high accuracy (72–95%) and discriminability (81–99%) in predicting regions exhibiting changes using individual subjects' pre-stimulation connectivity profile. We next investigated the brain dynamics *during stimulation* to determine how brain plasticity is induced. In each patient, we observed a four-phase response to repetitive stimulation, consisting of acute neural changes during and directly after each stimulation train as well as a buildup of effects across stimulation trains. The neural response to just one minute of stimulation reliably predicted long-term brain changes. Together this work sheds light on the mechanism underlying plasticity induction in humans. Furthermore, utilization of pre-stimulation network attributes and intra-stimulation cortical dynamics can be utilized to optimize brain stimulation technologies.
Keywords: ECoG, rTMS, plasticity

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A PILOT STUDY OF TRANSCRANIAL MAGNETIC STIMULATION OF THE MEDIAL PREFRONTAL AND CINGULATE CORTICES AND COCAINE SELF-ADMINISTRATION

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Previous studies have shown that repetitive transcranial magnetic stimulation (rTMS) may serve as a potential treatment for cocaine use disorder (CUD). This pilot study investigated the effect of rTMS on cocaine self-administration in the laboratory setting. For the self-administration sessions, CUD participants chose between smoked cocaine and an alternative reinforcer (money) in order to measure cocaine-seeking behavior. The rTMS was delivered with the H7 coil (provided by Brainsway), which directs stimulation to the medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC).
Volunteers with CUD were admitted to an inpatient research unit for the entire study. Subjects were assigned to one of three groups: high frequency (10 Hz), low frequency (1 Hz), and sham. Six participants were included in each group and the rTMS was delivered on weekdays for a total of 13 sessions. The cocaine self-administration sessions were performed at three points in time: at baseline (before rTMS, session 1), after 4 days of rTMS (session 2), and after 13 days of rTMS (session 3). During each self-administration session,the outcome measure was the number of choices for cocaine.
Our results showed a significant group by time effect ($p = .02$), where the choices for cocaine decreased between sessions 2 and 3 in the high frequency group only. There was no effect of rTMS on cocaine self-administration the sham or low frequency groups. In the context of the existing literature, these results contribute to the data indicating that high frequency rTMS may serve as a potential treatment for CUD.
Keywords: addiction, prefrontal cortex, stimulation, cocaine

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LEPIDIUM MEYENII (MACA) AND THE CEREBRAL STIMULATION FOR MOBILE PHONES: SOME ANSWERS IN AN ANIMAL MODEL

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Aim: To investigate the effect of *Lepidium meyenii* (maca) ecotype red, Peruvian Andean plant, on ovariectomised rats (Ov) exposed to radiation of second generation mobile phones in answering state.
Methods: Thirty-six female *Rattus rattus* var. albinus weighting 200- 250 g at the age 3 months, were randomly divided into six groups (n=6): Not ovariectomy (NOv), Ovariectomy - Not treatment (Ovnt), Ovariectomy-estrogen (Ove), Ovariectomy-estrogen-Radiation (OveR), Ovariectomy-Maca (OvM), Ovariectomy-Maca-Radiation (OvMR). After 80 days of ovariectomy and for 60 days, were administrated estradiol valerato orally 200 μg/kg body weight/day, to (Ove) and (OveR) groups and Maca orally 2 g/kg body weight/day to (OvM) and (OvMR) groups. Then, (OveR) and (OvMR) were exposed to calls /30 min/7 days, with GSM (850MHz) cell phone radiation. The rectal temperature measurement was taken before and after the exposure. Were tested the spatial memory in all the groups by Morris Water Maze (MWM) before ovariectomy and before the euthanasia. Was quantified Malondialdehyde chromogen parts (MDA), and cervical sample spinal cord tissue was harvested and fixed for histopathological microscopic examination.
Results: (OvMR) group presented better time spent that the group (OveR) with statistical significance ($p< 0.05$), minor stress oxidative expressed in MDA minor levels that (OveR) with significantly increased ($p< 0.05$), rectal temperature measurement was increased in both groups post exposition, but in (OvMR) was minor that (OveR) with ($p< 0.05$). Although both groups presented a spinal cord with histopathological damage with injury.
Conclusion: Maca would protect the memory, would diminish MAD levels, maintain the temperature but it would not protect spinal cord cells of injuries produced by the warming of the tisues during the exposure to radiations of mobile phones.
Keywords: electromagnetic, menopause, time latency, mobile telephony

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TRANSCRANIAL DIRECT CURRENT STIMULATION ALLOWS TO EARLY DETECT SYNAPTIC DYSFUNCTION AND MEMORY IMPAIRMENT IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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In the last years, transcranial direct current stimulation (tDCS) has been used to treat cognitive dysfunction in patients with Alzheimer's disease (AD) showing encouraging results. Here we asked whether tDCS applied before the onset of overt AD may be useful to predict future symptoms of disease.
To this aim we investigated the effects of anodal tDCS on synaptic plasticity and memory in a mouse model of AD (3×Tg-AD) before the phenotype was manifested (at 3 months of age) and compared these effects with those observed in age-matched C57BL/6 control mice. At electrophysiological level, we evaluated long-term potentiation (LTP) at CA3-CA1 synapses and neuronal excitability in CA1 neurons. Novel Object Recognition (NOR) task was used to test recognition memory. Finally, we performed Western Blotting to measure the expression levels of proteins involved in synaptic plasticity.
Our results showed that, in 3 month-old C57BL/6 mice, tDCS enhanced: i) LTP (81.1±7.0% vs. 50.8±4.9% in sham-stimulated mice, P=0.001); ii) number of action potentials (16.9±0.9 vs. 11.0±1.9, P=0.007) elicited by 300 pA depolarizing steps; iii) preference index in NOR task (70.7±0.8% vs. 64.2±1.3%, P=0.002); iv) $Ca_v1.2$ channel expression (P=0.0007), phosphorylation of CREB at Ser133 (pCREB; P=0.001) and CaMKII at Thr286 (pCaMKII; P=0.005). All these tDCS effects were, instead, not observed in 3 month-old 3×Tg-AD mice (LTP: P=0.4; action potential number: P=0.8; preference index: P=0.6; $Ca_v1.2$: P=0.06; pCREB: P=0.8; pCaMKII: P=0.5). Collectively our data show that, in the preclinical stage of an AD mouse model, tDCS fails to enhance synaptic plasticity and memory in contrast to the positive effects elicited in age-matched wild-type mice, thus suggesting that tDCS might unveil early synaptic dysfunction before AD onset.
This work was supported by: ONR Global (N62909-15-1-2002); Italian Ministry of Health (RF-2013-02356444; GR-2011-02349998); D1 Funds from Università Cattolica.
Keywords: tDCS, Alzheimer, biomarkers, LTP

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FOCAL TRANSCRANIAL MAGNETIC STIMULATION (TMS) OF THE RAT BRAIN: COIL DESIGN, C-FOS MAPPING AND ELECTROPHYSIOLOGY

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Introduction: Rodent studies could be of great value in understanding the neurobiological mechanism of TMS. Unfortunately, there is no commercial rodent TMS coil that can mimic the spatial focality of human TMS. We report a novel system capable of inducing focal stimulation of the rat and mouse brains, with an estimate focality of about 1 mm.

Theory: A key strategy in our coil design is the use of long magnetic core. Theoretically, the Maxwell equation $\nabla \times \boldsymbol{E} = \partial \boldsymbol{B}/\partial t + \mu_0 \boldsymbol{J}$ dictates that the induced $\boldsymbol{E}$ field is a function of how fast the $\boldsymbol{B}$ field changes over time. $\boldsymbol{B}(x,y,z) = \mu_r(x,y,z) \times \mu_0 \times \boldsymbol{H}(x,y,z)$, here μ_0 is a constant; $\mu_r(x,y,z)$ is relative permeability of the core material. $\mu_r(x,y,z)=1$ for air; the theoretical value of μ_r is 5000 for silicon steel. $\boldsymbol{H}$ is the magnetic field strength in free space (air core). It is apparent that the intensity and spatial distribution of the $\boldsymbol{B}$ field in relation to the $\boldsymbol{H}$ field is shaped by $\mu_r(x,y,z)$. By properly designing a magnetic core, thus the spatial distribution of $\mu_r(x,y,z)$, one can not only drastically ***enhance*** the $\boldsymbol{B}$ field, but can also ***guideand focus*** the magnetic flux.

Results: We have developed a TMS coil and impedance-matched driver circuits. The coil was carefully adjusted to the motor cortex representation of the hindlimb region (n=6 rats). We consistently observed contralateral hindlimb twitch to a single TMS pulse. We also measured motor evoked potential (MEP) in some of the animals via implanted microwires into the lateral gastrocnemius of the contralateral hindlimb muscle. We observed MEP signal with the delay, duration and amplitude consistent with the literature. We also mapped neural activity induced by TMS using c-fos immunochemistry (n=8 rats). Brain areas with Fos expressions are consistent with known projection pathways. This work was partially supported by NIDA-IRP, NIH.

Keywords: TMS, c-fos, MEP, rat

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EFFECT OF AN ELECTRICAL STIMULATION SESSION ON THE RIGHT INFERIOR FRONTAL GYRUS ON THE RESPONSE INHIBITION

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Introduction: Response inhibition is an executive function. This executive function is an important mental process necessary for behavior regulation and avoidance. The role of the right inferior frontal gyrus in the frontal lobe has been highlighted in recent studies on this function.

Method: In this study, we investigated the role of right inferior frontal gyrus in two types of fast and delayed response inhibition tasks by using electrical stimulation. To this end, we used the design of the between group. 117 students were randomly assigned into two groups of experimental, anodal stimulation of the right inferior frontal gyrus in two tasks, and four groups of control, anodal stimulation of the visual area and sham stimulation in both tasks. Simultaneously with the delivery of the electric current, the subjects performed the tow stop-signal and Go/No Go tasks.

Results: The results of multivariate analysis of variance analysis showed that there is a significant difference between the electrical stimulation of the right inferior frontal gyrus and the modulation of the inhibition parameters in the stop-signal task (p 0.05).

Discussion: These results indicate that electrical stimulation has an effect on modulating the latency response inhibition parameters. And the role of the right inferior frontal gyrus in this type of inhibition may be more specific. As the probability of its role in rapid inhibition control is questioned, or its examination with other areas of this gyrus is required. Generally, electrical stimulation may be a useful tool for modifying this cognitive function.

Keywords:

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IS COMORBID AUTISM OR BIPOLAR DISORDER A CONTRA-INDICATION FOR DBS IN PATIENTS WITH OCD?

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Introduction: Deep brain stimulation (DBS) is a safe and effective treatment for refractory obsessive-compulsive disorder (OCD). Refractory OCD often occurs with comorbid disorders. Autism spectrum disorder (ASD) and bipolar disorder (BPD) are regarded as contraindication for DBS because of supposed treatment non-response and stimulation induced (hypo)mania, respectively. We present 8 OCD patients with comorbid ASD or BPD who were treated with DBS of the ventral anterior limb of the internal capsule (vALIC).

Methods: Eight patients with comorbid ASD (n=4) or BPD (n=4) received DBS of the vALIC for treatment-refractory OCD and were followed for 1 year. Effectiveness of DBS was evaluated with the Yale-Brown Obsessive Compulsive Symptoms Scale (Y-BOCS) at baseline and 1 year after implantation. (Hypo)manic symptoms were measured by the Young – Mania Rating scale (YMRS).

Results: Following one year of DBS, mean Y-BOCS score of patients with comorbid ASD dropped from 34±3.0 to 21±9.9 (d=1.77, Z=-1.826, p=0.068). Two out of 4 patients were responders (Y-BOCS decrease of >35%) and one patient was a partial responder (Y-BOCS decrease of >25%). Mean Y-BOCS scores of patients with comorbid BPD dropped from 35±5.6 to 25±7.3 (d=1.54, Z=-1.841, p=0.066). One out of four patients was a responder and 2 patients were partial responders. We did not observe serious complications. All patients with comorbid BPD developed transient hypomanic symptoms (YMRS≤23, corresponding to mild symptoms) when DBS was activated or voltage increased. Hypomanic symptoms lasted between 7 and 30 days but did not require hospital admittance.

Conclusion: These preliminary results suggest that comorbid ASD and BPD in OCD should not be regarded as absolute contraindication for DBS of the vALIC. Effectiveness of DBS was comparable to DBS for OCD without comorbidity. Development of hypomanic symptoms should however be carefully monitored, and stimulation settings adjusted if necessary.

Keywords: Deep brain stimulation, obsessive-compulsive disorder, autism spectrum disorder, bipolar disorder

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TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION MODULATES LOCUS COERULEUS ACTIVITY IN MIGRAINE: A PRELIMINARY FMRI STUDY

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Migraine is a common episodic neurological disorder with unsatisfactory treatment options. Literature shows that vagus nerve stimulation (VNS) and transcutaneous auricular VNS (taVNS) can diminish pain and regulate mood, thus may hold the potential to relieve migraine symptoms. This study aims to investigate the neural pathways associated with taVNS in patients with migraine.

Twenty-nine patients with migraine were recruited from outpatient neurology clinics. All MRI scanning was conducted on a 3.0 T Siemens scanner. Each patient attended two MRI scans (receiving real and sham taVNS in random order), separated by at least one week. Each MRI scan included resting state fMRI, real or sham taVNS with a block design (6 minutes), continuous real or sham taVNS (8 minutes), and post-treatment resting state fMRI.

Data analysis on block fMRI data showed that real taVNS is associated with significant fMRI signal increases in the right striatum and thalamus, as well as fMRI signal decreases in default mode network (DMN) areas and brain stem areas, including the locus coeruleus (LC) / periaqueductal gray (PAG) and solitary nucleus. The sham taVNS also evoked similar fMRI decreases in the DMN, but no changes at the brain stem. Direct comparison between the real and sham taVNS showed that real taVNS produced greater deactivation at the bilateral medial prefrontal cortex/anterior cingulate cortex, precuneus/posterior cingulate cortex, hippocampus, and LC. Resting state functional connectivity (rsFC) analysis on pre- and post-treatment resting state fMRI data using the LC as a seed showed that real taVNS can produce significantly greater rsFC at the left operculum and amygdala, along with the right insula and hippocampus/para-hippocampus, compared to sham taVNS.

Our results suggest that taVNS can significantly modulate brain regions associated with pain modulation and vagus nerve pathway, which may shed light on the neural mechanisms underlying taVNS treatment of migraine.

Keywords: transcutaneous auricular vagus nerve electrical stimulation, migraine, fMRI, resting statee functional connectivity, locus coeruleus

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PAST, PRESENT, AND FUTURE PERSPECTIVE OF ELECTROCONVULSIVE TREATMENT IN SLOVAKIA