UNIVERSITÀ DI TRENTO

CIMeC Center for Mind/Brain Sciences

Transcranial Brain Stimulation in Cognitive Neuroscience Workshop

Rovereto (Italy) 2-3 December 2022

Center for Mind/Brain Sciences - CIMeC
University of Trento

3rd Edition

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1. The effect of bilateral frontal Transcranial Direct Current Stimulation on asymmetry of frontal brain activity

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Previous studies suggest that Transcranial Direct Current Stimulation (tDCS) aimed at enhancing right over left frontal brain activity improves self-regulation and inhibitory control. These behavioural effects are assumed to be due to a tDCS induced change in lateralization of frontal brain activity. However, it remains the question as to whether tDCS induced behavioural changes are mediated by shifts in brain activity lateralization. In the current study, we addressed this question. We employed a sham-controlled randomized design. In total, 65 participants (19 men, 46 women) between 18 – 58 years old (M=24, SD = 6) received either 20 min. of tDCS or sham-tDCS. tDCS consisted of 2 mA current delivered using the Starstim8 device from Neuroelectrics, with F4 (right frontal site) as anode and F3 (left frontal site) as cathode. Before and after the intervention 5 min. eyes-open and 5 min. eyes-closed resting state EEG was recorded. Results showed no statistically significant effect of tDCS relative to sham-tDCS on asymmetry of frontal brain activity indexed by frontal alpha (oscillatory) F4/F3 asymmetry. In conclusion, it may be that a mechanism other than asymmetry of brain activity drives the previously reported behavioural effects induced by F4/F3 2 mA tDCS.

2. The understanding of others' emotions relies on the involvement of segregated cerebellar regions: a study with transcranial magnetic stimulation

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Recent evidence suggests that the cerebellum is involved in socio-affective functioning, ranging from theory of mind to emotion perception abilities. However, whether its contribution may be ascribed to a single functional mechanism or a set of multiple functions (possibly mediated by different cerebellar subregions) is still unclear. By adopting a causative approach through the use of online Transcranial Magnetic Stimulation (TMS), the present study insights into the functional organization of the posterior cerebellum during social cognitive tasks. In particular, we hypothesized that low-level social cognitive operations, like the processing of emotional faces, recruit slightly more medial regions than complex social processes, like drawing higher-level emotional inferences that, in turn, rely on the activity of hemispheric (lateral) cerebellar regions. In two experiments, we asked healthy participants to either discriminate between emotional facial expressions (perceptual/low-level task) or to infer others' emotions by integrating facial and contextual cues (mentalizing/high-level task) while receiving TMS over the medial, the (left) lateral cerebellum, and the vertex (control condition). We found that interfering with the activity of both the medial and lateral cerebellum affected participants' performance in the discrimination of emotional faces. In turn, the ability to reason about others' emotional states at a higher level was affected selectively by TMS over the lateral cerebellum. Overall, our findings indicate for the first time that the cerebellum plays a causal role in different social cognitive operations and that segregated cerebellar regions exert partially distinguishable functions in social cognition.

3. Investigating the interaction between tACS aftereffects and cortical natural frequencies: a TMS-EEG study

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Compelling evidence of a consistent pattern of aftereffects following transcranial alternating current stimulation (tACS) is lacking. The interplay between tACS frequency and endogenous oscillatory activity (natural frequency) of the targeted cortico-thalamic module needs further investigation. We hypothesize that tACS effects can be predominant in the targeted cortical area's natural frequency regardless of the applied stimulation protocol. We measured cortical excitability and oscillatory activity following tACS of BA7 at its natural frequency (i.e. beta-rhythm) compared to a control frequency (i.e. gamma-rhythm).
Fifteen subjects participated in two TMS-EEG sessions. TMS was delivered over the left BA7 and the right BA6, before and after 15 minutes of tACS in the beta (18Hz) and gamma (40Hz) band over the right PPC. TMS-evoked potentials were recorded from 60 scalp electrodes. Cluster-based analyses were performed to compare the TEPs amplitude and oscillatory patterns before and after tACS stimulation.
Comparing TEPs amplitude triggered by parietal and frontal TMS, we found no modulation of cortical excitability after beta-tACS. Gamma tACS decreased frontal TEPs amplitude over tACS stimulation target around 200 ms post-TMS. No changes in the oscillatory profile were detected after beta-tACS, whereas we observed a bilateral increase in alpha power over frontal and central sites after gamma-tACS.
Albeit preliminary, our results do not provide strong evidence about the interaction between tACS frequency and endogenous rhythms in determining reliable patterns of aftereffects. Further studies are needed to clarify the neurophysiological underpinnings of tACS aftereffects.

4. rTMS-induced long-lasting language improvements associated with resting state functional connectivity changes in Primary Progressive Aphasia

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Primary Progressive Aphasia (PPA) is a clinical neurodegenerative syndrome characterized by language impairment (i.e., aphasia). There are three main PPA syndromes: the non-fluent/agrammatic variant (nfvPPA), the semantic form (svPPA), the logopenic form (lvPPA). Many patients do not fit perfectly into one of these three syndromes and other subtypes have been proposed: the mixed subtype (mvPPA) and the anomic subtype (avPPA).
5 male and 2 female (2 lvPPA, 2 nfvPPA, 1 mvPPA and 2 avPPA) patients underwent 10 consecutive daily sessions of repetitive Transcranial Magnetic Stimulation (rTMS) targeting the patients' left Broca's area. Immediately after each rTMS session, patients underwent one-hour Speech and Language Therapy (SLT), capitalizing the rTMS neuromodulatory after-effect. Before (T0), immediately after (T1), and one month (T2) after the rTMS intervention, language performance was tested with an extensive neuropsychological assessment and resting-state functional connectivity (rsFC) was measured with functional magnetic resonance imaging (fMRI).
At the end of the rTMS procedure, linguistic abilities (naming, semantic and phonemic fluency) were long-lasting enhanced in all patients. Moreover, we found a modification of the rsFC pattern between the left Broca's area and the Default Mode Network (DMN), specifically in the Medial PreFrontal Cortex (MPFC) and Posterior Cingulate Cortex (PCC).
rTMS over Broca's area combined with SLT led to significant and relatively persistent improvement in linguistic abilities associated to rsFC changes.

5. Stimulation of parietal cortices unveils asymmetric signal propagation dynamics

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TMS-EEG co-registration allows to examine differences in signal propagation dynamics. The purpose of this study is to characterize the emergence of visual awareness by stimulating a visually responsive portion of left or right parietal cortices to spot possible hemispheric asymmetries in conscious and unconscious processing. Twenty participants were tested. After the assessment of the individual phosphene threshold at which participants could perceive a phosphene in 50% of trials for both stimulation sites (i.e., electrodes P3 and P4), single-pulse TMS was administered at threshold intensity and participants had to report the presence or absence of a phosphene. Each experimental session consisted of 360 TMS pulses per site which was counterbalanced across participants. TMS-Evoked Potentials unveiled a significant main effect of stimulation site and phosphene awareness. Besides, the interaction between them was significant, where phosphene-present trials were contrasted against phosphene-absent trials, separately for each stimulation site. After left stimulation, analysis showed early clusters of significant activity over posterior regions. Instead, right stimulation displayed later centro-parietal clusters. Local mean field power analysis highlighted significant differences between ipsilateral and contralateral electrodes with respect to stimulation. This difference was even more pronounced for right stimulation than left stimulation, especially early in time. These results show that the stimulation of parietal cortices elicits different electrophysiological patterns, both per se and in the emergence of visual awareness. Such asymmetries provide further evidence for the hemispheric specialization hypothesis, showing that such differences are not limited to higher cognitive functions, but concern also lower perceptual mechanisms.

6. TMS-evoked potentials in successful ageing and Alzheimer's disease

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The cortical responses to a transcranial magnetic stimulation (TMS) pulse seen in electroencephalography (EEG), i.e., the TMS-evoked potentials (TEPs), rely on the integrity of the stimulated cortex and also on its white matter (WM) connections to neighboring and distant areas. Consequently, TEPs should be affected in pathological conditions associated with progressive WM damage, such as Alzheimer's disease (AD). Demonstrating that TEPs can track neurodegeneration would make TEPs both a potential novel biomarker for AD and possibly other neurodegenerative disorders. Previous studies have linked the propagation of TEPs in the cortex to structural networks, highlighting the relation between TEPs and WM tracts in healthy subjects. On these bases, we predicted that the TEPs in the AD group will have significantly lower amplitude and longer latency in the early part of the epoch, i.e., the part of the epoch less affected by TMS-induced sensory artifacts, than the healthy controls. We collected TEPs in healthy elderly individuals (N=28) and patients with Alzheimer's disease at various stages of the disease: mild-cognitive impairment (N=18), early-onset AD (N=13) and late-onset AD (N=25). TEPs were elicited from stimulation of parietal nodes of the default mode network as well as from stimulation of frontal nodes of the executive control network, as both networks are known to be affected by AD. We predict that the TEPs from the AD group will be significantly less intense in the early part of the epoch, i.e., the first 50 milliseconds, the part of the epoch less affected by TMS-induced sensory artifacts, than the healthy controls. In addition, we expect the early TEP components to be significantly slower in the AD group than in the control group.

7. More than meets the eyes: how interhemispheric electrophysiological asymmetries can elicit identical visual perceptions

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The visual system has been considered for a long time comparable across the two hemispheres. However, an increasing amount of data across the years has shown the existence of functional hemispheric differences in these brain areas. With this study we aimed therefore at characterizing the electrophysiological mechanisms responsible for visual perception, paying attention in particular to possible interhemispheric asymmetries in spatiotemporal dynamics.
To do so, 18 participants were administered TMS pulses at phosphene threshold intensity over left and right early visual cortices, while EEG signal was recorded. Participants reported the presence or absence of a phosphene after each TMS pulse. LMFPs revealed an effect of both site of stimulation (left vs. right TMS) and hemisphere (ipsilateral vs. contralateral to TMS): left TMS elicited late stronger activations in contralateral electrodes, while right TMS elicited early stronger activations. Interhemispheric signal propagation (ISP) index showed differences in how TMS-evoked activity diffused across the two hemispheres: left TMS-induced activity spread contralaterally more than right TMS-induced activity. As to phosphenes, different electrophysiological patterns reflected similar visual experiences: while right TMS-evoked phosphenes determined late, fronto-central and parietal activations, left TMS-evoked phosphenes were linked with early occipito-parietal and frontal activations, followed by later, more central ones. Our results show that left and right occipital TMS administration gives rise to different electrophysiological patterns, both per se and considering phosphene perception. These distinctive patterns seem to suggest different roles for the two hemispheres with regards to processing visual information and eliciting perception.

8. Impact of cerebellar non-invasive stimulation on cortical oscillatory activity: Insights from an ongoing TMS—EEG study in healthy human participants

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Oscillations are the hallmark of cerebellar activity and its communication with neocortical areas involved in learning motor skills. Yet, the distribution and the causal nature of cerebellar oscillations remain elusive. The present study aims to better understand the functional mechanisms by which the cerebellum synchronizes with widespread cortical regions. This will pave the way to identify and better modulate specific electrophysiological properties of these networks.
We sought to perturb the cerebellum with neuro-navigated transcranial magnetic stimulation (TMS) and characterize its synchronization patterns with the sensory-motor networks. In a block-design study, 20 healthy adult participants received either single-pulse or 4-pulses bursts of rhythmic (20 Hz) and arrhythmic (random) TMS delivered over the right cerebellum (Crus II), while electroencephalography (EEG, 63 electrodes) was recorded. The stimulation of a central occipital/parietal cortical site (POz) served as a control to assess the specificity of cerebellar stimulation. Noise-masking and sham stimulation were also used to attenuate and control the auditory responses triggered by TMS.
After cleaning and pre-processing, we computed the power and the inter-trial coherence of EEG signals elicited by TMS in frontal, central, and parietal areas. Current interim analyses support the feasibility of cerebellar TMS—EEG recordings, and our ability to perturb cerebellar oscillatory activity and record signs of effective connectivity with distal areas through oscillations, while minimizing unspecific effects (responses triggered by the TMS clicking-sound, scalp-tapping, etc).
The outcome of this study will characterize the neurophysiological properties of cerebello-cortical communication based on synchronization mechanisms, which may ultimately influence learning processes.

9. rTMS demonstrates the different contribution to grasping of two grasp-related areas of the human parietal lobe

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In the human brain, two parietal areas are known to be involved in grasping, the putative homologue of monkey dorsolateral area AIP (phAIP) and the putative homologue of monkey dorsomedial area V6A (hV6A), but their specific role in the encoding of grasping parameters is still under debate. The aim of this work is to investigate how specifically phAIP and hV6A are causally involved in the encoding of grasping variables such as grip aperture and wrist orientation. We stimulated these areas with repetitive transcranial magnetic stimulation (rTMS, 5 biphasic pulses at 20Hz) while participants were performing grasping actions (unperturbed grasping). rTMS over phAIP impaired the wrist orientation process, whereas stimulation over hV6A impaired grip aperture encoding. In a small percentage of trials, an unexpected reprogramming of grip aperture or of wrist orientation was required (perturbed grasping). In these cases, rTMS over hV6A or over phAIP impaired reprogramming of both grip aperture and wrist orientation. These results suggest that grip aperture and wrist orientation are differently encoded by the two grasp-related parietal areas. These results may be useful for establishing rehabilitation protocols in the case of brain damage, as well as in the use of phAIP and hV6A neural signals to specify the appropriate grasping parameters in the generation of accurate movements in brain-computer interfaces.

10. Post tCDS TMS-EEG responses in patients with post-stroke aphasia

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Noninvasive brain stimulation techniques, such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS), combined with speech and language therapy (SLT), might offer valid, additional strategies for post-stroke patients with aphasia (PWA). Literature reviews indicate that tDCS application is well tolerated, safe, and feasible. Language enhancement by tDCS is supposed to be linked to plastic changes at relevant cortical sites. However, direct electrophysiological evidence for this causal relationship in the clinical population is still missing.

We used a combination of TMS and electroencephalography (EEG) to explore the excitability modulation before and after active and sham tDCS in a double-blind, crossover, feasibility experiment. To date, four chronic non-fluent PWA underwent 8 weeks of linguistic exercises coupled with tDCS over the perilesional areas. To evaluate changes induced by tDCS, TMS-EEG responses over BA 6 were computed using different parameters; these data were compared with those recorded from 13 matched control people.

Our results suggest that TMS-evoked EEG responses recorded from the ipsilesional hemisphere are abnormal in PWA as indicated by Global Mean Field Power (GMFP), and Local Mean Field Power (LMFP) analysis. Specifically, we observed significant alterations in TEP amplitude and complexity, a pattern very similar to the one reported on patients with mild to severe motor deficits. Furthermore, this disequilibrium appears to be modulated by anodal tDCS, i.e., the GMFP and LMFP shifted after tDCS when the TEPs were recorded from the left hemisphere. No changes were detected when sham tDCS was delivered, indicating that the modification in cortical excitability recorded after tDCS sessions was due to an interaction between the neurophysiological modulation and cortical activity elicited by the linguistic tasks.

11. Phase-lag specific modulation of auditory perception by tACS

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Synchronization between auditory stimuli and brain rhythms is beneficial for processing auditory information. In principle, auditory perception could be improved by facilitating neural entrainment to sounds via brain stimulation. Here we present 2 experiments where we aimed to modulate auditory perception by perturbing neural entrainment to frequency modulated (FM) sounds using transcranial alternating current stimulation (tACS). In experiment 1, 2-Hz tACS was applied targeting auditory brain regions either with a standard or with an individually optimized electrode montage. Concurrent with tACS, participants listened to FM stimuli with modulation rate matching the tACS frequency but with different phase lags relative to the tACS, and detected silent gaps embedded in the FM sound. Gap detection was sinusoidally modulated by the phase of the 2-Hz FM stimulus into which the gap fell. Importantly, tACS modulated the amplitude of the FM-stimulus induced behavioral modulation – a behavioral signature of the strength of neural entrainment – in a phase-lag specific manner. Inter-individual variability of tACS effects was explained by the strength of the inward electric field depending on the field focality and the proximity of the electric field peak to the target brain region. Moreover, we observed lower inter-individual variability in the individualized-montage group compared to the standard group. In experiment 2, we replicated the tACS-lag specific effects from experiment 1 and showed that such effect is independent from the modulation depth of the auditory stimulus. Our results show that tACS can modulate auditory perception by interacting with stimulus-brain synchrony in the context of rhythmic sensory stimulation.

12. Specific cortical contribution in precision and power grip: a PMv-M1 cc-pas study

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Grasping actions are supported by a parietofrontal network, in which the ventral premotor cortex (PMv) and primary motor cortex (M1) represent critical nodes. Transcranial magnetic stimulation (TMS) is believed to target specific neural populations within M1, which are differently involved in power and precision grip.
In this study, we investigated how functional PMv-M1 connectivity drives the dissociation of these two actions at the neural population level. We applied a PMv-M1 cortico-cortical paired associative stimulation (cc-PAS) protocol, stimulating M1 both in postero-anterior (PA) and antero-posterior (AP) directions, to condition different M1 populations. We evaluated corticospinal excitability (CSE) and inhibition (cortical silent period [cSP]) in both PA and AP during isometric execution of precision and power grip.
After cc-PAS$_{PA}$, we observed a reduction in CSE during both actions; however, there was no modulation of cSP. In contrast, after cc-PAS$_{AP}$, the populations recruited by PA stimulation showed higher excitability during both precision and power grip. We suggest that these deeper populations could be significantly involved in the execution of both actions examined. In contrast, the populations recruited by AP stimulation showed increased excitability only during precision grip. These populations might be more involved in the execution of precision than power grip. Moreover, we observed an increase of cSP, after cc-PASAP, when tested with an AP coil orientation.
This study provides new insights into the specific neural populations involved in different actions. Further studies could elucidate how multiple populations drive hand-shaping in an ecological context.

13. The Effect of Intermittent Theta-Burst Stimulation on BOLD Signal Changes: A Concurrent iTBS/fMRI Study

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Three-minute 600 pulses of intermittent theta-burst stimulation (iTBS) has been recognized as the most promising transcranial magnetic stimulation (TMS) protocol for reducing depressive symptoms. However, the neuronal modulated mechanisms by TMS still need to be understood. With a novel concurrent TMS/fMRI setup and accelerated echo planar imaging (EPI) protocol, it allows mapping effects of iTBS inside the magnetic resonance imaging (MRI). In this study, 18 healthy participants underwent four sessions of scans. In the first session, we performed baseline MRI scans with a 64-channel head coil in a 3T Magnetom Prisma MRI scanner and measured individual resting-motor thresholds (rMT). From the second to the fourth session, we performed scans with the TMS-optimized 14-channel MR receive coils and MR-compatible TMS coil with a standard iTBS protocol. We randomized three conditions for each participant: 80% or 40% rMT intensity over the left dorsolateral prefrontal cortex (DLPFC) and 80% rMT over the left primary motor region (M1). In these sessions, we acquired a structural and three functional scans, resting-state fMRI (rsfMRI) immediately before and after TMS, and interleaved iTBS/fMRI. The results showed that during the 80% rMT stimulation over the left M1, the blood-oxygen-level-dependent (BOLD) signal significantly increased in the right motor region. Left DLPFC stimulation with 80% rMT intensity had significant BOLD activation on the right DLPFC and left inferior frontal gyrus. Another, the result of 40% rMT over the left DLPFC does not show significant BOLD activation on the stimulated hemisphere but the right inferior frontal gyrus. This finding indicated that with high stimulation intensity, both the stimulated and contralateral hemispheres have significant BOLD activation. In contrast, with low stimulation intensity, significant BOLD activation can only be found on the contralateral region.

14. Effects of very low intensity TMS on resting state neurophysiological activity: A TMS-EEG pilot study in the human primary motor cortex

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Low intensity TMS (LI-TMS, 0.1 V/m) has shown the ability to modulate neuronal excitability and promote circuit repair in rodents. However, in humans, Transcranial Magnetic Stimulation (TMS) is conventionally delivered at much higher current densities (65-95 V/m). Here, we aimed to determine the ability of LI-TMS at current densities similar to those proved efficient in rodents. To this end, first, we generated biophysical models of macro-scale (brain volume) and micro-scale (isolated neocortical neurons) cortical current distribution induced by low intensity TMS in the human head. On such basis, we determined the output intensity to induce LI-TMS to human brains with a commercial TMS device (Magstim SuperRapid[2] a 70 mm butterfly-coil) employed for human applications. Finally, a cohort of healthy participants (n=6) underwent a MRI neuronavigated TMS session in which under scalp EEG and EMG monitoring, we assessed the effects of short 4-pulse TMS bursts of either *single pulse*, *rhythmic* (20Hz), *arrhythmic*, or *sham* stimulation delivered to M1- First Dorsal Interosseous (FDI) hotspot at low (LI-TMS) compared to a conventional TMS intensity (60% MSO). Differences in power and interregional synchronization measures elicited at both intensities were estimated and compared across conditions. EEG analyses coupled to evidence from cellular models suggest the ability of LI-TMS to modulate membrane potentials facilitating spontaneous firing and elicit frequency-specific oscillatory activity at natural frequencies. Evidence on LI-TMS modulatory and entrainment effects will allow a more efficient use of this approach for human applications and drive the development of multifocal network stimulation devices able to optimally manipulate cerebral function.

Acknowledgements: ANR AAPG 'BrainMag'

15. Static magnetic fields reduce epileptic activity in a mouse model of dravet syndrome

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It is known that Static Magnetic Fields (SMFs) reduce cortical excitability and improve epileptic signs in a pharmacological model of epilepsy in rats. Here we test the efficacy of SMFs in a mouse model of Dravet Syndrome, a severe epileptic encephalopathy characterized by frequent and long lasting seizures. Experiments were carried out on conditional Scn1a -A1783V mice (n=20) which express the DS/SMEI-associated mutation A1783V in the Nav1.1 channel after Cre-mediated recombination. EEG was recorded continuously from sevoflurane anesthetized mice through two wires chronically implanted. Seizures were triggered by increasing temperature (0.3º/min) from 37º (baseline) to above 42º and maintained by 5 minutes. Protocol was made in the presence of a 0.5T Ni-Neodimium magnet or a sham replica, positioned 30 minutes before increasing temperature. In a subset of animals (n=4), an automatic epileptogenic event detection system detected 194% more incidences in the sham than in the magnet condition. When comparing a group of animals (n=4) in which placebo was applied in every session, versus a second group (n=3) that always received the magnet, the number of sessions with seizures dropped from 93% (26 out of 28 sessions) in the sham, to 37% (8 out of 22) in the magnet group. Furthermore, SMFs reduced by 45% the duration of the remaining seizures. SMFs were able to prevent or reduce the epileptic seizures in a model of DS and could be considered as a therapeutic approach.

Supported by:XUGA_ED431C_2018/24, Instituto_Salud_Carlos_III_PI21/0015, Asociación_Apoyo_Dravet

16. Targeting fronto-parietal connectivity with paired associative stimulation to modulate visuospatial bias

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Pseudoneglect is a visuospatial bias found in healthy individuals that consists of a behavioural advantage for left-hemifield stimuli. Evidence locates its anatomical substrate in a right-hemisphere fronto-parietal network that includes the frontal eye fields (FEF) and the inferior parietal lobule (IPL). However, the underlying neurophysiological mechanisms are yet to be defined.
We tackled this issue with a cortico-cortical paired associative stimulation (ccPAS) protocol targeting fronto-parietal connectivity. ccPAS is a class of transcranial magnetic stimulation (TMS) protocols that can induce spike timing-dependent plasticity-like mechanisms through the repeated, time-locked coupling of two TMS pulses.
In Experiment 1, 26 healthy participants underwent two counterbalanced sessions: a fronto-parietal ccPAS and a parieto-frontal ccPAS. In the fronto-parietal ccPAS, the first pulse targeted FEF and the second pulse targeted IPL. Conversely, in the parieto-frontal ccPAS the first pulse targeted IPL and the second pulse targeted FEF. In both sessions, the interstimulus interval (ISI) was 10 ms. Visuospatial bias was assessed with a landmark task before and after stimulation. We found that fronto-parietal (but not parieto-frontal) ccPAS induced a leftward shift of visuospatial bias – that is, a pseudoneglect increase.
Experiment 2 controlled for the time-dependency of ccPAS effects. 20 participants from Experiment 1 underwent the same fronto-parietal ccPAS, but with a longer ISI of 100 ms. No effects were found.
Our results show that right fronto-parietal ccPAS can modulate visuospatial bias, possibly through the induction of associative-like plasticity in the IPL. These results suggest a key role for intra-hemispheric right fronto-parietal connectivity in the genesis of pseudoneglect.

17. Scale-invariant corticospinal excitability modulation reflects multiplexed oscillations in the motor output

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While being remarkably smooth at first glance, voluntary movements are nevertheless marked by microscopic rhythmic discontinuities, such as submovements (2 Hz) and tremor (8 Hz). To date, it is unclear how the signals transmitted through the corticospinal system contribute to the macroscopic and microscopic architecture of movements. Here, we asked participants to perform a visuomotor tracking task requiring fine isometric finger force production with a sinusoidal pattern. The motor output shows microscopic ~2- and 8-Hz fluctuations, likely reflecting submovements and tremor, engraved in the macroscopic task-instructed 0.25-Hz periodicity. By assessing the electromyographic responses to Transcranial Magnetic Stimulation (TMS) applied over the primary motor cortex (M1) during task performance, we demonstrate that corticospinal excitability is consistently modulated over the three timescales. Surprisingly, this modulation spans a similar range across all scales, despite microscopic oscillations in the motor output being up to two orders of magnitude smaller than macroscopic oscillations. Thus, corticospinal excitability encodes movement at a relatively abstract level, which incorporates the temporal pattern in a scale-invariant manner, likely reflecting the hierarchical organization of sensorimotor processes.

18. Probing the functional relevance of pre-SMA and aIFG for controlled semantic processing with transcranial magnetic stimulation

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Recent inquiries indicate that general cognitive control areas contribute to semantic processing in the human brain. However, a consensus is still lacking about the precise extent of the multiple demand network (MDN) for cognitive control, its boundaries relative to core semantic processing regions, and the nature of its involvement in semantic cognition. Further investigations, beyond meta-analytic evidence, could help advance the current understanding of the functional relevance of domain-general areas for semantic processing.

The project aims at investigating network interactions between MDN areas and semantic regions by focusing on the contribution of the pre-supplementary motor area (pre-SMA), a region of the MDN showing strong functional associations with controlled semantic processing, in conjunction with the left inferior frontal gyrus as core semantic area. The first experiment, currently ongoing, is based on an offline dual-site transcranial magnetic stimulation (TMS) paradigm, testing the effects of left anterior inferior frontal gyrus (IFG) inhibition (1 Hz rTMS), left pre-SMA inhibition (1 Hz rTMS), and combined inhibition of both areas (1 Hz rTMS to IFG followed by cTBS to pre-SMA), on semantic and non-semantic fluency tasks. Stimuli set and TMS condition orders are counterbalanced across subjects. Subjects' performance at each intervention is compared with a sham session as a baseline.

A follow-up study will combine TMS and fMRI to explore the functional relevance of network interactions with effective connectivity analysis. These studies will help to elucidate the functional interaction of semantic-specific and multiple-demand areas in the context of semantic processing.

19. The role of the Somatosensory System in the generation and perception of emotions: a transcranial Alternated Current Stimulation (tACS) study

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Emotional experiences have a deep impact on our bodily states, such as when we feel ‘fear’ our body feels cold and unable to move, and when we feel ‘anger’ we close our fists and feel our face burning. Recent behavioural studies have shown that emotions can be mapped onto specific body portions, suggesting that emotions are represented in the somatosensory system. However, what is the role of the somatosensory system in the processing of emotions and, more specifically, in the generation of feelings of emotions?
To answer this question, we applied transcranial alternated current stimulation (tACS) to the somatosensory cortex of healthy adult participants at different frequencies while they saw emotional pictures taken from the IAPS database. We found that modulation of cortical excitability of S1 influenced subjective emotional ratings, particularly affecting Valence, and making the participants rating more pleasant, instead, we didn’t find a clear effect on Arousal (measured through the skin conductance response). Our results suggest a dissociation between the two dimensions of emotions: Arousal and Valence, with the latest being the only one affected by tACS applied on S1 at different frequencies. This is compatible with previous studies suggesting different neural substrates for Valence and Arousal, in which the Orbitofrontal cortex process valance and the amygdala preferentially process arousal. In general, our findings suggest that the somatosensory system plays a crucial role in the generation of emotions.

20. The effect of statistical learning on proactive motor control is modulated by transcranial random noise stimulation over frontoparietal cortex.

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Proactive motor control refers to endogenous preparatory mechanisms facilitating the selection of a specific motor effector, it is implicitly adjusted based on the global probability of event occurrence and it can be affected by statistical learning. This study aimed to investigate whether frontoparietal transcranial random noise stimulation (tRNS), which is known to interact with attentive functions, may enhance proactive motor inhibition driven by implicit statistical learning. To this aim, 40 healthy participants were asked to indicate a target in couple of stimuli, by a key pressing, using the hand assigned to a preceding cue. The task was performed before and after a training that could be coupled with tRNS over the left-intraparietal sulci and the left dorsolateral prefrontal area. For half of the participants, the training presented statistical imbalances of the target relative position, while in the other half, the training did not present such imbalance. Results showed that response times in the post-test were biased by the training type, and this pattern was enhanced by the left frontoparietal stimulation, compared to no stimulation. Our results suggest that tRNS has a potential in augmenting cognitive capacity in mediating the effect of implicit statistical learning over proactive motor inhibition.

21. A questionnaire to collect unintended effects of Transcranial Magnetic Stimulation: A consensus-based approach

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Transcranial magnetic stimulation (TMS) has been widely used in both clinical and research practice. However, TMS might induce unintended sensations and undesired effects as well as serious adverse effects (AE). AE are rare, whereas sensory sensations are more common, and they often represent a neglected factor during TMS studies that can affect participants' performance. Here, we present a questionnaire, the TMSens_Q, developed through the consensus of a group of international experts, with the aim to create a standardized tool that can be shared among researchers and clinicians to report undesired effects of TMS. The questionnaire will be presented together with some preliminary data about its application. In particular, the TMSens_Q includes 5 sections: 1) participant general information; 2) participant specific information; 3) TMS protocol; 4) TMS related sensations; 5) Serious AE. Data about TMS-related sensations are discussed considering the TMS protocol. This first application of the TMSens_Q showed that, during and after the stimulation, different sensory sensations are experienced by the participants depending on the applied TMS protocols. These sensory effects can affect behavioral performance and compliance with the study. We believe that systematically reporting information about potentially undesired TMS effects will provide a unique opportunity to quantify the incidence of minor sensory effects induced by the stimulation to reduce them in the long term. Matching discomforts and stimulation sensations with relative TMS protocols will help to monitor the safety of TMS, and it will improve the quality of data collection as well as the interpretation of experimental findings.

22. Modulating automatic imitation with a visuo-motor *Paired Associative Stimulation* protocol

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The mirror-*Paired Associative Stimulation* (m-PAS) is a crossmodal version of the PAS protocol that can induce atypical visuo-motor associations (i.e., new ipsilateral motor resonance responses, assessed through cortico-spinal excitability). This induction is achieved thanks to the repeated association of transcranial magnetic stimulation (TMS) pulses over the right primary motor cortex (M1) with visual stimuli depicting movements made with the right-hand – ipsilateral to TMS – index finger. In the present study, we deepen its behavioral correlates by exploiting a modified version of the *automatic imitation* task.

Thirty-three healthy participants underwent the m-PAS, and, before and after its administration, the *automatic imitation* task. Here, participants observed right or left hands moving the index or the little finger (visuomotor trials) or a neutral cue indicating which finger has to be moved (motor trials). In different blocks, participants were instructed to move the same finger of the same hand (congruent blocks) or the same finger of the opposite hand (incongruent blocks) observed on the screen. The imitative compatibility index (ICI, the difference between participant's reaction times in incongruent and congruent blocks*)* is calculated as a marker of *automatic imitation* and exploited as the main dependent variable*.*

Results show that the ICI is affected selectively by the m-PAS when the visual stimulus depicts the same movement conditioned during the protocol. This corroborates the evidence that the visuo-motor matching properties of M1 can be shaped by the m-PAS, suggesting that significant modulation also happened at a behavioral level, specifically for the visual stimuli conditioned during the protocol.

23. Closed-loop transcranial alternating current stimulation for enhancement and suppression of brain oscillations

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24. Is HD-tDCS efficacy on the executive vigilance decrement predicted by neuronal excitation/inhibition?

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Previous evidence shows that anodal high-definition transcranial direct current stimulation (HD-tDCS) over the right posterior parietal cortex (rPPC) can reduce the decrement of executive vigilance (EV). This is the ability to maintain a sustained state of readiness to react to unpredictable environmental changes. Cognitive load and neural oscillatory power appear to moderate tDCS efficacy on the EV decrement. Our previous results concerning the effects of stimulation on neural oscillations have, until now, been constrained to periodic activity (e.g., alpha and gamma power), without considering the contribution of aperiodic activity. The aperiodic exponent relates to neural states of excitation and inhibition and might underly domain-general processes such as attention. The exponent can be used to further explore the electrophysiological effects of tDCS and to predict stimulation efficacy. The present study used EEG data acquired from 180 participants during pre- and post-tDCS. Either anodal or sham HD-tDCS was applied over the rPPC in combination with an attentional task while modulating the cognitive load. We build upon previous research linking inter-individual variation in aperiodic activity to cognition, exploring how the aperiodic exponent relates to cognitive load and stimulation efficacy. Our findings may serve as a guide for future research in developing more specialised neuromodulation interventions to mitigate the inevitable decrement of vigilance over time.

25. Optimized dosing and targeting for transcranial magnetic stimulation during conceptual processing

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Conceptual knowledge is central to human cognition. Previous neuroimaging studies suggest that conceptual processing relies on the joint contribution of modality-specific perceptual-motor and multimodal brain regions. In particular, multimodal inferior parietal cortex (IPL) coupled with somatomotor cortex during action knowledge retrieval and with auditory cortex during sound knowledge retrieval. However, as neuroimaging is correlational, it remains unknown whether the interaction between modality-specific and multimodal cortices is causally relevant for conceptually-guided behavior. To tackle this issue, we applied inhibitory transcranial magnetic stimulation (TMS) over modality-specific cortex (somatomotor, auditory, or sham), before 24 healthy participants received TMS over multimodal cortex (IPL, or sham) during action and sound judgment tasks. To optimize the coil position and intensity for each stimulation target, we performed computational simulations of the TMS-induced electrical field (e-field). Specifically, we determined the coil position that maximizes the e-field strength in each target, and identified the stimulator intensity that elicits the same e-field in each target as in the primary motor cortex (M1) at resting motor threshold (RMT). While behavioral measurements are ongoing, simulation results show that e-field based dosing better matches the effective cortical stimulation than previous dosing approaches, both within and across participants. These results indicate that e-field based dosing may increase the stimulation efficacy and reduce both the within- and between-subject variability of TMS effects. Therefore, *a priori* e-field simulations have the potential to substantially improve TMS studies of higher cognition.

26. The role of frontal eye field in age-related differences to visual distractors during driving: a neuromodulation study

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The ability to suppress distractors during driving changes during lifespan. The aim of the present study was to investigate the effects of different tDCS montages on the inhibition of visual distracting stimuli on responses to critical events in young and older drivers. A driving simulator task was developed in which participants had to detect brake light events while they responded to one of two distractors (names of countries and cities that appear as road signs). Each participant completed three sessions comparing the effects of different tDCS montages, i.e. conventional, high-definition (HD-tDCS) and sham stimulations over a key cerebral area for distractors suppression, the frontal eye field (FEF). Results indicated an overall better performance under the HD-tDCS condition. In particular, young participants improved their performance both in breaking light RTs and in the second distracting task. Preliminary results on older participants seem to confirm and extend results on younger ones, indicating also an increased lane-keeping performance under HD-tDCS stimulation. Taken together these results are interesting from a theoretical and methodological point of view, by demonstrating a direct effect of FEF HD-tDCS in attentional response during an ecological driving task.

27. Amplitude modulating frequency overrides carrier frequency in tACS-induced phosphene percept

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The amplitude modulated (AM) neural oscillation is an essential feature of neural dynamics to coordinate distant brain areas. The AM transcranial alternating current stimulation (tACS) has recently been adopted to examine various cognitive functions, but its neural mechanism remains unclear. The current study utilized the phosphene phenomenon to investigate whether, in an AM-tACS, the AM frequency could modulate or even override the carrier frequency in phosphene percept. We measured the phosphene threshold and the perceived flash rate/pattern from 12 human subjects (four females, aged from 20–44 years old) under tACS that paired carrier waves (10, 14, 18, 22 Hz) with different envelope conditions (0, 2, 4 Hz) over the mid-occipital and left facial areas. We also examined the phosphene source by adopting ahigh-density stimulation montage. Our results revealed that (1) phosphene threshold was higher for AM-tACS than sinusoidal tACS and demonstrated different carrier frequency functions in two stimulation montages. (2) AM-tACS slowed down the phosphene flashing and abolished the relation between the carrier frequency and flash percept in sinusoidal tACS. This effect was independent of the intensity change of the stimulation. (3) Left facial stimulation elicited phosphene in the upper-left visual field, while occipital stimulation elicited equally distributed phosphene. (4) The near-eye electrodermal activity (EDA) measured under the threshold-level occipital tACS was greater than the lowest power sufficient to elicit retinal phosphene. Our results show that AM frequency may override the carrier frequency and determine the perceived flashing frequency of AM-tACS-induced phosphene.

28. The effect of bilateral frontal tDCS on electrophysiological correlates of attentional orienting to rewards.

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Substance-related and behavioural addictions have been associated with enhanced attentional bias to reward-associated stimuli. In the current study, we explored the effect of Transcranial Direct Current Stimulation (tDCS) on reducing electrophysiological reflections of attentional orienting towards intrinsic reward-associated stimuli. Sixty-five participants (19 men, 46 women) between 18 – 58 years old (M=24, SD = 6) were assigned to either tDCS or sham-tDCS intervention. The tDCs intervention consisted of 20 minutes of right frontal F4 anodal 2 mA stimulation, with the cathode at site F3 (left frontal). Before and after (sham-)intervention, participants performed a Visual Spatial Cueing (VSC) task, while EEG was recorded. In the VSC task, a cue indicates the most likely location (left or right) of the subsequent target to which a response is required. Our VSC adaptation included a neutral and food (intrinsic reward) context. The latter context was operationalized with target pictures depicting palatable food. Our results confirmed the validity of the paradigm in inducing attentional bias as indicated by faster responses to validly cued targets relative to invalidly cued targets. This effect was mirrored by an observed cue-associated Late Directing Attention Positivity Event Related Potential (LDAP ERP). In contrast to our hypothesis, attentional orienting (indexed by the LDAP) increased following tDCS relative to sham tDCS in the reward condition. Our results suggest that tDCS affects visuospatial attention via a mechanism other than shifting lateralization of frontal brain activity. One such alternative mechanism may involve tDCS associated enhancement of noradrenergic neurotransmission.

29. The effect of TMS current direction and pulse waveform on motor evoked potentials

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Transcranial magnetic stimulation (TMS) over the primary motor cortex (M1) elicits motor-evoked potentials (MEPs), a marker of cortico-spinal tract functioning. It is known that TMS pulse waveform and current direction influence MEPs, but the patterns of modulation are still controversial due to limited systematic investigation in within-subject design studies and small sample size in current literature.

In this study, we investigated the effect of three current directions – posterior-anterior (PA), anterior posterior (AP) and latero-medial (LM) – and two pulse waveforms – monophasic and biphasic – on resting motor threshold (rMT), MEPs latency and MEPs amplitude. Effects on rMT were tested as a positive control of experimental manipulation given that previous studies have consistently reported higher rMT for AP than for PA and for LM current directions, for monophasic waveform. 37 right-handed healthy participants underwent a session of TMS consisting in six blocks ($PA_{monophasic}$, $PA_{biphasic}$, $AP_{monophasic}$, $AP_{biphasic}$, $LM_{monophasic}$, $LM_{biphasic}$) where TMS was delivered over left M1 at rest while MEPs were recorded from the right-hand *abductor pollicis brevis* muscle.

Our positive control confirmed the effectiveness of TMS manipulation. Specifically, rMT in monophasic stimulation was higher for AP than for PA and LM directions. MEPs latency was affected by current direction: AP direction led to longer latency than PA and LM, both for monophasic and biphasic waveforms. No effects were found on MEPs amplitude in the different conditions. Our findings replicate and extend previous literature on how these TMS parameters affect MEPs. This can help shedding light on TMS functioning and on its sources of variability.

30. Susceptibility to neuromodulation in the healthy brain: the role of white matter variability

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Transcranial Magnetic Stimulation (TMS)-induced neuromodulation is related to structural properties of white matter tracts. In patients with brain lesions, white matter properties have been linked with the recovery potential of TMS treatments. In healthy individuals, white matter microstructural variability also correlates with TMS effects. Tracts connecting the TMS-targeted region and other key regions are fundamental to explain TMS effects. Recently, some studies from our group have shown an association between TMS effects and indirect white matter tracts (not innervating the targeted region), probably due to compensatory processes supported by different anatomical networks. For example, phasic alerting produced a reliable behavioral boosting of conscious access, which was modulated by the stimulation of the supplementary motor area. This TMS effect correlated with the integrity of the right ventral branch of the Superior Longitudinal Fasciculus (SLF). Nevertheless, these (and similar) results have been observed with limited samples (~20 participants). Currently, we are developing two projects in which we aim to replicate these findings with larger samples (~50 participants). We are using a paradigm in which different attentional networks are manipulated (i.e., phasic alerting, and exogenous and endogenous orienting) while measuring its effects on the conscious perception of near-threshold targets. We hypothesize that TMS effects will correlate with the indexes of microstructural white matter properties of relevant tracts, such as the SLF and the Inferior Fronto-Occipital Fasciculus. Other data-driven approaches are envisioned (such as Tract-Based Spatial Statistics) to explore the role of other tracts in the correlation between white matter integrity and TMS effects.

31. Is attentional capture by a color singleton modulated by previous stimulus-response association?

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On the one hand, a color singleton captures attention in a visual search task, increasing reaction time. On the second hand, a color that was previously responded to in a Go/NoGo task captures attention and decrease reaction time when it is the target in a visual search task. Action upon a feature seems to modulate its salience in a visual search paradigm. We aimed at going further into this link between attentional control and motor control by exploring the specificity and automaticity of stimulus-response association.
In a first part, participants learnt the association between motor response and visual stimulus (specific action-color association). In the second part, the previously selected colors served as distractors in a visual search display in which participants had to indicate the orientation of a line contained in the target, defined by its shape. We recorded behavioral performance as well as eye movements and muscular activity of effectors involved in the second part of the task.
We replicated increased reaction times and decreased accuracy in presence of visual singletons in a search display. However, we did not found any interference between the stimulus-response association and the effector involved in the response during the second phase, at least on behavioral measures.
Benefits from including TMS techniques in this experiment will be twofold: with single-pulse TMS, we could evaluate the level of automatic activation of the response associated with the stimulus; and with repetitive TMS, we could modulate the effects of salient singleton in a visual search display.

32. Is the ACC crying for help? Characterizing the neural network of performance monitoring by implementing simultaneous TMS-EEG

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A fundamental mechanism of cognitive control is to adapt behaviour after committed errors to prevent future errors. These adaptative processes (e.g., measured as post-error slowing, PES) are triggered by the performance monitoring system, represented by the *error-related negativity* (ERN) in the event-related potential. The ERN, originating in the anterior cingulate cortex (ACC), reflects automatic error processing, while the required behavioural adaptation is assumed to be implemented by the dorsolateral prefrontal cortex (DLPFC). Yet, it is unknown whether the functioning of the ACC is independent of subsequent processes associated with the DLPFC.

Here, we probe the functional relationship between the ACC and DLPFC by (i) disrupting activity within the (right) DLPFC through triple-pulse TMS shortly after errors, and (ii) observing changes in ERN peak amplitude after DLPFC stimulation compared to a control stimulation condition (primary motor cortex). To this end, we applied simultaneous TMS-EEG, while participants engaged in a demanding cognitive control task (i.e., the speeded-inference game).

Data from the first participants of the ongoing study (n = 21) show that interfering with DLPFC activity reduces PES, while other behavioural measures such as response accuracy or response time are unaffected. In addition, we observe a higher ERN peak amplitude after DLPFC stimulation in comparison to the control stimulation. This suggests that disrupting the functioning of the DLPFC immediately after errors reduces adaptive processes, which is accompanied by an intensified error signalling. These preliminary results indicate that the ACC and DLPFC might build the interdependent core of the performance monitoring system.

33. Does the Vertex Potential reflect the activation of the extralemniscal system?

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Sudden sensory changes elicit a transient, large and widespread biphasic negative-positive deflection in the ongoing electroencephalogram: the Vertex Potential (VP). The VP has been traditionally interpreted as a results of modality-specific sensory processing. Given the several properties shared by both the VP and the extralemniscal system (e.g. their supramodality, tendency to habituate, and sensitivity to pharmacological compounds), we propose that the VP reflects the cortical consequence of extralemniscal processing. Also, the extralemniscal system has widely diffused thalamic and cortical targets, produces global arousal, and modulates other brain systems and processes. Therefore, if the VP truly reflects extralemniscal activation, it should similarly influence ongoing sensory and motor processing. In a first experiment we explored how VP modulates early somatosensory processing, probed by recording somatosensory evoked potentials (SEPs) in healthy human participants. The amplitude of the P45 SEP component was modulated as function of the VP phase: P45 was reduced during the negative and enhanced during the positive VP wave. Crucially, these effects were enhanced when single-trial SEPs were binned accounting for the trial-by-trial latency jitter of the VP. In a second experiment, also in healthy volunteers, we explored the VP modulation of corticospinal output, by simultaneously recording VP and TMS-induced motor-evoked potentials (MEPs). MEP amplitude was clearly modulated by the VP phase, but in opposite direction compared to SEPs: an initial MEP increase was followed by a decrease. Overall, these results provide strong evidence that the VP exerts phase-dependent modulation of both early sensory and motor processing.

34. Probing cerebellar involvement in cognition through neuromodulation: A meta-analysis on the effectiveness of non-invasive cerebellar stimulation

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The cerebellum is increasingly attracting neuroscientists interested in neuromodulation. Recently, cerebellar activity has been targeted by non-invasive brain stimulation (NIBS) techniques including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) to investigate the involvement of the cerebellum in a wide range of cognitive functions. Though promising, the strength of the conclusions drawn from single studies may be constrained by several aspects such as the kind of NIBS and stimulation parameters. The present study aims to assess the effectiveness of non-invasive cerebellar stimulation in altering cognitive-related behavioral performance in healthy participants.

A PRISMA search was conducted and 58 studies matched our eligibility criteria (25 TMS, 33 tDCS studies). Hedges' g was used to quantify effect sizes for changes in cognitive performance after real vs. sham/control stimulation. Type of NIBS (low- and high-frequency TMS, anodal and cathodal tDCS), stimulation site (right, left, and medial cerebellum), and stimulation protocol (performance measured during or after stimulation) were included as moderators in an extension of linear model for meta-analysis.

Results showed that NIBS effects were moderated by the kind of stimulation, revealing an effect of low- and high-frequency TMS in reducing cognitive performance. No evidence of modulation was found for tDCS. Analysis on the stimulation site showed an effect of NIBS only when the right cerebellum was targeted.

These findings indicate that NIBS administered over the cerebellum modulates cognitive performance and suggest that the kind of stimulation and targeted site play a key role in determining the effectiveness of non-invasive cerebellar stimulation.

35. Probing the cortical network underlying semantic interference and phonological facilitation in picture naming: a TMS-EEG study.

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In picture-word interference (PWI) paradigms, semantic interference (SI) and phonological facilitation (PF) respectively increase or decrease naming latencies depending on the nature of the relationship between targets and distractors (Schriefers et al., 1990). The behavioral consequences of these effects are well-known, but their timing and the involved brain structures are still controversial (Nozari and Pinet, 2020), as the involvement of a left fronto-temporo-parietal network is unclear (de Zubicaray and Piai, 2019). We used TMS-EEG co-registration to investigate brain spatial-temporal activations related to PF and SI. Sixteen healthy participants were asked to perform PWI in which they had to name target pictures simultaneously presented with either semantically-related, phonologically-related or unrelated written distractors. Single pulse TMS was delivered over the left inferior parietal lobule (lIPL) or left mid-temporal gyrus (lMTG) at two onsets (i.e., 250ms and 400ms after picture presentation) to track lexical selection and word-form retrieval time-course, while TMS Evoked Potentials (TEPs) were recorded from 60 scalp electrodes. PF was abolished while SI increased when targeting the lIPL at 250ms. Accordingly, cortical excitability increased over centro-parietal electrodes around 50ms post-TMS in PF and SI trials. No modulation was observed for neutral trials nor when TMS was applied at 400ms post target. MTG stimulation did not specifically modulate the different experimental conditions. Parietal TMS effects occur in a time window critical for lateral inhibition mechanisms in selection by competition processes, suggesting a neural substrate shared by lemma and phonological levels and thus influencing both PF and SI.

36. Non Invasive oscillatory neuromodulation of cortical vestibular functions: method and future implications

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Vestibular cortex is a multisensory associative region. Low-frequency Galvanic Stimulation (1 or 2 Hz), corresponding to the physiological oscillatory processing of the vestibular core regions and organ receptors, is responsible of transient symptoms of kinetosis, oscillopsia and postural instability. In a randomized, double-blind, controlled trial, we show how, using tACS, it's possible to evoke transcranial oscillatory potentials, biophysically modelled to reach the putative vestibular cortex, able to tune this "sixth sense" in a frequency-specific manner, producing transient and controllable behavioral effects in healthy subjects.

We asked to thirty (30) healthy subjects to stand in the center of a stabilometric platform, while wearing the cap for tACS delivery, for five consecutive recording sessions, including baseline, 1 Hz, 2 Hz, 10 Hz stimulation and Sham. The 1 Hz and 2 Hz stimulations represented the experimental conditions, while the 10 Hz and Sham stimulations represented the control conditions. During the recovery phase, subjects answered the Simulator Sickness Questionnaire (SSQ), regarding the symptoms of motion sickness.

Significant effects are shown in both the experimental conditions (1Hz, 2Hz stimulation) compared with the Sham condition. A significant difference emerges also between both experimental conditions and the 10 Hz stimulation condition.
Results demonstrate how the human vestibular cortex can be immediately perturbated by transcranial oscillatory potentials in a frequency-specific and controllable manner. Conversely, in this patient, the 10 Hz stimulation significantly reduced his chronic vestibular symptoms, opening the possibility for a new interventional neuromodulatory strategy for vestibular diseases such as motion or cybersickness.

37. Inhibiting anterior insula changes interoceptive accuracy: a combined TMS-fMRI study

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The insular cortex (IC) is involved in sensing and interpreting visceral signals, an ability called interoception, the lack of which is considered a transdiagnostic risk factor for psychopathology. It is still unknown whether it is possible to modulate insular activity to change interoception using noninvasive brain stimulation techniques. Transcranial magnetic stimulation, including theta-burst stimulation (TBS), has proven to be an effective method to non-invasively modulate cortical regions' activity, producing facilitatory (iTBS) or inhibitory (cTBS) effects. By combining TBS with fMRI, we hypothesized that iTBS and cTBS would affect IC activity and, consequently, interoception. Thirty-six participants (18 F; M_{age}: 23.78 ± 3.56 years) volunteered for this study. cTBS and iTBS, over the right anterior insula, and sham stimulation over vertex were administered in a counterbalanced order across participants. After each stimulation, participants performed the heartbeat counting task and were scanned while performing an explicit emotional judgment task. During this task, they saw disgusting (or, as control, neutral) images that have proven to consistently activate the insula. We found preliminary evidence indicating that cTBS is able to change bilateral anterior IC activation. Specifically, cTBS reduced the bilateral activation of the IC during disgusting blocks and reduced participants' ability to accurately detect their heartbeats compared to sham. Given the growing use of TMS protocols in psychiatry, current results could be used to inform the conduction of clinical trials aimed at actively changing the IC activity, for example, in patients showing alterations in interoception (e.g., anxiety disorders) or increased disgust sensitivity (e.g., obsessive-compulsive disorders).

38. Effects on implicit motor learning after gamma tACS on bilateral primary motor cortex

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Oscillatory neural activity in gamma frequency band plays a crucial role in motor control and learning. Transcranial alternating current stimulation (tACS) may modulate endogenous oscillations related to movement, possibly causing behavioral changes. tACS effects are commonly studied during the execution of motor tasks, but they have been shown also to outlast the end of the stimulation.

Our study investigated the effects of the induction of gamma (40 Hz) oscillations in healthy adults on implicit motor learning. Thirty participants performed a computerized serial reaction time task (SRTT) before and after a 20-minutes session of tACS. The stimulation was delivered at 2mA through two electrodes positioned over left and right primary motor cortex. Sham was used as control on the same sites. The SRTT required the execution of repetitive movements in response to sequential visual stimuli. It was composed of 8 blocks. In blocks 1 and 6 visual stimuli were randomly distributed over the sequence.

Results revealed a significant main effect of time session: reaction times (RTs) were faster in the post-tACS phase with respect to the pre-tACS phase, showing an implicit motor learning effect. The sequential blocks showed faster RTs compared to the first random block. Moreover, the inference generated by block 6 slowed down RTs in the late sequential learning blocks. However, no significant difference emerged from the contrast between real and sham tACS.

Our results did not support evidence of an aftereffect on implicit motor learning induced by gamma tACS when stimulating bilateral primary motor cortex.

39. The Interhemispheric Equilibrium - a Biomarker of Attentional Performance

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Unilateral stroke can disrupt the equilibrium between hemispheres, which is necessary for efficient attentional deployment. Given the variability characterizing stroke patients' cognitive profiles and the classical neuropsychological tools' lack of sensitivity, we used a combination of behavioral and imaging techniques to identify biomarkers of interhemispheric equilibrium that predict attentional performance. Since the posterior parietal cortex (PPC) is a crucial node of the dorsal attention network and the PPC-to-PPC communicationsupports the interhemispheric equilibrium, we investigated whether the PPC-to-PPC communication predicts attentional performance. Given that the PPC is also a generator of alpha oscillations and alpha power correlated with attentional deployment, we tested whether interhemispheric asymmetries in alpha predict attentional performance.

The within-subjects experiment consisted of two sessions. In the first session, healthy participants underwent resting-state fMRI that allowed us to identify individualized TMS targets. In the second session, participants underwent both Rest- and TMS-EEG recordings, 100 TMS pulses at 65% of the maximum stimulator output over the right and 100 over the left PPC individualized target. EEG recordings were preceded by a set of behavioral tasks quantifying different components of attention such as visuospatial attention, attentional orienting and reorienting, and temporal selective attention.

Preliminary results showed that the interhemispheric signal propagation (IPS) from right to left PPC predicted participants' performance in task quantifying spatial and temporal attention, while both the PPC and FEF alpha asymmetry index predicted participants' search efficiency.

This is the first fMRI-guided TMS-EEG study to investigate ISP and alpha asymmetry index as possible biomarkers for attentional performance.

40. Adaptive plasticity in the reading network investigated through combined neurostimulation and neuroimaging

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The classical reading network in the human brain comprises (a) the left inferior frontal gyrus (IFG), (b) the ventral occipito-temporal cortex (vOTC) and (c) the temporo-parietal cortex (TPC). The left TPC is crucial for sound-letter mapping and significantly underactive in dyslexia. To confirm the causal role of this region in typical readers and test the potential to alleviate reading difficulties by facilitating this region in dyslexia, we combined repetitive transcranial magnetic stimulation (rTMS) with functional neuroimaging (fMRI). 28 neurotypical readers received inhibitory rTMS and 26 adults with dyslexia received facilitatory rTMS to the left TPC before they overtly read simple and complex words and pseudowords during fMRI. In the dyslexia group, rTMS altered speech onsets, reading times and accuracy, and led to higher activation of the right precuneus during word, and the right insula during pseudoword reading. In neurotypical readers, we found a marginal effect of TMS on speech onsets for complex words and changes in activation patterns in the left IFG for both types of stimuli. In terms of effective connectivity within the classical reading network, neurotypical readers show an increase in connectivity from the left vOTC to the left TPC during active TMS, which can be interpreted as compensation. In the dyslexia group, we find a marginal effect of facilitation of the left TPC leading to decreased functional coupling from the left vOTC to the left TPC. Overall, we suggest that TMS improves reading performance in dyslexia and results in functional short-term reorganization within the reading network.

41. Join the action: top-down and bottom-up information modulate different neurophysiological indexes

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In Joint Action (JA), prior top-down knowledge is integrated with bottom-up evidences to optimize coordination. We designed a transcranial magnetic stimulation (TMS) protocol to investigate the neurophysiological fingerprints of these two processes.
We used a cooperation task in which a confederate has to open either one of two bottles: one held by a mechanical clamp (no_JA) and the other by the subject (JA). In half of the trials, the subject was not being informed from the beginning about the target bottle of the action (K vs. no_K). Yet, after movement onset, they can extract information from confederate's kinematics.
Single-pulse TMS was delivered over the left primary motor cortex to collect motor evoked potentials (MEP) and cortical silent periods (cSP) from the opponens pollicis (OP). The TMS pulse was delivered in four timings: rest, onset of confederate's movement, pre-shaping, grasping.
Subject's CSE is modulated if prior information about confederate's choice is available. Differently, cSP is modulated regardless prior information only when kinematic features are accessible.
Our results are imputable to the concurrent activation of two complementary inferential processes during JA. The first one might encode contextual abstract information and is reflected in CSE modulations. The other might encode partner's kinematic features and is reflected in a modification of cSPs. These findings suggest that CSE and cSP might constitute the neurophysiological fingerprint of the two complementary processes naturally at play during JA coordination.

42. Working memory training combined with transcranial direct current stimulation in healthy older adults

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Working memory is a key function to maintain and, at the same time, manipulate information, and is fundamental to everyday activities. Working memory is, however, subject to decay with age. Recent studies have pointed out that modulating cortical plasticity could induce a lasting improvement of cognitive functions. Interventions to manipulate plasticity include, amongst others, transcranial direct current stimulation (tDCS), cognitive training, or a combination of both, but their effectiveness in the elderly is still under debate. Our study aims to investigate the effectiveness of working memory training (WMT) combined with tDCS in healthy older adults. To this purpose, we conducted a double-blind randomized sham-controlled experiment in which thirty-four older adults were randomized into two groups: active tDCS + WMT and sham tDCS + WMT. Anode electrode was placed to the right dorsolateral prefrontal cortex (DLPFC). Participants performed an adaptive spatial working memory (nBack) task during 5 consecutive days for 20 minutes, while receiving either ACTIVE or SHAM tDCS. Performance was quantified during training as the average 'n' level reached during a session. Repeated measured ANOVA (STIMULATION x DAYS) showed that all individuals improved their performance during training, but the improvement was larger in the ACTIVE than in the SHAM group. Our study further supports the beneficial effects of combining working memory training with tDCS of the DLPFC in healthy older adults. Future work will investigate the neural correlate of these stimulation-related improvements and their maintenance over time.

43. Short-term network reorganization in cognition after inferior parietal lobe perturbation.

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The inferior parietal lobe (IPL) is an important hub of neural network function across multiple cognitive states, contributing to "task-negative" networks (default mode network; DMN) and "task-active" networks. To investigate flexible network behavior in cognition, we combined spaced double continuous theta burst stimulation (cTBS) with functional magnetic resonance imaging (fMRI) in both task and rest states. Thirty healthy, young volunteers participated in three measurements in which posterior IPL was inhibited using either right, left, or sham cTBS, prior to a three-task fMRI experiment encompassing the key cognitive domains attention, semantics, and social cognition. Additionally, all participants completed three pre-post stimulation resting-state fMRI sessions.
We identified 11 large-scale connectivity networks of interest that organized during the tasks and assessed stimulation-induced changes of interactions between network pairs within each domain. Compared to sham, cTBS decreased several network interactions during social cognition, primarily from the posterior subnetwork of the DMN that includes posterior cingulate cortex (pDMN-PCC) to task-positive networks. Stimulation increased interactions between default mode subnetworks and control networks during semantics. Only right-hemisphere stimulation influenced network connectivity during attention, with a mix of inhibition and facilitation. Collectively, our results demonstrate that beyond inducing local changes, cTBS influences large-scale network interactions in a domain-specific manner. The observed patterns suggest that the most complex cognitive task shows relatively high responsiveness to stimulation, with more distributed changes across networks, while overall effects exhibit distinct alterations between task-active and task-negative networks.

44. Bilateral parietal tACS within the beta band improves spatial vision in crowded scenes

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Visual crowding refers to the difficulty of identifying an object when surrounded by closely arranged flankers. In contrast to the extensive characterization of the spatial properties of crowding, less is known about its neurophysiological underpinnings. Recently, beta-band activity (15-30 Hz) has been shown to be related to the processing of information in crowded scenarios. In the present study, by using bi-focal high-definition tACS we aimed at reducing the effect of visual crowding during letter orientation discrimination as well as to investigate the tACS-induced modulation on the beta-band oscillatory dynamics. Participants (N=22) were asked to report the orientation of a peripheral target letter positioned nearby two flankers in a vertical array, while the target-flankers distance was manipulated. In three experimental sessions, taking place in separate days, we administered beta-band tACS with a right fronto-parietal montage, a bilateral parietal montage, as well as a sham protocol. EEG was recorded before, during, and after the task. At a behavioral level, participants reported higher accuracy and lower thresholds for letter identification when the stimulation was applied with a bilateral parietal protocol with respect to sham. Electrophysiological results showed a significant reduction in beta power over parietal sites after the bilateral parietal tACS and sham condition. In order to better disambiguate these results, we parameterized the periodic (oscillatory) and the aperiodic (1/f) components of the EEG spectrum separately. In terms of pure oscillations, a significant beta-band power reduction was found only after bilateral parietal tACS. In terms of aperiodic activity, we noticed a wide-band (1-18 Hz) power reduction after sham as compared to the active stimulation protocols, which may have caused the overall reduction in power found this experimental condition. These results suggest that neural oscillations in the beta band represent a fundamental rhythm of communication between the dorsal and the ventral visual pathways. They could provide important clinical insights in the development of tACS-based neuro-rehabilitation trainings for patients that exhibit stronger visual crowding, such as those with dyslexia, macular degeneration, or amblyopia.

45. A preregistered TMS-EEG study to investigate effective connectivity in borderline personality disorder

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People with borderline personality disorder (BPD) show alterations in empathic abilities, which may involve automatic simulation processes relying on mirror-like mechanisms in the somatosensory domain. In the tactile mirror system (TaMS), the observation of a touch on someone else's body activates the same cortical network involved in tactile perception, including the primary somatosensory cortex (S1). While TaMS alterations have been suggested in BPD, its neural dynamics in terms of effective connectivity is underexplored.

Here, we aim at comparing BPD and healthy controls in the empathic abilities, measured by self-report questionnaires, and in TaMS effective connectivity, obtained by concurrent transcranial magnetic stimulation and electroencephalographic recording (TMS-EEG). TMS evoked potentials (TEPs) are recorded from 74 EEG-channels after right S1 stimulation during the presentation of touch stimuli. Touch stimuli consist of real tactile stimuli on participants' hand and of visual touches, either on a hand or on an object. TMS is delivered with different time intervals after the onset of touch stimuli (20 ms or 150 ms). To improve methodological rigor and transparency, hypotheses, methods and planned analyses have been preregistered on Open Science Framework before data collection (in progress).

As expected based on the existing literature, preliminary results show lower cognitive empathy in BPD (n=13) compared to controls (n=14). Moreover, the observed TEP components at 50 and 100 ms are consistent with previous findings on healthy subjects after S1 stimulation.

Findings from the present study will shed light on a putative neurophysiological candidate for BPD empathic dysfunctions, namely TaMS connectivity pattern.