finding converging modulatory effects in response to NIBS over this large-scale system.

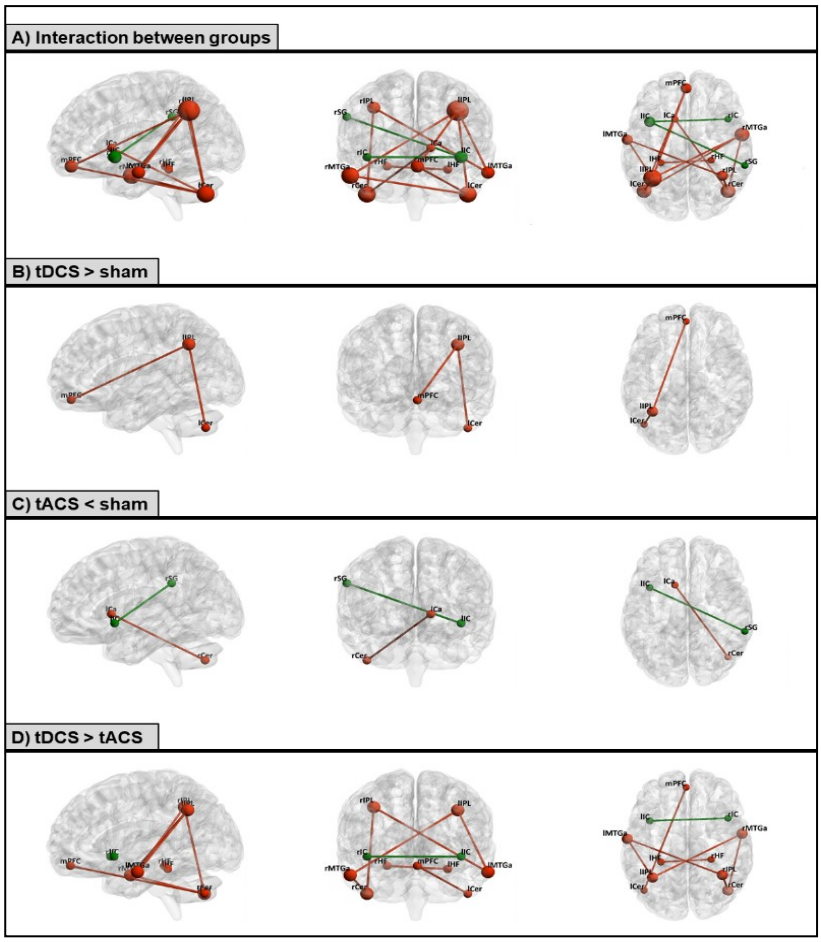

Fig. 1. Seed-to-seed significant results within the DMN (in red) and the ECN (in green) for: A) interaction between groups, B) tDCS > sham, C) tACS < sham and D) tDCS > tACS.

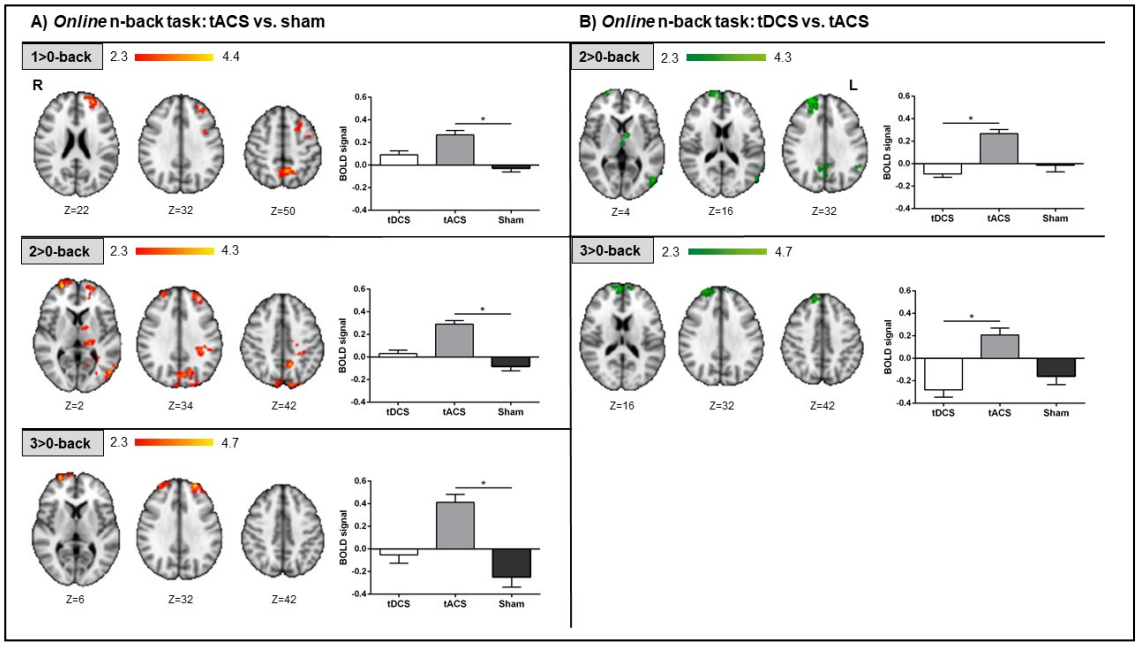

Fig. 2. Online n-back task fMRI results. A) tACS vs. sham fMRI results are shown in red-yellow. B) tDCS vs. tACS fMRI results are shown in green. Left**:** Statistically significant fMRI activity maps on

the standard MNI for each contrast of interest and groups comparison. Right: Plots of mean BOLD signal values at the neuroimaging clusters where significant differences between groups were found. Data are represented as mean with *SEM*. *Abbreviations:* tACS, transcranial alternating current stimulation; tDCS, transcranial direct current stimulation; BOLD, *blood-oxygen-level- dependent*.

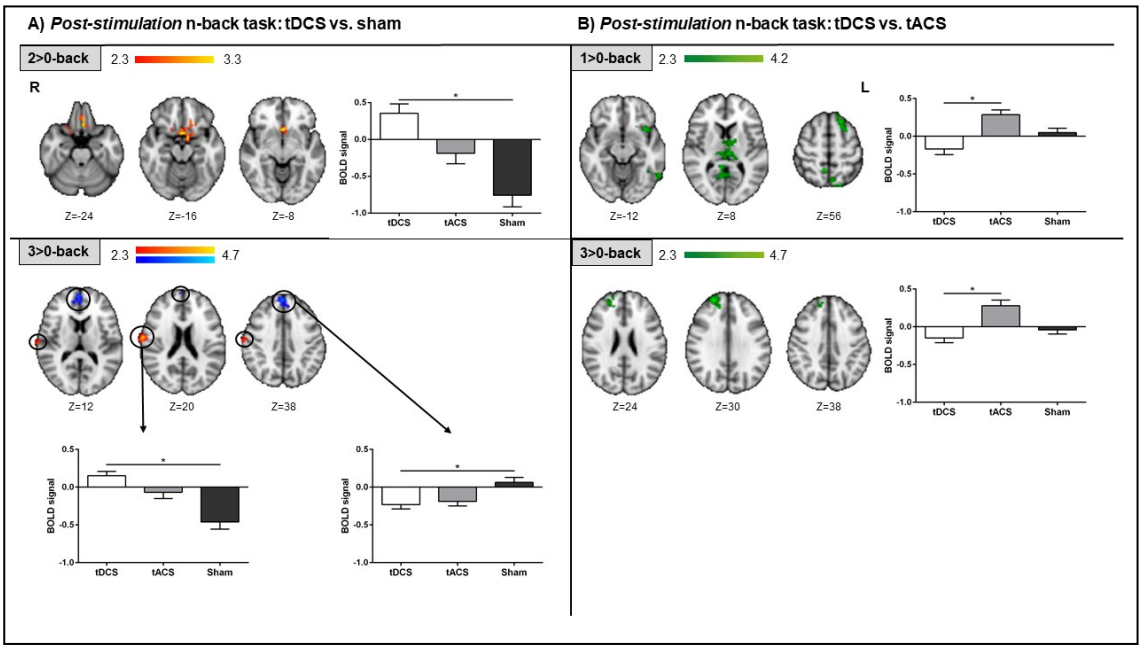

Fig. 3. Post-stimulation n-back task fMRI results. A) tDCS vs. sham fMRI results are shown in red-yellow for higher activations and blue-lightblue for lower activations. B) tACS vs. tDCS fMRI results are shown in green. Left*:* Statistically significant fMRI activity maps on the standard MNI for each contrast of interest and groups comparison. Right: Plots of mean BOLD signal values at the neuroimaging clusters where significant differences between groups were found. Data are represented as mean with *SEM*. *Abbreviations:* tDCS, transcranial direct current stimulation; tACS, transcranial alternating current stimulation; BOLD, *blood-oxygen-level-dependent*.

10. Mechanisms of the focusing effect of dopamine on the LTP-like plasticity

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Dopamine plays a key role in various cognitive functions including learning and memory as well as neural processes related to synaptic modifications like long-term potentiation (LTP) and long-term depression (LTD), both of which are NMDA receptor-dependent and important neuronal substrate for learning. Dopamine is proposed to facilitate learning via enhancing the signal-to-noise ratio of neural network activity, as a result of the balance between distinct regulations of dopaminergic receptor subtypes, particularly D1 and D2. It is further hypothesized that dopamine focuses LTP-like plasticity via a D2 receptor-dependent NMDA receptor activity reduction. In this study, we explored the NMDA mechanisms underlying dopaminergic modulation of LTP-like plasticity induced by transcranial direct current stimulation (tDCS) over the left motor cortex. 11 healthy, non-smoker and right-handed participants were recruited and received 12 sessions of anodal tDCS (1 mA, 13 min) and pharmacological intervention which was applied as a combinations of dopamine agents (D2 agonist Bromocriptine, as well as L-Dopa for general dopamine activation) with three dosages of NMDA agonist (i.e., D-Cycloserine 50, 100 and 200 mg) and placebo. Cortical excitability was monitored using transcranial magnetic stimulation-induced motor-evoked potential amplitudes. Preliminary results show a nonlinear dosage-dependent effect of D-Cycloserine on LTP-like plasticity under dopamine and D2 agonist agents. In general, our study supports the assumption that NMDA-receptor activity has facilitatory effects on neuroplasticity in the human motor cortex.

11. The impact of chronotypes and time of the day on tDCS-induced motor cortex plasticity, cortical excitability, and cognition

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Objective: Chronotype (i.e., morningness vs eveningness) refers to an endogenous disposition towards sleep and wakefulness, which affects the physiological functions of the brain and cognition. However, the impact of chronotypes on neuroplasticity and brain physiology has not been systematically investigated yet. We investigated the effects of chronotypes on motor cortex plasticity, induced by the transcranial direct current stimulation (tDCS), cortical excitability measured by the transcranial magnetic stimulation (TMS), and cognitive functions.
Methods: Twenty-four healthy, right-handed, non-smoker participants (10 males, mean age =25.41, SD=5.17) were divided into groups of early-chronotype (ECs) (morning-type, N=12) or late-chronotypes (LCs) (evening-type, N=12) based on their Morningness-Eveningness Questionnaire (DMEQ) scores. All participants received anodal, cathodal and sham tDCS (1 mA, 7 min) over the primary motor cortex in the morning (at 8:00) and evening (at 19:00), and motor-evoked potentials (MEP) were measured up to 30-min following tDCS. Additionally, cortical excitability was measured at the same time in the morning and evening with different TMS protocols including motor thresholds, Intracortical Inhibition, and Facilitation (SICI/ICF), Short-latency Afferent Inhibition (SAI), I-wave facilitation and input-output Curve. Participants attended 8 sessions in total. Additionally, participants performed a series of cognitive task (i.e., SRTT, Stroop, and N-back) once in the morning and once in the evening the same time.
Results: Motor cortex plasticity was significantly increased and decreased following anodal and cathodal tDCS compared to sham tDCS in both groups. ECs showed significantly increased and decreased levels of excitability after anodal and cathodal tDCS in the morning, compared to evening. Conversely, LCs showed significantly increased and decreased levels of plasticity after anodal and cathodal tDCS in the evening compared to morning. Furthermore, ECs showed increased cortical excitability, slope of the input-output curve, ICF, and I-wave facilitation but decreased SICI and SAI in the morning whereas LCs showed this pattern of response in the evening. Similarly, participants showed significantly better performance in the SRTT, Stroop and N-back tasks in their respective chronotypes.
Conclusions: Motor cortex plasticity, cortical excitability and cognition are strongly dependent on chronotypes and time of the day in ECS and LCs individuals.

12. Effects of one session of anodal tDCS over Wernicke's area on verbal learning and memory

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Wernicke's area, a critical component of the cortical language network, is functionally related to the comprehension of oral and written language. Recent evidence suggests that this cortical region may be related to verbal learning as well. It can be hypothesized that different degrees of neuromodulation on this area could determine its effect on word learning. In this study, the influence of the application of anodal transcranial direct current stimulation (tDCS) over Wernicke's area at different intensities on word learning was explored. The effect of anodal tDCS on performance in a word learning and recall task was analyzed in three different groups (0.5 mA of intensity vs. 1.5 mA vs. sham tDCS). The results reveal that 1.5 mA anodal tDCS improved performance. The number of words learned in this condition was higher compared with stimulation at 0.5 mA current strength and sham stimulation. In addition, stimulation at 1.5 mA specifically prevented the interference effect over word learning, compared to the other two tDCS conditions. These results show an intensity-dependent effect of anodal tDCS on verbal memory formation. These findings are discussed regarding the language functions of Wernicke's area and the ability of tDCS to modulate the activity and functionality of this cortical region at different intensities.

13. tDCS and semantic processing: speeding up word recognition in older adults with verbal memory difficulties

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Introduction: Studies, that combine transcranial direct current stimulation (tDCS) of the temporal cortex with language tasks, show promising results in increasing effects of memory training [1,2,3,4]. With respect to the usage of tDCS in neurorehabilitation of patients with language specific memory deficits, the stimulation of the left temporal cortex could be of great potential. Neuronal changes due to temporal lobe damage elicit deficits in semantic processing and semantic memory [5,6,7]. In order to investigate the effectiveness of tDCS of the left temporal cortex in patients with language specific memory deficits we conducted an experiment using an auditory word recognition task. In addition, we also measured pure motoric reaction times.
Method: 15 older individuals with language specific memory deficits (8 f, ∅ = 76.8y, SD = 6.7y, 62-91y) participated in this sham-controlled and double-blinded study. All participants were righthanded and monolingual native speakers of German. Participants completed two sessions (sham and anodal tDCS), counterbalanced between subjects, with a washout period of at least 10 days. During stimulation, participants had to memorize auditorily presented words in a learning phase, followed by a recognition phase, in which they had to recognize learned words out of twice as much distractors (semantically or phonologically related words). Decision times were taken via button press. 20 minutes of 1.5 mA anodal tDCS was applied to the left temporal cortex during both the learning and the recognition phase. Additionally, a pure motoric reaction task was carried out before and after each experiment to measure participants' individual reaction time independent of a cognitive task. We hypothesized that anodal tDCS would lead to improved word recognition performance compared to sham.
Results: Results indicate a positive influence of anodal tDCS compared to sham for participants with memory deficits. Shorter decision times in the tDCS-condition illustrate improved verbal memory processing visible in marginally significant results (but with strong effect size) for correct answers, ($F(1, 11) = 4.625$, $p = .055$, $r = 0.54$) and incorrect responses ($F(1, 10) = 14.266$, $p = .004$). Pure motor reaction times are not influenced by tDCS ($F(1, 13) = .030$, $p = .865$).
Discussion: In participants with language specific memory deficits the combination of an auditory word recognition task with anodal tDCS of the left temporal cortex speeds up recognition performance. In contrast to the decision time in the recognition task, the motoric reaction time is not influenced by stimulation. tDCS of the left temporal cortex may therefore be promising to support cognitive training in patients with language specific memory deficits.
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14. Direct Evidence for Modulation of Single Unit Activity by tDCS in the Intact Somatosensory Cortex of Rats

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Transcranial direct current stimulation (tDCS) has been known as a non-invasive brain stimulation technique to modulate cortical excitability. In most animal experiments, craniotomy and durotomy over the cortex were an inevitable step to record single unit activity in the cortex. These procedures hamper a study to evaluate the effect of tDCS on cortical activities. To overcome this problem we introduced the new recording method that directly measure single unit activity in the cortex during tDCS without the craniotomy. Under urethane anesthesia, a small-sized craniotomt over the ventral surface of the brainstem was made in adult rats. Tetrode wire electrodes were inserted into the brainstem and then reached to the somatosensory cortex after fixing a tDCS electrode on the skull. Single unit in each electrode were isolated extracellular and their activities were measured before and after anodal or cathodal tDCS with different currently intensity of 50 – 200 μA. Cathodal tDCS decreased neural firing rates in the somatosensory cortex with dose-dependent manner. Oppositely, we found significant current intensity-dependent increase in single unit activity for about 30 min following anodal tDCS. This up-regulation of single unit firing by anodal tDCS was block by pretreatment of glutamate recepter blocker. Using our new recording method, we confirmed modulated neural activities in somatosensory cortex of rats vary depending upon the polarity of tDCS.

15. Sustained attention combined with transcranial direct current stimulation (tDCS) in healthy aging

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Sustained attention is crucial for people to focus on target activities among a variety of distracting information to meet daily life needs. Recently, it has been shown that sustained attention can be improved by transcranial direct current stimulation (tDCS) in some pilot studies. It is hypothesized that combination of sustained attention training with tDCS in the elderly might have synergistic effects. This has however not been systematically explored so far, and the optimized intervention protocols remain to be determined. In this double-blind study we explored systematically the tDCS parameters regarding electrode montage and stimulation intensity to optimize the effects on sustained attention training. Participants aged from 60 to 85 years received sham, 2mA and 3mA anodal tDCS in three different montage groups: left, right, or bilateral dorsal lateral prefrontal cortex (DLPFC) stimulation, while performing sustained attention training task. Continuous Performance Test (AX-CPT) were measured before and after intervention as outcome measures. Preliminary data demonstrated that combining tDCS with sustained attention training has distinct effects among different montages in healthy elderly.

16. Age-related differences in default-mode network connectivity in response to intermittent theta-burst stimulation and its relationships with maintained cognition and brain integrity in healthy aging

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Background: The default-mode network (DMN) is affected by advancing age, where particularly long-range connectivity has been consistently reported to be reduced as compared to young individuals. We examined whether there were any differences in the effects of intermittent theta- burst stimulation (iTBS) in DMN connectivity between younger and older adults, its associations with cognition and brain integrity, as well as with long-term cognitive status.

Methods: Twenty-four younger and 27 cognitively normal older adults were randomly assigned to receive real or sham iTBS over the left inferior parietal lobule between two resting-state functional magnetic resonance imaging (rs-fMRI) acquisitions. Three years later, those older adults who had received real iTBS underwent a cognitive follow-up assessment.

Results: Among the younger adults, functional connectivity increased following iTBS in distal DMN areas from the stimulation site. In contrast, older adults exhibited increases in connectivity following iTBS in proximal DMN regions. Moreover, older adults with functional responses to iTBS resembling those of the younger participants exhibited greater brain integrity and higher cognitive performance at baseline and at the 3-year follow-up, along with less cognitive decline. Finally, we observed that 'young-like' functional responses to iTBS were also related to the educational background attained amongst older adults.

Conclusions: The present study reveals that functional responses of the DMN to iTBS are modulated by age. Furthermore, combining iTBS and rs-fMRI in older adults may allow characterizing distinctive cognitive profiles in aging and its progression, probably reflecting network plasticity systems that may entail a neurobiological substrate of cognitive reserve.

References:

Abellaneda-Pérez, K., Vaqué-Alcázar, L., Vidal-Piñeiro, D., Jannati, A., Solana, E., Bargalló, N., Santarnecchi, E., Pascual-Leone, A. & Bartrés-Faz, D. (2019). Age-related differences in default-mode network connectivity in response to intermittent theta-burst stimulation and its relationships with maintained cognition and brain integrity in healthy aging. NeuroImage, 188, 794–806. https://doi.org/10.1016/j.neuroimage.2018.11.036

17. Development of Quantitative Measurement Device for Spasticity in Children with Cerebral Palsy

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Spasticity is one of the commonest problems and is also a major challenge for the rehabilitation of children with cerebral palsy (CP). To determine the effect of therapeutic interventions such as rehabilitation protocols, botulinum toxin injections or orthopedic surgeries for reducing spasticity, it is needed to have an objective and quantitative method for the spasticity assessment. However, the current clinical assessment method (e.g. Modified Ashworth Scale) for spasticity measurement is still needed to reduce the subjective biases. To improve the accuracy and reliability of spasticity measures, this study developed a relevant assessment device to quantify the level of spasticity in the lower limb in children with CP. The assessment system consists of a pressure sensor, joint angle calculation algorithm, electromyography (EMG) system. Based on several quantitative sensors, the joint resistance, angular displacement and EMG activity of knee flexor and extensor muscle during stretch were collected for further analysis. The viscous and elastic components were derived to represent the velocity-dependent properties of the knee joint during the stretch. Compared to healthy control, the level of the viscous component was significantly higher in CP subjects with spasticity. The significant increase in viscous component correlated well with the modified Ashworth scale. This integrated evaluated approach could provide a unique opportunity to objectively quantify the severity of spasticity and improve the accuracy and reliability of clinical spasticity assessment method for children with Cerebral palsy.

18. Educational effects of a nursing department/clinical engineering department collaboration class designed to promote an understanding of ME devices in emergency care

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In emergency medical settings (e.g., emergency medical center, intensive care unit), various ME devices are used to save lives, for life support, and to monitor patients. Understanding the mechanisms of these devices, as well as their effects on the human body and therapeutic purposes, is essential for nursing care practice. In this study, an interdepartmental collaboration class was taught by faculty members of nursing and clinical engineering departments, mainly focusing on three representative ME devices (PCPS, IABP, and CHDF). We aimed to verify the educational effects of the class based on changes in student knowledge and awareness regarding ME devices, as well as what they learned.
From October 2017 to February 2018, 80 third-year students at A University attended a class in which faculty members of the clinical engineering department demonstrated the use of actual ME devices to students. This class was intended to promote an understanding of ME devices in preparation for on-site visit/practical training in an emergency medical center and intensive care unit as part of an adult acute-stage nursing practicum. Before the class, faculty members of the nursing department presented assignments, such as key points of the on-site visit. Records regarding changes in student knowledge and awareness about ME devices after the class and what they learned from the class were subjected to content analysis.
Before the class, students had an image of ME devices as having "complicated and confusing" structures and being "far from nurses," and had a "strong awareness that they were not good at handling them." However, this awareness changed after the class as they observed how the actual devices moved (e.g., "the structure and circuit of the devices looked simple in light of principles and their basis," "I no longer feel like I'm bad at handling them," "ME devices are directly connected to patient life," and "they are indispensable tools for nursing work").
With regard to learning, content analysis revealed the following: 1. ME devices protect patient lives but with high risk; 2. ME devices are a part of the patient’s body; 3. Alarms include patient complaints/distress; 4. Awareness of nursing with a sense of responsibility; and 5. Collaboration based on understanding the characteristics of other professions.
The emergency medical setting is an extraordinary place for students, and their knowledge about life supporting ME devices is limited to the aspect of treating diseases. However, by observing how the devices operate in practice and asking questions, students were able to imagine and perceive them as familiar issues. Moreover, they realized the need for learning, and this became a motivation to learn. Life-supporting ME devices are highly invasive to the body. Thus, nurses must hone their observation skills in order to notice even small changes in patients in a state of tension. Promoting an understanding of ME devices could also provide the opportunity for nurses to perceive their own identity and evaluate their role as a nurse. Our findings suggest that the trial collaboration class by nursing and clinical engineering departments had the educational effects of increasing student knowledge and awareness.

19. Analysis of Waiting Time from Order Histories

Shusaku Tsumoto (Shimane)

Hospital information system starts from introduction of order-entry system and has been developed into the system storing almost all information about clinical actions, where users can browse them through the window system. The most important characteristics is that each stored event is linked with time stamp, which can be used for temporal data mining to extract useful information about hospital management. In this paper, we focus on waiting time that is defined as the difference between reservation and actual inspection by doctors, and attributes related with waiting time. The results shows that groups of doctors, reservation time and divisions contributes to the length of waiting time.

20. Comparison of one-session anodal tDCS effects on fine motor control in subacute and chronic stroke patients

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*- presenting author

Objective: To compare the application of tDCS in subacute and chronic stages of stroke in order to define an optimal time-window for stimulation.
Methods: Anodal and sham tDCS was applied to M1 of 13 stroke patients in balanced cross-over design during subacute and chronic stages of stroke. The Jebsen-Taylor Hand Function test, evaluating the time required for performance of everyday motor tasks, was employed.
Results: The repeated-measure ANOVA showed significant influence of stimulation type, the test performance time relative to stimulation (during or after tDCS) with no overall influence of the stage of stroke. The interaction TYPE*TIME*STAGE was significant. The effect after anodal tDCS in the subacute stroke was significantly higher compared to the effects in all relevant conditions including the chronic stage (Figure 1). Yet, on the individual level, this type of response was present only in six patients (Group 1). On contrary, patients of Group 2 showed small responses (1-1.3% improvement compared to sham) in the chronic stage. These effects were significantly higher compared to those in the subacute stage (Figure 2). All Group 1 patients were women; six men and one woman belonged to Group 2. No other difference in clinical characteristics between groups was seen.
Conclusions: For some patients tDCS treatment in the subacute stage of stroke can be superior over the treatment in the chronic stage. However, the possibility that other patients might show opposite effects, cannot be ruled out.

21. Effective utilization of e-learning for Japanese geriatric nursing

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Introduction

E-learning offers numerous opportunities for students to interact with each other and with their teachers in an electronic manner. These interactions can be via e-mail, by posting on discussion boards, or through conversations in chat rooms. Of course, the world as a whole will continue to use language and terminology in different ways, but the term, 'virtual learning environment (VLE)' is used here to refer to a variety of online interactions that take place among students and teachers. Many available software systems offer VLE, both as commercial and open source software (OSS). Moodle is one such system that has been increasing in global popularity as an e-learning system. In particular, the Japanese nursing education field has recently focused in more on e-learning as a learning support method. Our university also has an e-learning system that enables students to learn using Moodle. Moodle is a free, online Learning Management system enabling educators to create their own private website filled with dynamic courses that extend learning, anytime and anywhere. Whether you're a teacher, student or administrator, Moodle can meet your needs. Moodle's extremely customizable core comes with many standard features. Moodle was created from 1999-2001 in Austria by Martin Doubiamas and colleagues.
Here, we present some of the approaches we have taken in our use of Moodle in the Geriatric Nursing education program at Tottori University.

Nursing Education in Japan

We have several methods of nursing educations. At the university level, nursing students receive 4 years of education that aims to fulfill their eligibility requirements to pass the examination to become registered nurses. The eight major subjects are as follows: Fundamentals of Nursing, Adult Nursing, Geriatric Nursing, Home Care Nursing, Pediatric Nursing, Women's Health Nursing, Community Health Nursing, and Mental Health Nursing.

Geriatric Nursing Education at Tottori University

At Tottori University, the Geriatric Nursing component of the program comprises two classes and one practicum, which are taught over the course of a year and target second-, third-, and fourth-year students. To begin, students take an Introduction to Geriatric Nursing from April to July. This is followed by Geriatric Nursing, which is taught from October through January. Finally, the practicum in Geriatric Nursing on third level students. Moodle is used continuously in the classroom lectures.

Using Moodle in Geriatric Nursing Education

Our students are able to access Moodle at all times from their internet sources, which include smart phones, laptops, and any other device with internet. We ready some word file paper and comments for class in Moodle. Students are required to access Moodle and prepare for class by reading papers pertaining to the classroom lecture topic.

Introduction to Geriatric Nursing

This class was a 90-minute lecture, comprising 15 classroom lectures over the course of 4 months. This class aims to ensure that students understand aging-related changes and the current realities and challenges faced by the elderly in Japan. Students are led in this class to consider nursing care for elderly individuals based on their understanding of the concepts of death, living, and aging-related changes.

Geriatric nursing

Geriatric Nursing is also a 90-minute lecture class, also comprising 15 classroom lectures over the course of 4 months. This class aims to teach students to understand nursing planning as it

pertains to the recovery period in elderly individuals. Students are tasked with creating a care plan for an elderly individual who has suffered from cerebral infarction.

Using Moodle to teach Introduction to Geriatric Nursing and Geriatric Nursing

Moodle of introduction of Geriatric nursing is composed 16 category. Each paper used in the classroom lecture is uploaded to Moodle. Students are required to access Moodle prior to attending class and confirm the content of the upcoming class. This is a natural way to ensure that students are better prepared to learn in the class to come. In addition, each student is required to submit a report following each class, which increases their motivation to prepare and listen in class.

Discussion

Effective utilization of the Moodle e-learning system in Geriatric Nursing

We summarized the effectiveness of using Moodle as an e-learning system in the Geriatric Nursing program based on student-written reports.

1. Continued interest in Geriatric Nursing

Students are required to view the papers pertaining to the classroom lecture prior to attending that particular lecture. As such, they come to class having already read the paper pertaining to the relevant lecture topic. Moreover, they can access the content of the classroom lecture at all times. Several of our students commented that “I am still interested in Geriatric Nursing even after 4 months.” Their continuous interest in problems faced by the elderly in Japan is reassuring with regard to this learning method. Tubaishat (2018) said Facebook™ can be used as an instructional tool to support nursing education.

2. Saving on the cost of paper for classroom lecture classes

Our students have numerous opportunities to use the computer in their university education. As such, nearly all students have their own laptops and are admit to ready paper of classroom lecture any materials. Some students read the papers required for the lecture class on their computers, rather than actually printing a hard copy. As we have roughly 80 students, this saves an immense amount of paper and the cost required to print hard copies of the papers each year.

Reference:

Tubaishat Ahmad (2018.08-10) Student nurses' perceptions of Facebook™ as an interactive learning platform in nursing education, Contemporary nurse, Vol. 54issue (4-5), PMID: 30296928DOI: 10.1080/10376178.2018.1530944.

22. Temperature and humidity characteristics of two kinds of skin cleaning towels that affect sensation

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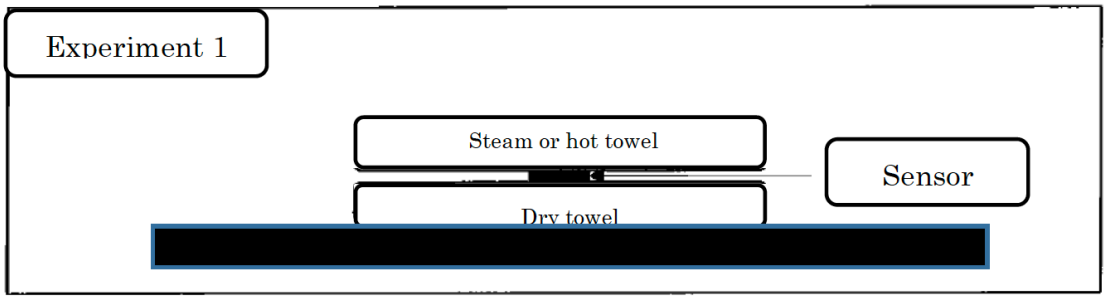
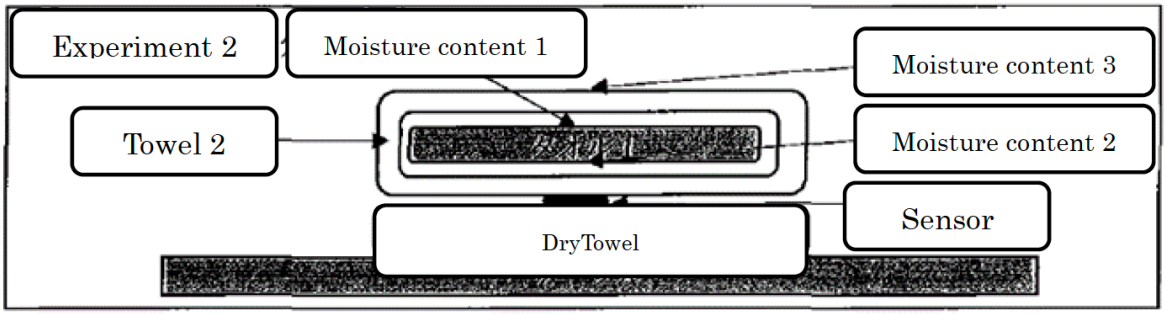
Aim: Traditionally, hot towels have been used by nurses to clean the patient's skin. The authors examined the effect of the steam towel approach in which a small amount of boiling water is poured into a dry towel. They found that the steam towel had a relaxing effect on the brain waves. Therefore, this study aims to clarify the differences in the properties of hot and steam towels.
Method: Data on the temperature, humidity, and keratin-containing water of the two samples, namely, hot and steam towels, were collected using measuring devices.
1. Definition of terms
(1) Steam cloth is a towel obtained by dripping approximately15–20ml of hot water at90 °Cor more on a dry towel, leading to transpiration.
Steps on how to make the steam cloth (towel 1):
i) Fold the towel in half.
ii) Weigh the T-fal electric kettle before adding water.
iii) Boil the water by using the T-fal electric kettle, open the eight fold towel 1,and pour the boiling water at the center of the towel.
iv) Weigh again the T-fal electric kettle containing the hot water.
v) Twist the towel that is dripping with hot water by hand, and steam the hot water contained in the towel.
vi) Weigh the steam towel.
vii) Slap the steamed towel on to a palm and spread the steam.
viii) Open in quarters.
(3) Steam towel set
The steam towel set is a towel in a state in which the eightfold steam towel (towel 1) is folded in four and placed between dry towels (towel 2).
(2) A hot towel is a towel containing approximately100ml of water soaked in 70 °C water and squeezed tightly.
Steps on how to make the hot towel (towel 1):
i) Fold the towel in half.
ii) Dip the eightfold towel in approximately 70 °C of warm water, remove it, and squeeze it by hand.
iii) Weigh the hot towel.
iv) Open the towel in fourfold.
(3) Hot towel set
The hot towel set is a towel in which the hot towel (towel 1) is folded in four and placed between dry towels (towel 2).
2. Measurement conditions
(1) The implementation date was on February 26, 2019 at 9:30 AM to 11:30AM.
(2) The average environment indoor temperaturewas22.70 °C, and the average indoor humiditywas32.83%.

(3) The towels used were white towel, green towel, and another white towel weighing at 101.62, 67.43, and 43.14g, respectively.
3. Measuring equipment
(1) The temperature/humidity sensor probe, that is,THP-728 (SHINNEI Technology Co., Ltd.),of a temperature/humidity measuring instrument was connected to the network-type temperature/humidity meter, that is,TRH-7X,to measure the temperature and humidity. Data were gathered in a personal computer by using temperature/humidity-meter data acquisition software (NSD-0025).
(2) The horny-moisture meter called Moisture Checker, which was manufactured by Scalar Corporation (MY-808S), was used to measure the horny-moisture content.
(3) The balance used was Sartorius KK BP 1200 (minimum display,0.01g).
(4) T-fal electric kettle
(5) Thermometer
(6) Towels used were white and green towels weighing at approximately 43 and 63–69g, respectively.
4. Implementation procedure
Experiment 1(G.1)
A sensor was placed on top of a dry white towel, and the temperature and humidity of towels 1 and 2 were measured. Specifically, the sensor was placed on the top center of a dry fourfold white towel. Next, a steam towel or dip towel, which was made in the following procedure, was placed on top of towel 1. Subsequently, the temperature and humidity were measured for 1 minute at the intervals of 0and5 second sand then recorded as the measuring data.



G.1. Experiment 1 Design

Experiment 2(G.2)
A sensor was placed on top of a dry white towel, followed by a towel set. The temperature and humidity were measured in between by using the temperature/humidity sensor to also measure the moisture amount of the towel surface according to the following three points:
・Water content measurement point
・Water content 1: top of towel 1
・Water content 2: lower part of towel 1
・Water content 3: upper part of towel 2



G.2. Experiment 2 Design

Experiment 3

Using the towel set prepared in the same procedure as Experiment 2, we wiped the human arm (the measurement site was a fixed point of approximately 10cmfrom the right-forearm inner elbow to the periphery), and the moisture amount on the skin surface was finally measured.

5. Measurement result

Experiment 1Result

The steam towel contained approximately12–16mlof hot water at approximately92 °C, whereas the hot towel contained approximately90–100mlof hot water at 70 °C.

The average surface temperature and humidity were 52.13 °C and 98.00RH for the steam towel and 52.97 °C and 96.33RHfor the squeezed towel (Tables 1 and2).

Transpiration was relatively active but had no statistically significant difference, given that transpiration was relatively active by pouring hot water at 20 °Cor more from the squeezed towel to the steam cloth p> 0.10(Graphs3and4).

The steam cloth maintained a higher surface temperature than the squeezed towel after 2 seconds.

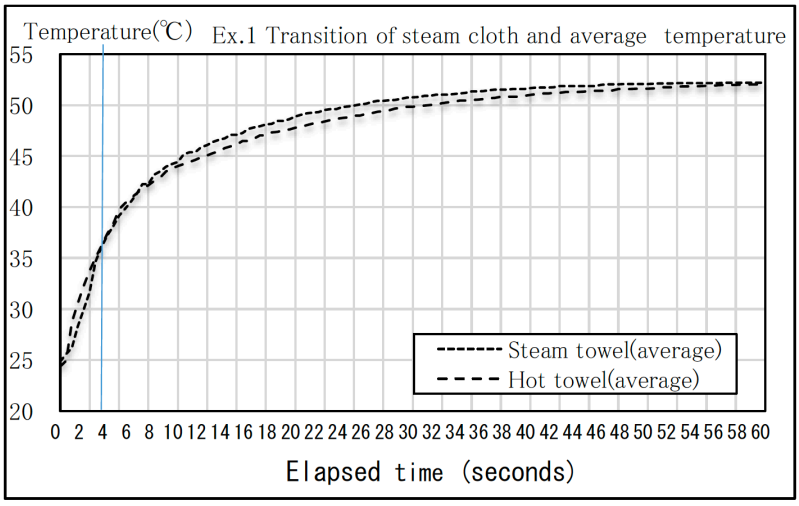
The steam cloth maintained more vigorous transpiration than the squeezed towel after approximately2 seconds.

Table 1. Measurement time of the steam towel, shape, weight, temperature, and humidity

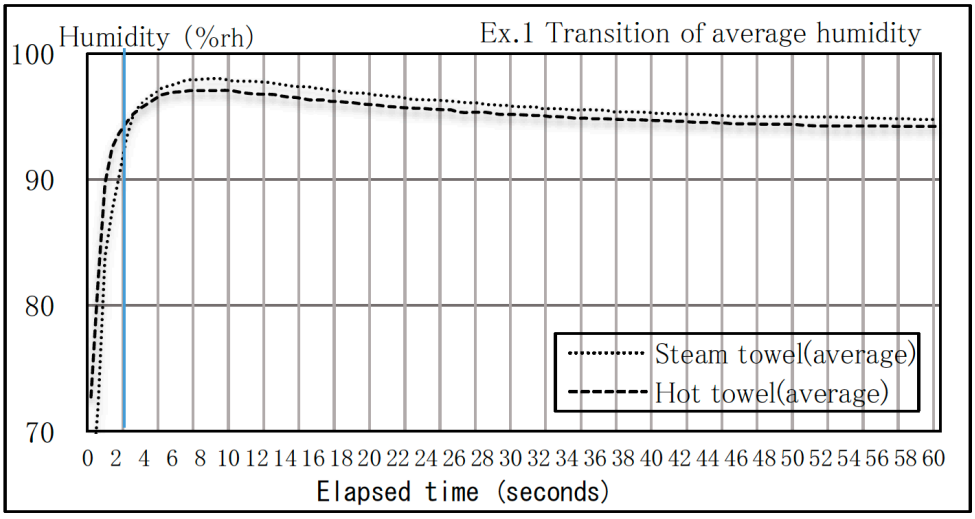
	Start testing	towel weight (g)					
		Before use	After use	Hot-water amount poured (g)	Hot-water temperature (℃)	Maximum water temperature (℃)	High humidity (RH)
First time	2019.2.26 10:15	65.34	78.49	13.15	90	51.9	97.7
Second Time	2019.2.26 10:20	65.50	80.99	15.49	94	50.7	96.6
Third time	2019.2.26 10:25	67.42	79.45	12.03	93	53.8	99.7
Average	—	66.09	79.64	13.56	92.33	52.13	98.00

Table 2. Measurement time of the hot towel, shape, weight, temperature, and humidity

	Start testing	towel weight (g)		Amount of immersion water (g)	Hot-water temperature (℃)	Maximum water temperature (℃)	High humidity (RH)
		Before immersion	After immersion				
First time	2019.2.26 09:45	67.38	166.60	99.22	70	55.0	95
Second Time	2019.2.26 09:50	67.37	158.74	91.37	70	52.0	97
Third time	2019.2.26 09:55	65.82	162.00	96.18	70	51.9	97
Average	—	66.86	162.45	95.59	70.00	52.97	96.33



G.3. Temperature result of Experiment 1



G.4. Humidity result of Experiment 1

Experiment 2Result
A sensor was placed on top of a dry white towel and measured with a towel set across the temperature/humidity sensor.
In the case of the towel set that wrapped Experiment 1 in the dry towel, the steam towel set contained approximately17.2ml of hot water at around92.3 °C, whereas the hot towel set contained approximately82.6mlof hot water at 70 °C (Tables 5 and6).
The average temperature and humidity of the steam towel set were lowered from 52.13 °C to 3.83 °C by wrapping the steam towel set with a dry towel at 48.3 °C, whereas those of the hot towel set decreased from 52.97 °Cto 5.70 °C by wrapping it with a dry towel at 47.9 °C. The humidity showed saturation, indicating that active transpiration had occurred (Graphs 3 and 4).
Although temperature drop may have been affected by the temperature of the injected hot water, such temperature can eventually lead to a cleaning optimum temperature state of approximately 52 °C.
In the case of a towel set, exceeding the skin temperature can reach around 20 seconds.
The towel set may be suitable for cleaning beyond20 seconds and for acupuncture to be placed in contact with the skin (Graph 5).
When the humidity of the towel set passed through the dry towel, transpiration can be maintained without being influenced by the temperature of the injected hot water (Graph 6).

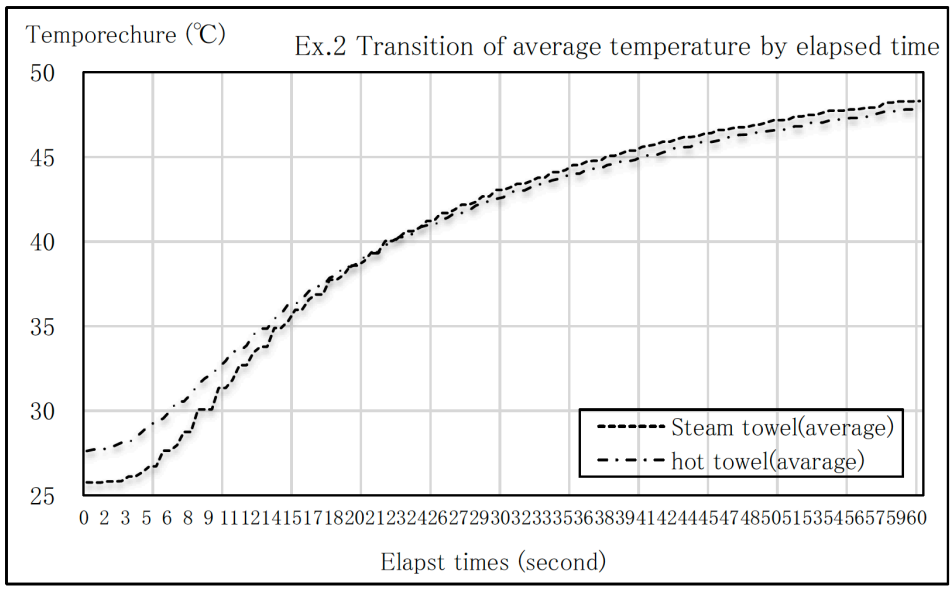
Table 3. Measurement time of the steam towel, weight before and after cleaning, water content, pouring temperature, maximum temperature of towel, humidity, and skin moisture after cleaning

		Towel weight (g)		Hot-water	Hot-water	Maximum water	High
	Start testing	Before use	After use	amount poured (g)	temperature (℃)	temperature (℃)	humidity (RH)
First time	2019.2.26 10:30	66.65	86.55	19.90	93	49.7	99.9
Second Time	2019.2.26 11:00	67.06	84.82	17.76	92	46.7	99.9
Third time	2019.2.26 11:10	68.97	82.80	13.83	92	48.4	99.9
Average		67.6	84.7	17.2	92.3	48.3	99.9

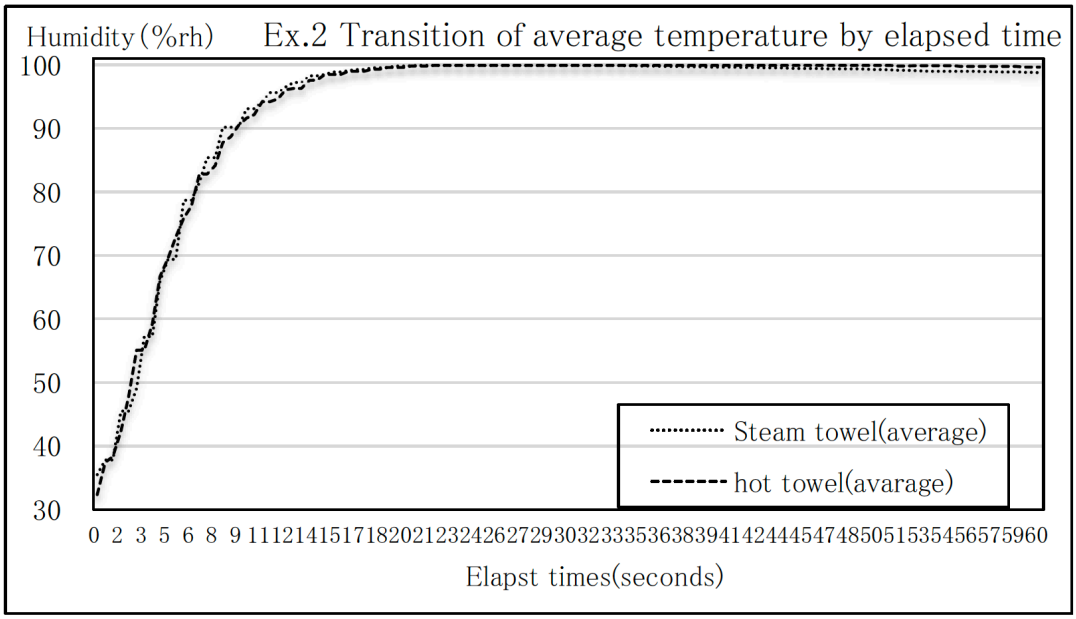
Table 4. Measurement time of the hot towel, weight before and after cleaning, water content, pouring temperature, maximum temperature of towel, humidity, and skin moisture after cleaning

		Towel weight (g)					
	Start testing	Before use	After use	Hot-water amount soaked (g)	Hot-water temperature (℃)	Maximum water temperature (℃)	High humidity (RH)
First time	2019.2.26 11:20	67.23	142.54	75.31	70	49.2	99.9

Second Time	2019.2.26 11:00	64.88	148.95	84.07	70	48.6	99.9
Third time	2019.2.26 11:10	66.46	154.93	88.47	70	45.8	99.9
Average		66.2	148.8	82.6	70.0	47.9	99.9



G.5. Temperature result of Experiment 2

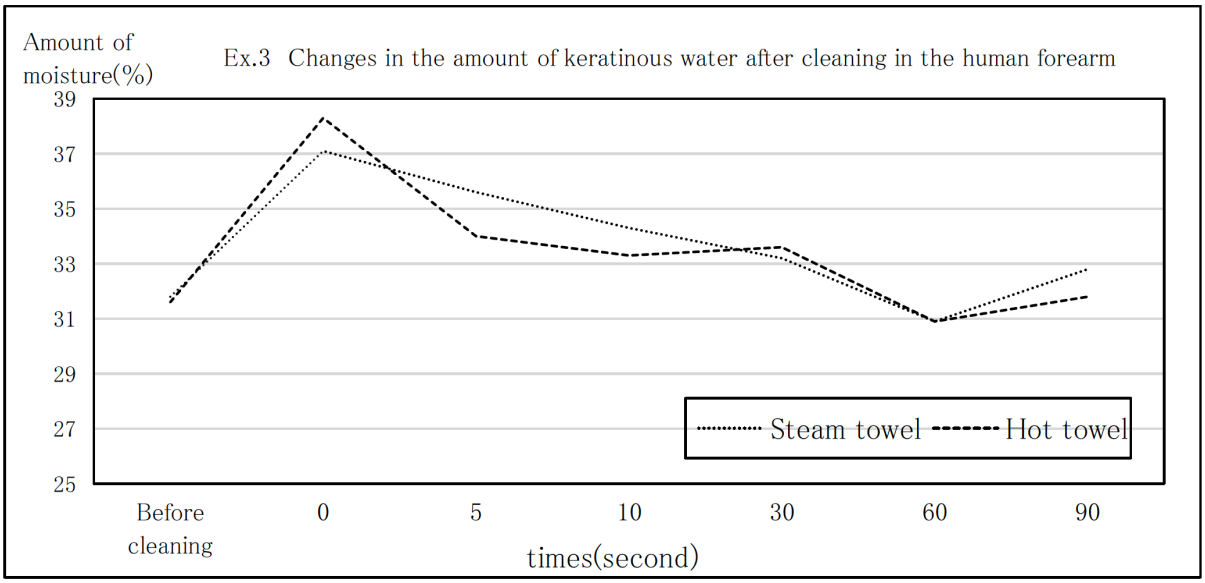


G.6. Humidity result of Experiment 2

Experiment 3Results
As a result of skin cleaning with two towel sets, no significant difference was found according to the Mann–Whitney U Test (p> 0.10, Graph 7).

Table 7. Cutaneous water content of skin after cleaning by the two towel sets

	Experiment start date	Towel weight (g)		Amount of hot water poured (g)	(°C)	Water content of human forearm (%)						
						Before cleaning	After cleaning (seconds)					
		Before cleaning	After cleaning				0	5	10	30	60	90
Hot towel	2019.2.26 11 : 40	63.6	75.68	12.08	92	31.8	37.1	35.6	34.3	33.2	30.9	32.8
Steam towel	2019.2.26 11 : 50	65.31	156.38	91.07	70	31.6	38.3	34.0	33.3	33.6	30.9	31.8



G.7. Changes in the amount of keratinous water after cleaning the human forearm

Consideration

The two experimental samples also differed in the temperature of the pouring water by 20 °C. In addition, it had a similar surface temperature and humidity, although the amount of pouring differed. However, the transpiration between the steam cloth and the squeezed towel without wrapping with a dry towel was relatively active but not significantly different. In the previous measurement of our brain waves, this steamed cloth caused a relaxing effect compared with the squeezed towel with 52 °C of hot water. This phenomenon may have been affected by the differences in the sensation of the towel surface. The number of measurements should be repeated and verified.

Conclusion

Although the two towel sets had similar characteristics, the difference between the temperature and the amount of hot water poured into the towel may affect the skin sensation. Thus, we need to examine the rubbing phenomenon between the skin and the towel surface.

23. Improvement of Retinex Algorithm for Medical Image Enhancement

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Recently, many patients are at risk of diagnostic error due to a chronic shortage of doctors all around the world. In particular, Japan has a small number of doctors per head of population compare with the other developed countries. One of the causes of oversight of the lesion in regular examinations is the overburden for one doctor. We argue that the appearance improvement of the medical image is essential to reduce the risk of diagnostic error.
In this paper, we apply Retinex algorithm which ensures detail and brightness enhancement to medical X-ray images with the aim of reducing the burden on doctors. Even though the application of Retinex algorithm for medical X-ray images was suggested to be an effective means to grasp the presence or absence of a lesion in some conventional researches, Retinex algorithm is not applied in actual medical field works. Therefore, we discover the obstacle in field application and propose the improvement method of Retinex algorithm.

24. Morse Code: A Window on Language Decoding in the Brain

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In natural languages, single words are processed rapidly, and low sampling rates of functional brain imaging techniques pose an unsolved problem regarding disentanglement of neural correlates of various linguistic components, including phonological, lexical and semantic components (Friederici, 2002). Resembling letter-by-letter translation, Morse code can be used as a model to slow down the cognitive process of word recognition. More specifically, decoding Morse code requires sound pattern analysis and mapping these patterns onto phonemes (sublexical analysis), followed by phonological assembly, and mapping the resulting phonological structures onto semantic structures (lexico-semantic processing). In the current project, we used Morse code to get further insights into sublexical and lexico-semantic processing by study a specific type of access to the semantic system, namely the non-lexical route as described in the conceptual framework of the connectionist dual process (CDP+) model (Zorzi, 2010; Taylor et al., 2013).
Using functional Magnetic Resonance Imaging (fMRI), we investigated 34 right-handed subjects who had previously learned to decode 12 letters of Morse code; here, they decoded three-letter words and nonwords in a lexical decision task. By investigating specific time domains as well as contrasts between words and nonwords (Figure 1), different processing phases (Sublexical, lexical, semantic) were identified using general linear models (GLM) and multi-voxel pattern analysis (MVPA).

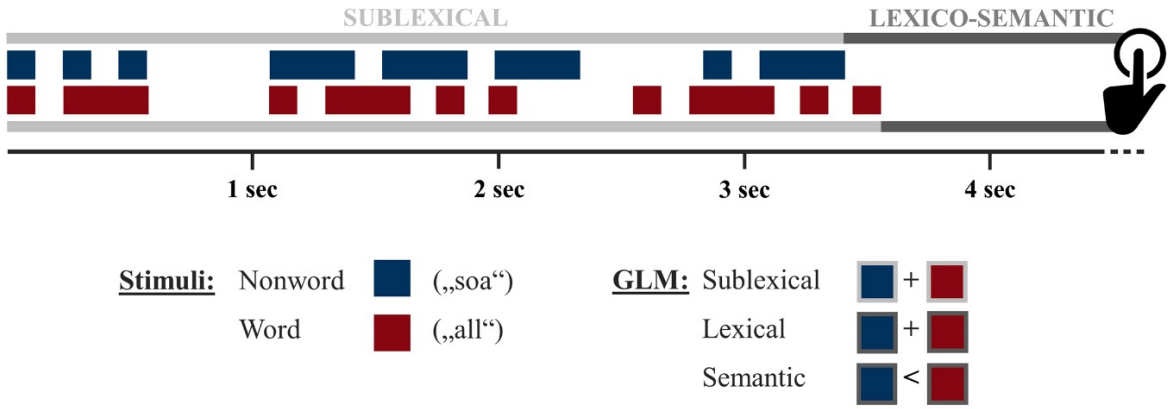

Figure 1:General linear model
Analysis of sublexical (light grey) and lexico-semantic (dark grey) processing step for words (red) and nonwords (blue red) presented via Morse code. The feedback of the subjects was done with the left hand (black).

In the sublexical phase, brain activation was observed in the left inferior parietal lobule, the supplementary motor area, the left premotor cortex and the left inferior frontal cortex, comprising Broca's area (Figure 2). In the lexico-semantic phase, brain activity spread out into the insular cortex, as well as within the parietal lobule. When contrasting activity elicited by words versus nonwords (semantic processing), significantly more activation was observed in the ventral part of the left inferior frontal cortex/insular cortex, the medial prefrontal cortex (anterior cingulate cortex/superior frontal cortex), the precuneus and the left angular gyrus. By training a linear binary support vector machine in a leave-one-subject-out approach on the whole brain (MVPA), additional involvement of the left middle temporal gyrus and temporal pole in semantic processing were identified. These regions are known to play a critical role within the semantic system.

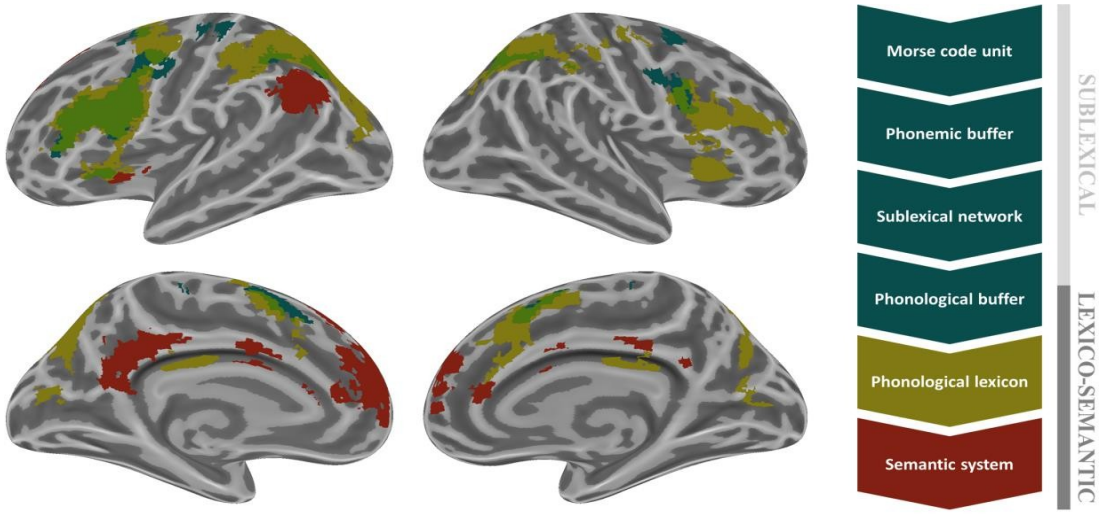

Figure 2: Morse code processing

Summarized results of the general linear model (GLM) for processing of Morse code (left) according to the connectionist dual process model (CDP+: Right) for processing encoded language. Sublexical processing is shown in blue, lexical processing in yellow and semantic processing in red colors. Overlaps are shown in the corresponding colors.

By using Morse code, we were able to disentangle the different phases of linguistic analysis (language decoding) in a way, that different processing stages, which followed one after the other, could be studied despite the low temporal resolution of fMRI. Here, our data suggesting that the sublexical and lexico-semantic analyses are two distinct processes that rely on neighbouring, partially overlapping networks. Where early sublexical processing is associated with activation in brain regions that are implicated in the analysis of sound patterns and the generation of phonemes (DeMarco et al., 2017), the later lexico-semantic phase is associated with activation in brain regions that are implicated in access to the phonological lexicon (Protopapas et al., 2016) and subsequent lexical decision-making, as well as the semantic system comprising regions of the Default Mode Network (Binder et al., 2009). More specifically, whereas encoded language (graphemes, Morse code or any other code) is initially an external stimulus that undergoes analysis and processing within the task-positive network (here, the sound pattern-to-phoneme conversion and subsequent storage in the phonological buffer), the resulting word then gains access to the task-negative network (DMN). In this way, semantics could be an interlink between these task-positive and task-negative networks.

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25. Fusion of Touch and Vision with Floating Image Visualization

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We have been developing floating touch as an addition to floating image displays, to increase the user immersion in the interface. We report on our latest version that improves on previous floating touch displays, by allowing the sensing of contours, surface shape, and roughness, by precise control of a transparent plate moving into or out of the floating image plane. Experiments with user perception indicate that floating touch provides a separate channel besides vision. We have also developed a simple game that uses floating touch to give direct feedback to the user. We are now trying to use this method as a new multi-modal user interface, augmenting visualization to help interpreting medical images and similar complex information.

26. Comparison of acquired knowledge by nursing students for learning elderly dementia care between a digital learning and a text-book study

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1. Introduction: The number of dementia patients is increasing. Therefore, it is thought that a measure that deals with this dementia issue is needed. We aim to improve dementia education to solve the shortage of skilled staff. In our previous study, we developed a learning system as digital game-style about dementia care for nursing students. The user of the system plays a role of a nurse in a hospital. An elderly woman with dementia stays in the hospital and the user of the game is to take care of her. She express some symptoms of dementia and the nurse is expected to react properly by selecting the most appropriate candidate words for what the elderly woman says. Her symptoms get changing in corrects or errors by uses' selecting as the game's scenes go on. They can experience dementia care by seeing her changes in virtual reality. The digital learning materials also contain the test from the previous national nursing exams. We evaluate the effects of the learning system by comparing the test performance and the contents of acquired knowledges of two groups, A : the students from one group studied the dementia care using the digital learning material, and B: the students from the other group studied from the conventional text book. In this study we compared the differences of acquired knowledges of A group with B group.

2. Methods

2.1. Subjects: The participants were 18 nursing students (who had acquired credits of practical subject of Elderly Nursing).

2.2. Experiments: We divided students into two groups of A and B at random. A group: the students studied the dementia care using the digital learning material, and B group: the students studied it from the conventional text book. Both groups studied about the subject for one week. Before and after conducting the experiment, they answered 40 questions about dementia cares on tests and the questionnaire about the contents of acquired knowledges in this study and learning attitude (frequency, hours and so on) in each group after the experiment. In this study we compared the difference of acquired knowledges of A group with B group. This study was approved by the researcher's Ethics Committee.

3. Results and Conclusions: The contents of the acquired knowledges of Group A were "the way of talking to the dementia elderly person", "how to communicate for the dementia elderly person", "how to take care of their daily life movement", "importance of the environment around them". On the other hand, those of Group B were "the prevention of dementia", "the characteristic of dementia", "the kind of dementia" ,"about dementia symptom (core symptom and Behavioral and Psychological Symptoms of Dementia)." In other words, the students could learn the communication methods and methods of the care by simulating some scenes with the dementia elderly person in the digital game-style learning system and could understand important concepts for dementia and systematic knowledge with text-book.

27. tDCS-induced reconsolidation memory effects in Subjective Cognitive Decline (SCD) are related with structural brain integrity

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Introduction: Transcranial Direct Current Stimulation (tDCS) is technique that allows modulating cognition in older adults (Flöel A, et al., NeuroImage, 2014; 85(Pt 3): 934-47). In this vein, a recent study evidenced that tDCS entails capability to strengthen episodic memory in subjects with subjective cognitive decline (SCD), (Manenti R, et al., FrontAgingNeurosience, 2017; 9: 401), who are at risk to develop dementia (Jessen F, et al., Alzheimer's&Dementia, 2014; 10: 76-83). The main goal of the present study was to corroborate whether tDCS applied over the left dorsolateral prefrontal cortex (l-DLPFC) improves episodic memory consolidation in SCD participants after a contextual reminder and to elucidate its putative associations with brain integrity.

Methods: Thirty-eight elders (mean age = 62.29±1.55; 19 females) with SCD but normal neuropsychological profile were randomly assigned to receive active (N=19) or sham (N=19) tDCS in a double-blind design. Participants underwent a verbal learning task with 15 words (DAY-1) and 24h later (DAY-2) stimulation was applied during 15 min at 1.5 mA using 5x7 sponge electrodes after a contextual reminder. The anodal electrode was positioned over the l-DLPFC and the cathode on the right orbital region. Delayed recall and recognition were measured one day after the stimulation session (DAY-3) and at 1-month follow-up (DAY-30). In addition, we acquired 3T structural magnetic resonance images (MRI) data and performed cortical thickness (CTh) analyses with FreeSurfer Software Suite (https://surfer.nmr.mgh.harvard.edu/).

Results: We identified a group*time interaction in recognition (F=7.399, p=0.010). Specifically, recognition scores declined between DAY-3 and DAY-30 for the sham participants (t=4.003, p=0.001), while subjects at the active tDCS group maintained a stable recognition across measures (t=0.900, p=0.380; Figure 1). No significant differences were found between groups regarding CTh analyses. However, within the active group, a significant negative correlation between CTh and DAY-3 recognition scores was revealed within two areas located over the right medial orbitofrontal and middle temporal cortices (Figure 2).

Conclusions: These results support recent independent findings indicating that within the context of a reconsolidation experiment, tDCS holds potential to improve memory amongst older adults with SCD up to 1 month. Further, the neuroimaging results suggest greater immediate effects of memory reconsolidation through tDCS amongst those SCD individuals exhibiting greater brain atrophy.

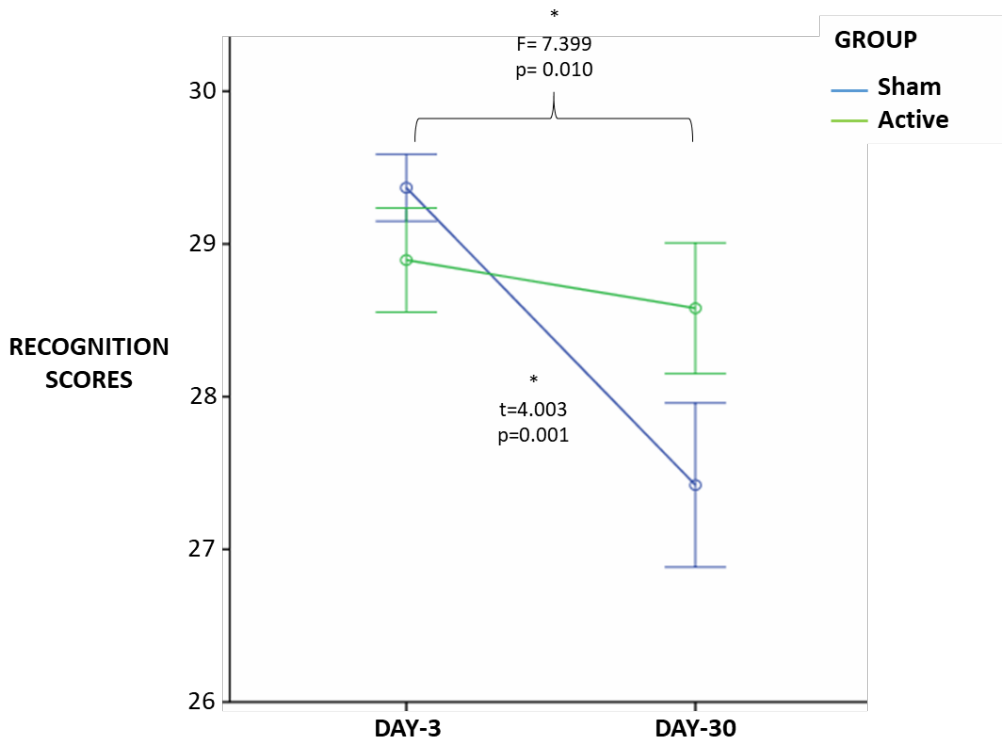

Figure 1. Plot showing the time*group interaction regarding the recognition scores. The sham group showed a significant decline after 1-month follow-up, while there was no a significant difference between DAY-3 and DAY-30 for the active group.

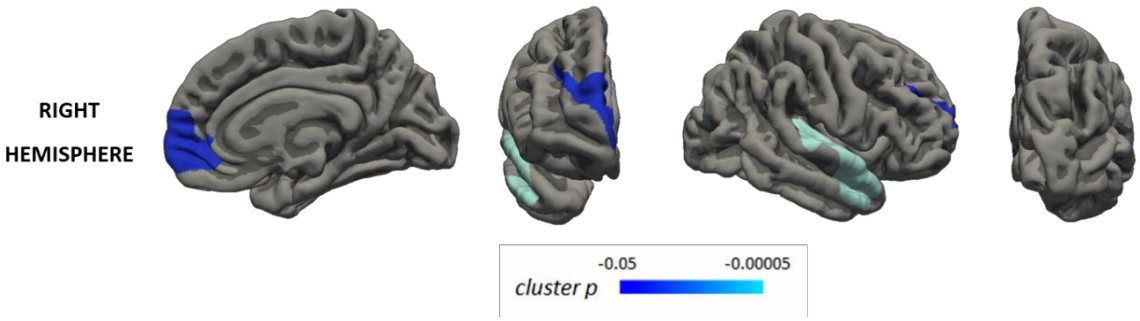

Figure 2. Vertex-wise CTh maps of significant clusters surviving FWE multiple comparison correction with a final cluster-wise $p < 0.05$. The clusters identified as negatively correlated with the recognition scores at DAY-3 for the active group are shown in blue

28. Consequences of prefrontal tDCS on inhibitory control and reactive aggression in alcohol dependent patients and tobacco users

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High impulsivity and pathological aggression are a hallmark of a number of psychiatric disorders, including substance use. Impulsiveness does not only contribute to the likelihood of initial substance use, it is also a strong predictor of relapse rates among patients with substance use disorder. Moreover, substance use is associated with an increased risk for aggressive behavior, which is further demonstrated by the fact that a multitude of violent acts is committed under the influence of alcohol. Thus, interventions to increase impulse control and reduce aggressive behavior are highly warranted. Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique to alter cortical excitability, presents a powerful tool to increase neural activation associated with cognitive control. In a double-blind, sham-controlled study, we investigated the effect of anodal tDCS over the right DLPFC on aggressive and impulsive behavior in a sample of 18 patients with alcohol dependence, 17 chronic tobacco users and 16 healthy matched controls. Following active but not sham stimulation, we observed increased response inhibition in alcohol dependent patients and chronic tobacco users. No differences in aggressive behavior were detected between individuals that received active tDCS and individuals that were treated with sham stimulation. However, results revealed reduced reactivity to high provocation following active but not sham tDCS in healthy controls and alcohol dependent patients. The current study suggests that anodal tDCS over the right DLPFC may help to increase impulse control and to reduce aggressive reactions to high provocation in selected individuals.