XXII National Congress of the Italian Society of Psychophysiology

PROCEEDINGS - ABSTRACTS

Main lectures

Symposia abstracts

Abstracts

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of the Italian Society of Psychophysiology

MAIN LECTURES

The placebo effect

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The placebo effect is an organic or mental change that occurs as a result of the symbolic meaning that is attributed to an object or event within the healing context. Therefore, the placebo effect is a window into mind-brain-body interaction, doctor-patient relationship, psychotherapy, as well as the psychological component of physical performance. Recently, several studies have identified the changes that occur in the brain of patients following the administration of a placebo, particularly in pain, Parkinson's disease, and performance in sport and extreme environments. What is emerging from these studies is that placebos activate the same mechanisms that are activated by drugs.

Translating brain-machine interfaces to end-users: lessons and challenges

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In the framework of the European project TOBI, we have developed a variety of BCI prototypes that have been extensively tested by motor-impaired users after a short training period. A substantial number of tests have been carried out at end-users' home and clinics, outside well controlled laboratory conditions. Equally significantly, non-BCI experts (assistive technology professionals and therapists) have run many of these tests independently or with a minimum of remote assistance from researchers. A central concern in our research is how to facilitate the operation of brain-controlled devices over long periods of time. This is a challenging problem due to the limited (and variable) information carried by brain signals we can measure, no matter the recording modality. I will argue that efficient brain-computer interaction, as the execution of voluntary movements, requires the integration of several parts of the CNS and the external actuators. In this talk I will summarize this work and the main lessons learned from this major effort, highlighting new principles incorporated in the brain-controlled devices.

SYMPOSIA ABSTRACTS

A neuropsychological approach for placebo analgesia

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Acute and chronic pain conditions are often present in elderly individuals, but only a small minority of patients with dementia are prescribed analgesics and thus, these patients may be severely undertreated for their pain. To further exacerbate the situation, even when patients with dementia receive analgesic treatment, they have shown a reduced placebo analgesia effect and thereby a reduced response to pain medication. In particular, in the third section of the symposium Martina Amanzio will focus on placebo analgesia by giving an overview of how psychological and neurophysiological elements of expectations may influence placebo analgesic responses in patients with dementia and how to optimize the therapeutic context to achieve better outcomes.

A neuroaesthetic study by neuroelectric imaging during the observation of the Michelangelo's Moses sculpture

Babiloni F. [1, 2] **- Cherubino P.** [1, 2, 3] **- Graziani I.** [1, 2] **- Bagordo G.M.** [4] **Cundari C.** [4] **- Borghini G.** [1, 2] **- Aricò P.** [1, 2] **- Maglione A.G.** [1, 2, 5] **Vecchiato G.** [1, 2]

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Recent studies have been showed as the perception of real or displayed masterpieces by ancient or modern painters generate stable neuroelectrical correlates in humans. In this study, we collected the neuroelectrical brain activity correlated with the observation of the real sculpture of Michelangelo's Moses within the church where it is actually installed in a group of healthy subjects. In addition to the cerebral activity also the heart rate and the galvanic skin response were collected simultaneously, to assess the emotional engage of the investigated population. The Moses sculpture was

observed by the group from three different point of views, each one revealing different details of the sculpture. In addition, in each location the light conditions related to the specific observation of the sculpture were explicitly changed. Results showed that cerebral activity of the subjects varied significantly across the three different views and for light condition against no light condition ($p < 0.04$). Furthermore, the emotional engage estimated on the whole population is higher for a point of observation in which the Mose's face is directed toward the eyes of the observers ($p < 0.02$). Finally, the cerebral appreciation of the investigated group was found maximum from a perspective in which all the details of the sculpture could be easily grab by the eyes. Results suggested how the perception of the sculpture depends critically by the point of view of the observers and how such point of view can produce separate emotional and cerebral responses.

Modulation of neural activity with light: optogenetic probes and photovoltaic interfaces

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Modulation of neuronal activity is a principle strategy in neuroscience research and in treatment of neurological and psychiatric disorders. Optical techniques, aimed at manipulating neuronal activity, comprise a distinct class, characterized by the use of targeted light stimuli to initiate neuronal responses. This class offers several important advantages over chemical or electrical stimulation. The recent discovery of light-sensitive ion channels from algae was the starting point for the development of a novel photostimulation method, termed optogenetics. In this technique, a gene coding for light-activated ion channels or pumps, such as the excitatory channel rhodopsins or the inhibitory halorhodopsins/archeorhodopsins, is introduced into the tissue. The gene construct can be delivered in a variety of ways, including electroporation, transfection, or viral vectors. Subsequently, the expression of the exogenous protein renders neurons light-sensitive. Inclusion of cell-type specific promoters can ensure that expression of the light-activated protein is restricted to the desired cell-type. Since its initial discovery, optogenetics research has generated a whole range of suitable proteins, which are activated optimally by various stimulus wavelengths, and display diverse properties regarding ion selectivity and kinetics. Lastly, neuronal activity can be optically modulated by application of a photoisomerizable molecule, called a photoswitch, which can regulate the activity of ligand-gated channels or receptors. In this case photoisomerization of the photoswitch leads to delivery/removal of the ligand to its binding site on the channel or receptor. Recently, a novel approach has been added to the class of optical techniques. This approach involves the generation of light-sensitive photovoltaic interfaces to excite neurons

that are in close vicinity to the photovoltaic material. We have exploited an organic photovoltaic blend for neuronal stimulation via a photo-excitation process. The use of an organic film made of a donor-acceptor blend (P3HT:PCBM) is able to trigger neuronal firing upon illumination at high temporal and spatial resolution. We have also demonstrated that this bio-organic interface restores light sensitivity in explants of rat retinas with light-induced photoreceptor degeneration. These findings suggest that bio-organic hybrid opto-neural interfaces can play an important future role in sub-retinal prosthetic implants.

Basic forms of neuroplasticity and their potentialities for neurorehabilitation

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Neuropsychological or cognitive rehabilitation has undergone a considerable theoretical and practical development as a specialized field of research and clinical application in its own right. Its possibilities of intervention have been considerably expanded after the abandonment of a wrong belief in the immutability of the central nervous system and the growing evidence in favour of the existence of a considerable degree of neuroplasticity even in the mature and aged brain. Modulation of synaptic transmission and synaptogenesis, the staple mechanism of neuroplasticity in development, maturation and learning, is also assumed by most to underlie functional recovery in the damaged central nervous system. In order to achieve a true scientific rationale for neurological and neuropsychological rehabilitation, it will be necessary to fully understand the actual overlaps and the actual differences between the mechanisms of repair and re-organisation after brain damage and those of physiological development and normal learning.

The multisensory brain

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Multisensory integration is a fundamental property of the brain; it refers to the process by which the brain integrate and co-modulate incoming stimuli from the different senses. Multisensory integration allows the human brain to consider multiple sensory stimuli (e.g., visual, auditory, tactile inputs) simultaneously and construct a unified

perception of the environment based upon these simultaneous inputs. The effective combination of sensory information is a perceptual strategy that allows for enhanced identification of external stimuli, in turn facilitating behavioural responses to them, particularly when the input from one sensory modality is ambiguous. However, the presence of a complementary sensory component can even alter a percept entirely, as in the case of cross-modal illusions. Although multisensory interactions have been mainly ascribed to the activity of higher-order hetero-modal areas, recent evidence shows that multisensory convergence may arise even in primary sensory areas. Indeed, a growing body of evidence from neuroimaging and non-invasive brain stimulation studies demonstrate interactions in primary sensory areas, which can improve or even alter perceptual and cognitive processes, up to social behaviour. Moreover, the recent research on multisensory integration in pathological conditions, such as in stroke, migraine and autism, is further increasing our understanding of the importance of efficient integration of sensory inputs in everyday life, and how alterations of this process may dramatically influence human behaviour. In this context, of great interest is the potential of driving multisensory integration with therapeutic purposes. For instance, neuropsychological evidence indicates that spared multisensory mechanisms can compensate for modality-specific perceptual or cognitive impairments that follow a brain injury. The emerging view is that different cross-modal plastic changes can result following damage to sensory-specific and hetero-modal areas, and we can modulate such post-injury cross-modal plasticity to improve multisensory integration for driving functional recovery. This places greater emphasis on the development of multisensory-based rehabilitation approaches that take advantage of the innate tendency of the human brain to integrate sensory information for optimal performance.

Aesthetic appreciation and perceptual ambiguity

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In the last few years the investigation of the neurocognitive correlates of the aesthetic experience received increasing interest thanks to the opportunities offered by the improvement of neuroimaging techniques. In fact, they allow for testing the hypotheses concerning psychological mechanisms underlying aesthetic appreciation. In particular, the modulatory influence of perceptive processes on aesthetic experience has still to be clarified. In order to explore such relationship we performed an fMRI study on the neural correlates of aesthetic appreciation in the presence of perceptual ambiguity. Participants were asked to judge the pleasantness/beauty of four stimuli categories: ambiguous art masterpieces (Arcimboldo's portraits), non-

ambiguous art masterpieces (Renaissance portraits from XVI century), ambiguous non-artistic stimuli (illusory pictures of objects that can be perceived as faces), and non-ambiguous non-artistic stimuli (pictures of faces). The comparisons within each category showed that neural activity is significantly modulated by the valence of the aesthetic appreciation for ambiguous art masterpieces. Namely, areas related to face perception proved to be less activated when the masterpiece was appreciated, while they were recruited when it was not. Results will be discussed in the light of current knowledge on aesthetic appreciation processes.

Pain in mild cognitive impairment and dementia

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Pain in dementia has recently become a topic of great interest. Based on clinical findings of reduced pain report and diminished prescription of analgesics in demented patients, the question has arisen of whether pain processing might be changed in this patient group. In order to answer this question experimental studies are indispensable because only these allow to assess changes in the pain system itself. The focus of the talk will lie on experimental findings on pain processing in patients with dementia and in patients with Mild Cognitive Impairment. It will be discussed how the neuropathological degeneration affects the processing of pain as well as the various responses to pain. Moreover, promising new pain assessment strategies will be presented, with a special focus on the facial expression of pain.

Brain development and effects of stimulant medications in ADHD

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Disturbances in the basal ganglia portions of cortico-striato-thalamo-cortical circuits likely contribute to the symptoms of attention deficit hyperactivity disorder (ADHD). The author will illustrate the results of a previous study investigating the morphological features of the basal ganglia nuclei (caudate, putamen, and globus pallidus) in children with ADHD. The study involved 47 individuals with combined-type ADHD and 57 healthy comparison subjects, aged 7 to 18 years, examined in a cross-sectional case-control study using anatomical magnetic resonance imaging. Overall the brain volumes were significantly smaller only in the putamen, whereas

analysis of the morphological surfaces revealed significant inward deformations in each of the three nuclei, caudate, putamen, and globus pallidus, in positive correlation with the ADHD symptoms. Moreover, outward deformations of all basal ganglia nuclei were observed in ADHD children treated with stimulants compared with those ADHD not treated. These stimulant-associated enlargements were in locations similar to the reduced volumes detected in the ADHD group relative to the comparison group. Conclusions: These findings potentially represent evidence of anatomical dysregulation in the basal ganglia in children with ADHD and suggest that stimulants may normalize morphological features in children with ADHD.

Compromised neural development in schizophrenia: the interaction of genetic and environmental factors

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Schizophrenia is a debilitating brain disorder, one that compromises the highest expressions of human mind, including perception, reasoning, emotion, and social behavior. There is agreement that the impact of genetic variation can be large, although seemingly multiple relatively common variants may set the stage for the disease, without major causative factors. It has been hypothesized that the etiology of schizophrenia takes effect during neurodevelopmental stages. However, it is difficult to directly test this hypothesis, since schizophrenia is usually diagnosed in adulthood. We used a novel approach to interface genetic variation with physiological and behavioral data. The gene GRIN2B, coding for the GluN2B subunit of the N-methyl-D-Aspartate glutamatergic receptor, was selected because of its role in neural development and in working memory. Genetic variants in the gene were selected for their association with GRIN2B mRNA expression. The effects of multiple variants were then collapsed into a poli-loci score indexing mRNA expression. The score was used as a predictor of fMRI activation and connectivity during working memory performance in healthy controls and in patients with schizophrenia; cognitive phenotypes were also tested. Results show that the composite effect of multiple genetic variants reflecting GRIN2B gene expression correlates with imaging and cognitive phenotypes. Furthermore, we extended these results using a gene coexpression network technique aimed at studying the interactome of genes related with dopaminergic transmission. Current evidence supports the idea that genetic variants in genes involved in neural development are associated with the imaging and cognitive phenotypes found in schizophrenia.

Methods of pain evaluation: the PAIC tool

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Pain is often not recognized and thus undertreated in people with cognitive impairments (such as dementia). The reason is that people with cognitive impairments are less able to communicate to their care-givers that they are in pain, resulting in reduced quality of life. Generally, pain is assessed using self-report scales where the person indicates the level of intensity and discomfort experienced. However, clinical evidences show that these scales are inadequate to recognize pain in persons with cognitive impairments. Consequently, there is an urgent need to improve pain management in these vulnerable populations. The European COST action TD1005: "Pain assessment in patients with impaired cognition, especially dementia" has developed a new scale (PAIC scale). This talk will present examples of this work and discuss future possibilities.

Reward mechanisms and artefacts fruition: neurophysiological and personality components

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Artefacts appreciation, including artworks as well as handicraft and industrial products, involves the audience by an emotional point of view, guides motivational level and affects decision making. Moreover, it is well known that individual differences based on personality correlates play a key role in determining evaluation, preference and subjective responsiveness to specific features of a good. Emerging evidence suggests that these behaviors could rely on reward mechanisms, according to the approach-withdrawal motivational model of emotion, and that the left prefrontal brain activity may reflect the strength of the reward-related behavioral activation system (BAS and BAS-reward). Although it has been demonstrated that the DLPFC is a key structure in processing rewarding information, little is known about the relationship between neurophysiological and personality correlates supporting artefact appreciation and preference. Therefore, the present study aimed to explore the impact of reward mechanisms and their prefrontal correlates to support cognitive and emotive processes during the presentation of different artefacts (videos). Inhibitory rTMS (1 Hz) was applied on DLPFC to 24 participants, while electrocortical activity (EEG) and behavioral self-report evaluation were recorded. Two control

conditions were included in the experimental design to control the simple stimulation effect (sham condition with absence of TMS stimulation) and the localization effect (control site condition, F3/F4 stimulation). Results showed that, in comparison to sham and control condition, F3 low-frequency stimulation (inhibitory effect) induced increased prefrontal alpha activity (brain activity reduction) during the processing of emotionally involving videos, suggesting a decreased interest due to the deactivation of reward-related mechanisms. In addition, theta activity was modulated by BAS-reward component. In conclusion, this study supported the prefrontal approach-withdrawal motivational model of emotion applied to artefacts processing, and suggested that some goods may elicit a stronger subjective response in terms of rewarding-power, resulting in a greater modulation of the prefrontal system. These results were revealed in both electrocortical responses and explicit subjective evaluation, and were supported by personality attitudes.

Bridging events and actions: P3b reflects activation of stimulus-response links

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It has been proposed that, by its being related to the decision on how to respond to stimuli, the P3b component of event-related EEG potentials reflects linking of responses to stimuli. This is in contrast to the traditional "stimulus evaluation" view which holds that P3b depends on processing of stimuli only. To further explore this matter, we used the oddball-effect on P3b in two standard paradigms: choice-response to frequent and rare stimuli, and prediction of such stimuli. Relevant stimuli were random series of two letters, one frequent and one rare. In prediction tasks we studied whether the feedback-P3 evoked by the letters to be guessed was increased by rare stimuli or rather by rare combinations of guesses and stimuli. The latter was true, which may mean that P3 reflects the link made from the perceived stimuli to the preceding related guess response. In the choice-response tasks, rare or frequent stimuli (S1) were followed by ancillary stimuli (S2). Rare S1s evoked a large oddball effect on P3b when S2 was irrelevant. This oddball effect became abolished when both S1 and S2 were relevant for responding. We suggest that P3b arises when some firmly associated stimulus-response link which is not in an active state has to be reactivated for responding.

ORAL AND POSTER PRESENTATIONS ABSTRACTS

Use of rTMS in the treatment of Primary Progressive Aphasia (PPA)

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rTMS improve action naming in subjects with aphasia in neurodegenerative disorders. Only a few cases has been reported in the scientific literature about the rehabilitation of Primary Progressive Aphasia (PPA) using rTMS and our study aims to contribute to the actual debate over this subject. As part of ongoing study protocol we present data of six patients affected by (PPA) nonfluent type, that have completed the treatment until the present day. In our study, a randomized cross-over single-blind trial, patients undergo two consecutive treatment cycles (for three weeks, five days a week); a cycle of combined speech therapy and real rTMS, and another cycle of combined speech therapy and sham rTMS. Each patient is assigned to a starting cycle upon randomization. The patients' performance is evaluated on a battery of language (Italian version of AAT) and on a test of verbal fluency, before and after every cycle. Statistical analysis of the scores on the AAT test has not yet revealed significant differences. The test scores of verbal fluency has shown, however, significant variations in patients treated at the end of treatment with real rTMS compared with the cycles in which the same patients were treated with sham rTMS. In particular, patients treated with sham rTMS increased the performance value of 8.8% at the end of the cycle; whereas patients treated with real rTMS improved their performance of 31% at the end of the cycle. In conclusion, the preliminary results of this study suggest that the association between speech therapy and real rTMS could increase performance on tests of verbal fluency in patients with PPA.

No causal effect of left hemisphere excitability in the genesis of neglect

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Most of the neurorehabilitative interventions using non-invasive brain stimulation techniques after brain damage base their rationale on the theoretical framework

of interhemispheric rivalry models, which postulate the existence of reciprocally interactive opponent processes exerted by the two hemispheres. According to these models, neglect (i.e., the inability to report, respond, or orient to stimuli presented on the opposite side of the brain lesion) is caused by the inactivation of the right damaged hemisphere together with the simultaneous hyperactivation of the intact, contralesional, left hemisphere, this latter due to the release of inhibition from the damaged one. The present study represents an attempt to directly test the predictions of interhemispheric rivalry models inducing neglect-like bias in healthy participants by means of repetitive transcranial magnetic stimulation (rTMS) applied over the right hemisphere while concurrently recording the electroencephalographic (EEG) activity. The combination of these techniques allows to measure specific neurophysiological markers of cortical activity (i.e., TMS-evoked potentials, TEPs) both over the stimulated right cortical area and the contralateral homologous area in the left hemisphere, thus representing a direct and univocal measure of cortical excitability. Fourteen healthy volunteers performed a line bisection task and a simple detection task of unilateral checkerboards stimuli. Both tasks were performed either before and after 30 minutes of low frequency rTMS (1 Hz) over the right posterior parietal cortex. The EEG signal was continuously recorded throughout the experiment. The efficacy of rTMS in inducing neglect-like phenomena was confirmed by the results of the line bisection task where participants showed a rightward deviation after rTMS, a performance comparable to that of neglect patients. Moreover, TEPs showed that low frequency rTMS induced a comparable reduction of cortical excitability of both the stimulated (right) and the contralateral (left) hemisphere. Behavioural and EEG data obtained during the detection tasks confirmed the inhibitory effect of rTMS, testified by a lengthening of reaction times and a reduction of the amplitude of P200 component generalized to both the right and the left visual stimuli. This evidence is in direct contrast to the predictions put forward by the inter-hemispheric rivalry models according to which the reduced excitability of the right parietal areas induced by a real or virtual brain lesion should produce an increased cortical excitability in the contralateral homologous areas as a consequence of the release of reciprocal inhibition of the two hemispheres. The results of the present study are consistent in demonstrating that the parietal imbalance, with the relative hyper-activation of the left hemisphere, is not causative of spatial neglect but possibly reflects a long-term maladaptive plastic reorganization that follows a brain lesion.

Interactions between motor simulation and action pre-selection during action observation

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Motor simulation is an effect obtained during the observation of others' actions and it is described as the automatic activation of the motor representation correspondent

to the action observed. Since, according to this view, action execution and action observation should share both the same neural circuits and similar mechanisms, it is interesting to pose the question about how the pre-selection of actions to be performed in response to observed actions influences the simulation effect. In particular the present work aims to understand whether pre-selecting actions that are not the same actions observed (NOT-OVERLAP task) affects the motor simulation effect in a different way compared to the condition in which the pre-selected actions to be performed are the same as the ones that participants will be observed (OVERLAP task). In the present experiment two force sensors were placed respectively between the participants' index and thumb, and on the ulnar side of the forearm. Participants were presented with a hand which could either grasp an object placed between the index and the thumb, or it could extend these two fingers in order to touch an object placed outside the hand. The hand could become either yellow or light-blue at different delays from the presentation of the action (16-33-50 ms, 100-116-133 ms, 150-167-183 ms, 200-216-233 ms). The relation between color and action observed was completely independent. Each time the hand became colored, a transcranial magnetic stimulation pulse was delivered on the participants' motor cortex in order to evoke both motor evoked potentials from intrinsic hands muscles and to record the pulse-inducted force on the force sensor placed between participant index and the thumb. In one task (OVERLAP task) participants were required to squeeze/release the sensor between their fingers if the hand became yellow/blue. In the other task (NOT-OVERLAP task) participants were required to abduct/adduct their forearm if the hand became yellow/blue. Results showed that a simulation effect was found on the pulse-generated force in the 150-183 ms time-window in the OVERLAP task, but not in the NOT-OVERLAP task. However in this last condition a simulation effect was detected later within the 200-233 ms. These findings clearly showed a modulation of the simulation effect between the two conditions showing in particular an inhibition of the simulation effect at early time-windows when the pre-selected actions were not the same as the ones observed. However, the motor simulation was evoked at later time-windows. These results enrich the complexity of a dual-route model of visuo-motor transformations applied by our group to action observation.

Stimulus- or movement-locked cortical potentials? Similarities and differences

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Event-related potentials (ERPs) are time-locked voltage fluctuations in the electroencephalogram (EEG) usually induced by sensory events (typical ERPs) and by

motor acts (movement-related cortical potentials, MRCPs). Different components have been observed in both of them. The typical ERPs include early components (the P1, N1 and P2 for visual ERPs) within 200 ms post-stimulus that are mainly modulated by perceptual features and attention, and later component, as the N2 and P3, which are related to cognitive processing of the stimulus. The MRCPs include the Bereitschaftspotential (BP) or readiness potential (RP), a slow rising negativity associated with the motor preparation. Recently, other cortical activities have been observed over the prefrontal cortex: the prefrontal negativity (pN) preceding and overlapping the BP, and the prefrontal positivity (pP) following response-related stimulus presentation. In case of movements initiated by external stimuli both stimulus- and movement-locked cortical potentials can be considered; however, even though the ERPs and MRCPs are well known, none has tried to overlap and directly compare both of the waveforms to understand similarities and differences between these two kind of EEG segmentations. The participants were asked to perform a simple (SRT) and a discriminative (DRT) visuo-motor response task. In order to align stimulus- and movement-locked ERP waveforms, the subjects with the smallest standard deviation (SD) of the response time (RT) were selected. 27 young subjects (mean age ± SD: 34.8 ± 11.3; 6 females) were included in the analyses. The epoch length was selected based on the averaged RT (213 ± 17 ms and 440 ± 17 ms for the SRT and DRT, respectively) in order to allow the alignment of both ERPs and MRCPs on the same time scale. Results were comparable for both SRT and DRT. The prefrontal negativity (pN) was not different between ERPs and MRCPs ($t < 1$). The BP was larger in the MRCP than ERP ($t = 2.17$, $p = 0.015$). The P1, N1 and N2 components were larger in the ERPs than MRCPs (all $ps < 0.001$). The P3 was larger in the MRCPs than ERPs ($t = 1.94$, $p = 0.0002$). The pP was not different between ERPs and MRCPs ($t < 1.5$). Concluding, the prefrontal components were not affected by the event alignment. Conversely, the P1, N1 and N2 components were more stimulus- than motor-related, whereas the BP and the P3 were more related to the movement initiation. The P3 is considered a sort of cognitive reaction to target stimuli, more specifically, it is thought to reflect processes involved in stimulus evaluation and categorization. Therefore, the finding that this component is mainly driven by motor control and is only in a less extent due by perceptual events, sheds light into the origin of this well-known component suggesting a main role in the last phase of movement selection and execution.

Action observation combined with peripheral electrical nerve stimulation increases motor efficiency

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Human action observation (AO) is known to affect the activity of the primary motor cortex (M1) and, as result, the human motor behavior. Several studies showed that during AO M1 excitability increased and participants' motor response was influenced by the observed motion. However, the AO effects may vanish if motor practice is not concurrent or immediately follows it. This suggests that a prompt comparison between the visual and the somatosensory representations of movement could be necessary to induce plasticity in M1 and to make the behavioral modifications long-lasting. In a previous study we showed that M1 excitability increased after a conditioning protocol where AO was combined with a peripheral nerve stimulation (PNS), whereas the effects of AO and PNS alone vanished immediately after video observation. The increased M1 excitability was still present 45 minutes after the combined stimulations (AO-PNS) and was specific for the stimulated muscle. Thus, we concluded that plasticity in M1 can be induced by the activation of the mirror neuron system but only in an associative context (e.g., afferent signals from periphery). In the present study we tested whether the M1 plasticity induced by AO-PNS could have a behavioral correspondence dealing with changes in motor behavior such as an increased efficiency in finger-tapping movements. Thirty-one participants were randomly assigned to four groups: (1) AO-PNS group: 9 participants observed a 14-minutes video showing a right hand that performed a finger-tapping movement at 3 Hz (a frequency that is expected to be higher than the natural one that is on average 2 Hz) and contemporarily received an electrical stimulation at the median nerve of the right hand; (2) AO group: 8 participants observed the same video of the AO-PNS group; (3) PNS group: 6 participants received the same electrical stimulation of the AO-PNS group; (4) CTRL group: 8 participants observed a 14-minutes video showing different landscape images. Before and 30 minutes after the conditioning protocols the participants performed for 2 times a finger-tapping movement (thumb towards index-middle-ring-little repeated 4 times) to test whether the different stimulations affected the motor response. As behavioral outcome we considered the percentage of changes in movement frequency – (POST/PRE)*100. Results showed that the conditioning protocols significantly affected participants' movement frequency. Although in all groups the finger-tapping frequency slightly increased, probably due to a motor learning effect, in the AO-PNS group the percentage of changes was significantly higher than in the others groups. This result suggested that the AO-PNS stimulation was able to induce long-lasting behavioral

changes. This effect, coupled with the know long-lasting increase of M1 excitability after AO-PNS, strengthen the possibility to apply this combined stimulation in a rehabilitative context to obtain a maximal outcome in term of motor efficiency.

Cerebellar current stimulation modulates pain perception in humans

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Cerebellum is involved in a wide number of integrative functions, but its role in pain experience and processing is poorly understood. Here, we evaluated the effects of transcranial cerebellar direct current stimulation (tcDCS) on pain by studying the changes in perceptive threshold, pain intensity (VAS: 0-10) and laser evoked potentials (LEPs) variables (N1 and N2/P2 amplitudes and latencies) in healthy volunteers. Fifteen healthy subjects were studied before and after anodal, cathodal and sham transcranial cerebellar direct current stimulation (tcDCS: 20', 2.0 mA). LEPs were obtained using a neodymium: yttrium-aluminium-perovskite (Nd: YAP) laser. VAS was evaluated by delivering laser pulses at two different intensities, respectively two and three times the perceptive threshold. Cathodal polarization dampened significantly the perceptive threshold ($F[2, 28] = 18.67$, $p < 0.0001$) and increased the VAS score ($F[2, 28] = 31.448$, $p < 0.0001$), while the anodal one had opposite effects ($p < 0.0001$). Cathodal tcDCS increased significantly the N1 ($F[2, 28] = 102.281$, $p < 0.0001$) and N2/P2 ($F[2, 28] = 65.77$, $p < 0.0001$) amplitudes and decreased significantly their latencies ($p < 0.0001$), whereas anodal tcDCS elicited opposite effects ($p < 0.0001$). Sham stimulation was ineffective. Motor thresholds assessed through transcranial magnetic stimulation were not affected by cerebellar stimulation ($F[4, 56] = 0.339$, $p = 0.851$). The cerebellar direct polarization is able to modulate pain perception and its cortical correlates in humans in a polarity specific manner. While cathodal tcDCS increases amplitudes and decreases LEPs latencies,

then dampening the inhibitory tone the cerebellum exerts on brain targets, anodal polarization elicits opposite effects, thus resulting in an analgesic action. Motor cortex activation does not contribute to the analgesic effects of the anodal cerebellar stimulation. As DCS is effective on both N1 and N2/P2 components, we speculate that the cerebellum is engaged in pain processing by modulating the activity of both somatosensory and cingulate cortices. Our findings indicate a cerebellar effect on pain experience and prompt further investigation aimed at assessing whether the cerebellar direct current polarization could be used as a novel and safe therapeutic tool in chronic pain patients.

Spinal direct current stimulation modulates short intracortical inhibition in humans

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Transcutaneous Spinal Direct Current Stimulation (tsDCS) is a new and safe neuromodulation technique for modulating spinal cord excitability in humans. Despite its growing use, to date whether and how tsDCS induces functional changes in the human brain is still unknown. Here, we assessed changes in intracortical excitability in healthy subjects following tsDCS applied over the thoracic spinal cord; to this end, we evaluated changes in cortical Silent Period (cSP), paired-pulse Short Intracortical Inhibition (SICI) and paired-pulse Intracortical Facilitation (ICF). ICF and SICI depend on different intra-hemispheric networks: paired-pulse TMS at Inter-Stimulus Intervals (ISIs) between 6 and 25 ms hinges on excitatory glutamatergic pathways within primary motor cortex, while SICI, at ISI < 6 ms, mainly accounts for GABA(A) receptors. Ten healthy subjects were studied before (T_0) and at different intervals (T_1 and T_2) after anodal, cathodal and sham tsDCS (20', 2.0 mA) applied over the lower thoracic spinal cord (T10-T12). At each time point we assessed changes in cSP, SICI (ISI = 3 ms) and ICF (ISI = 9 ms); SICI and ICF were obtained with a subthreshold conditioning stimulus (S1) followed by a suprathreshold test stimulus (S2). Motor Evoked Potentials (MEPs) were recorded from First Digital Interosseus (FDI) and Abductor Hallucis (AH) muscles. Cathodal tsDCS increased the MEPs amplitude at inter-stimulus interval of 3 ms, while anodal one elicited opposite effects (FDI:

p 0.0023, AH: p = 0.0004). No significant change in cSP duration was found for recordings made from upper (p = 0.25), as well as from lower limb (p = 0.41); similarly, tsDCS did not modify MEPs amplitude at ISI of 9 ms (FDI: p = 0.39, AH: p = 0.45). tsDCS modulates intracortical excitability in a polarity specific manner. In particular, the reduction of SICI without interfering with cSP and ICF prompts a specific impairment of inhibitory GABA(A)ergic drive. The possibility to modulate brain processing of motor and multisensory ascending inputs makes tsDCS a useful approach to restore spinal drive through non spinal mechanisms; in this view, tsDCS could be useful, especially as an early rehabilitation strategy in patients with acute brain lesions, when other NIBS tools are not indicated due to safety concerns, as well as in the treatment of pain syndromes or in cognitive rehabilitation.

Why do you like Arcimboldo's? Effect of perceptual style on aesthetic appreciation of ambiguous artworks

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Visual aesthetic experience reflects the state of the mind and the brain when visual artworks are being viewed. It has been hypothesized to arise from the interaction between top-down orienting of attention and bottom-up perceptual facilitation. In the present study we investigated whether perceptual style, biasing the orientation of visual attention, leads to a preference for a particular level of a percept (i.e., Global or Local) and thus affects the aesthetic appreciation of ambiguous portraits, such as those of Arcimboldo, which are characterized by part-whole ambiguity. In the present study 50 participants (27 women) were classified as having Global (N = 24) or Local (N = 26) perceptual style by using the Navon task. Then, they were asked to aesthetically judge two different types of artworks, the portraits of Arcimboldo and Renaissance painters. We found that perceptual style affects both the degree of perceived ambiguity in Arcimboldo's artworks and their aesthetic appreciation. Specifically, participants with Local perceptual style judged Arcimboldo's portraits as being more ambiguous than did participants with a Global perceptual style. They also liked Arcimboldo's portraits more than did participants with a Global perceptual style. With regard to the Renaissance portraits, these effects were not observed for either pleasantness or ambiguity. Our findings suggest that aesthetic judgment is a consequence of the interaction between individual personal perceptual style and the perceptual features of artworks. Taken together with previous neuroimaging evidence, this result also indicates that the aesthetic pleasure experienced when viewing ambiguous portraits, such as those of Arcimboldo, is connected more with local processing of the object than with global processing of the face.

Psychophysic and cortical source analysis of movement illusions induced by vibratory stimulation

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It is known that vibratory stimuli applied to muscle tendons induce illusory perception of movement. Tendon muscle vibration, indeed, activates spindle receptors and almost selectively elicits trains of action potentials in the primary endings connected to Ia afferent fibers, which are then interpreted as muscle lengthening and limb displacement. However, while the anatomical substrate that may mediate such illusions is quite defined, their functional and psychophysical correlates are understudied. The present research aims at qualifying and investigating vibration-induced movement illusory perceptions in terms of their electrophysiological and psychophysical features (frequency, strength, and duration of illusion). 17 right-handed volunteers took part to the study, two of them who never reported movement illusions was then excluded from the analyses. Participants were asked to wear a 28-channel EEG system and a wrist splint on the right forearm. A vibratory stimulator was then placed perpendicularly to the flexor tendons and the arm was hidden behind a screen. The vibratory stimulation was at a frequency of about 90 Hz. The experimental design included 15 trials and participants were asked to report whether they felt their right hand moving during stimulations and to qualify those perceptions based on psychophysics features. EEG frequency data were analysed and used as input for signal source localization (sLORETA). The analysis of psychophysical data revealed significant correlations each other. In particular, the more frequently participants reported movement illusions the stronger their perception, and participants who perceived stronger illusions over-estimated their duration. The analysis of EEG data contrasting baselines and stimulation trials inducing movement illusions highlighted a significant decrease of upper-alpha power – mirroring greater activation – especially in insular and prefrontal areas. Finally, correlation analyses between psychophysical and cortical localization data yielded significant relationship between the activation of parietal areas and the frequency of illusory perception. Present findings point out a clear consonance between psychophysical and electrophysiological features of motor illusory phenomena and suggest that pre- and post-central structures may play different roles in their definition. The advanced analyses of EEG components, in particular, helped in shedding light on the potential contribution of superior parietal areas to conscious feeling of movement – even if illusory.

Patients with mild cognitive impairment have an abnormal upper-alpha event-related desynchronization/synchronization during a task of temporal attention

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There are several evidences indicating that an impairment in attention-executive functions is present in prodromal Alzheimer's disease and predict future global cognitive decline. In particular, the issue of temporal orienting of attention in patients with mild cognitive impairment (MCI) due to Alzheimer's disease has been overlooked. The present research aimed to explore whether subtle deficits of cortical activation are present in these patients early in the course of the disease. We studied the upper alpha event-related synchronization/desynchronization phenomenon during a paradigm of temporal orientation of attention. MCI patients (N = 27) and healthy elderly controls (N = 15) performed a task in which periodically omitted tones had to be predicted and their virtual onset time had to be marked by pressing a button. Single-trial responses were measured, respectively, before and after the motor response. Then, upper-alpha responses were compared to upper-alpha power during eyes closed resting state. The time course of the task was characterized by two different behavioral conditions: (1) a pre-event epoch, in which the subject awaited the virtual onset of the omitted tone, (2) a post-event epoch (after button pressing), in which the subject was in a post-motor response condition. The principal findings are: (i) during the waiting epoch, only healthy elderly had an upper-alpha ERD at the level of both temporal and posterior brain regions; (ii) during the post-motor epoch, the aMCI patients had a weaker upper-alpha ERS on prefrontal regions; (iii) only healthy elderly showed a laterality effect: (a) during the waiting epoch, the upper-alpha ERD was greater at the level of the right posterior temporal lead; (b) during the post-motor epoch, the upper alpha ERS was greater on the left prefrontal lead. The relevance of these findings is that the weaker upper-alpha response observed in aMCI patients is evident even if the accuracy of the behavioral performance (i.e., button pressing) is still spared. This abnormal upper-alpha response might represent an early biomarker of the attention-executive network impairment in MCI due to Alzheimer's disease.

TMS-EEG decay artifact: a new adaptive algorithm for signal detrending

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TMS-EEG represent one of the most promising methods in the investigation of the brain dynamics. However, during EEG, the discharge of TMS may generate a decay artifact that can last for tens of milliseconds. Such artifact represents a problem for the analysis of the TMS-evoked potentials (TEPs). So far, two main strategies of correction have been proposed involving the use of a linear detrend or independent component analysis (ICA). However, none of these solutions may be considered optimal: firstly, because in most of the cases the decay artifact shows a non-linear trend; secondly, because the ICA correction (1) might be influenced by individual researcher's choices and (2) might cause the removal of physiological responses. Our aim is to verify the feasibility of a new adaptive detrend by comparing it with the ICA correction. Thirty-six healthy volunteers were stimulated with 50 TMS pulses over the left M1. The peak-to-peak amplitude and the morphology of the TEPs were compared among three conditions: RAW (no correction of the decay artifact was applied); ICA (the decay components were extracted and removed by ICA); ALG (the decay artifact was corrected through the use of an adaptive algorithm). To assess whether the artifact correction significantly affected also the physiological responses to TMS, we examined the differences in the -100 +400 ms time window after the TMS pulse, across the three conditions, by means of a non-parametric, cluster-based, permutation statistical test. Then, we compared the peak-to-peak TEPs amplitude within the detected time windows. The grand-averaged EEG response revealed 5 main peaks: P30, N45, P60, N100 and P180. Significant differences (i.e. Monte Carlo p-values < 0.05) among the three conditions were detected in a cluster nearby the TMS coil, and specifically over FC1 (all the components); CP1 (P30/N45 and N45/P60) and FC2 (N45/P60 and P60/N100). Repeated-measures ANOVA revealed a higher peak-to-peak amplitude in 5 of the 8 TEPs after ICA correction, compared to the RAW and ALG conditions. Our results showed that the ICA correction significantly affected the amplitude and the morphology of most of the analyzed TEPs. On the other hand, when our algorithm was used, the amplitude and the morphology of the peaks did not differ from the original signal (i.e. RAW condition). The present results showed that our adaptive detrend is a reliable solution for the correction of the TMS-evoked decay artefact, especially considering that, contrary to ICA, (1) it is not dependent from the number of recording channels, (2) it does not affect the physiological responses and (3) it is completely independent from the experimenter's choices.

Inter-hemispheric interactions between brain stimulation procedures in a highly lateralized brain function

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Many cerebral functions are lateralized, i.e. they rely on the activity of a specialized (dominant) cortical region in one hemisphere. The role of the contralateral (non-dominant) cortex and its interplay with the dominant cortex are matter of debate. In the present study inter-hemispheric relations were investigated by means of bilateral cortical stimulation in a well-established lateralized function such as spatial attention. The symptom of contralateral hemi-inattention is produced mainly by right-sided lesions. This asymmetry is explained alternatively by models that imply inter-hemispheric competition, inter-hemispheric collaboration or inter-hemispheric independence. The aim of this study was to investigate inter-hemispheric dynamics of spatial attention in healthy individuals. Two Experiments were run. In the Experiment 1 we verified whether single Transcranial Magnetic Stimulation (TMS) pulses applied over the right parietal cortex (CP4/P4 coordinates) 150 ms from the tachistoscopical presentation of a bisected line could induce a right shift in the perceived midpoint. Experiment 2 was run to investigate inter-hemispheric interactions. The "neglect-like" effects of right parietal TMS shown in Experiment 1 were primed with 15 minutes of cathodal transcranial Direct Current Stimulation (tDCS) previously applied to the contralateral left hemisphere (CP3/P3 coordinates). Control conditions included Sham TMS and Sham tDCS in a 2 × 2 design. The subjects' performance was measured by d' analysis and by fitting the responses to a psychometric curve and subsequent extraction of the threshold and slope. The results of Experiment 1 confirmed that single-pulse TMS over right parietal cortex delivered at 150 ms from stimulus onset can transiently induce effects equivalent to neglect in healthy individuals. The results of Experiment 2 indicated that left tDCS alone was capable of inducing contralateral hemi-inattention. The effects of right TMS were not modified by left tDCS. The results support an independence model of inter-hemispheric interactions in attentional functions, though a collaboration model cannot be excluded.

Temperament, character and QEEG in children with ADHD-C and ADHD-C+ODD

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Low levels of harm avoidance, reward dependence, self-directedness (SD), cooperativeness (C) and high novelty seeking (NS) are the distinctive temperament and character traits of ADHD-C children when assessed with Junior Temperament Character Inventory (JTCI). Typical patterns of resting EEGs in ADHD children show abnormal values of absolute power in theta, alpha and beta bands while frontal hyper-coherence in the theta and beta bands. ADHD is frequently associated with oppositional defiant disorder (ODD) but no clear neurophysiological evidence exists that distinguishes the two groups. Aim of this study is to combine personality inventory and qEEG to identify biomarkers that could be used to discriminate between the two groups. 29 ADHD-C and 22 ADHD-C+ODD children participated in the study. All the subjects met the DSMV criteria for these disorders. JTCI and 2-5 minutes of artefact-free EEG were collected and analysed. Stability based Biomarkers identification, a modification of the technique proposed by Wehrens and colleagues, 2011 was applied to the JTCI and to the EEG separately and combined. This technique is aimed to diminish the negative effects produced by the high number of variables, compared to the small number of subjects. The biomarkers are extracted in a multivariate analysis, which preserves the correlation between the variables, eliciting a group of biomarkers with a reasonable predictive performance. To measure the classification power of the selected set of biomarkers the stable ROC technique was used. The ROC area was calculated for the 10, 20 and 100% of False Positive (FP). The ADHD-C+ODD children had significant higher values of NS (Z score = 2.35), and significant lower values of SD (Z score = -2.39) and C (Z score = -2.88) than ADHD-C children. TCI measurements showed a high regression between the two groups: SD (m = -1.3, p < 0.001) and C (m = -2.4, p < 0.001) showed the highest scores during the biomarkers selection procedure (90%). NS (m = 0.86, p < 001) was selected about 70% of the times. t-tests of qEEG (FDR corrected for multiple comparisons) for all sources and frequencies revealed group differences at 1.95 Hz and at 9.75 Hz (ADHD-C<ADHD_C+ODD). The classification method showed that TCI and qEEG when analyzed together, had the best discriminant power, especially at the low FP range (AUC = 0.9 at FP = 0.10, AUC = 0.96 at FP = 0.20). The most significant classifiers (channels and frequencies) were F4 at 1.17 Hz and at 5.47 Hz and F8 at 17.58. The right prefrontal and frontal areas that regulate attention and behaviour are impaired in the two groups.

Visuospatial attention in cerebral palsy: an eye movement study

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The tight link between visuospatial attention and eye movements has been well-established from behavioral and neurophysiological studies. Moreover, neuroimaging evidence strongly supports the hypothesis that oculomotor areas provide signals for overt and covert shifts of attention. However, albeit in a more complex way, visuospatial attention interacts also with other goal-directed motor systems, such as those controlling limbs for common visually-guided tasks (e.g., ambulation or pointing, reaching and manipulating salient objects). Furthermore, early motor deficits might affect the development of the attentional system. In the present study we tested visuospatial attention abilities in 7 children (5 males, mean age: 11.6 years) with cerebral palsy (CP), which is one of the most common cause of physical disability in childhood. All CP subjects suffered from spastic hemiplegia or diplegia. Visuospatial attention was investigated by recording eye movements while subjects executed visually-guided saccades randomly towards one of 4 possible positions marked by placeholders equally distributed around a central fixation cross. A cueing paradigm was also administered: a placeholder flashed for 50 ms (cue) at the same spatial position of the target (valid condition), or at a different location (invalid condition). The visual cue did not predict the position of the target, whose onset occurred 150 ms later. Saccade latency and accuracy of CP subjects were compared with those of a typically developing (TD) reference group of 13 participants (mean age: 12.3 years). On average, CP and TD subjects showed a similar performance in the saccadic task, being both groups quick to react to the onset of the visual target. Moreover, in the spatial cueing task, a coupling between the task-irrelevant location of the cue and the direction of a following overt shift of attention emerged, being saccadic latencies of CP and TD subjects faster to valid targets. However, PC children were more frequently (on mean, in 30% of trials) attracted by the onset of the cue, suggesting the tendency to execute ocular movements towards the target of the exogenous attention. Furthermore, during the fixation of the central cross, the CP group often performed saccadic intrusions, which were always aimed at orienting the gaze to one of the placeholder. This occurred irrespectively of whether CP children executed the saccadic or the cueing task and clearly shows a difficulty of patients to suppress overt ocular movements towards the target of the endogenous attention.

From a clinical perspective, the present work encourages efforts to design reliable procedures, using eyetracking techniques combined with cognitive protocols, aimed at improving the assessment of people suffering from motor impairments, in the field of neuropsychological, neurological and psychiatric aspects. Indeed, motor deficits make often difficult to apply procedures typically employed by clinicians and cognitive neuropsychologists, like paper-and-pencil tests or manual reaction time paradigms. This represents a crucial limitation in the diagnostic and rehabilitative fields considering that the brain damage that leads to CP, as well as to other neurological disorders affecting muscle tone, movement and motor skills, is usually accompanied by other deficits including visuospatial attention abilities.

Nocebo-induced changes of corticospinal excitability: a TMS study

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Behavioural evidence shows that believing in the detrimental effects of a treatment on motor performance leads to a worse motor outcome (the so-called nocebo effect). The neurophysiological underpinnings of this effect are still completely unknown. By using transcranial magnetic stimulation (TMS) over the primary motor cortex, we investigated whether a nocebo modulation of force could change the excitability of the corticospinal system. A total of 36 healthy volunteers were recruited and divided into two groups: experimental (18 subjects) and control (16 subjects) group. Force production was obtained by asking participants to perform abduction movements with the right index finger against a piston connected to a force transducer. We designed a protocol consisting of three sessions: baseline, manipulation and final. The baseline and final sessions were identical in the two groups and served to control any nocebo effect, which was instead induced during the manipulation session. To induce this effect, we applied a treatment consisting of peripheral low frequency transcutaneous electrical nerve stimulation (TENS) for 5 minutes over the muscle specifically involved in the task (i.e., the first dorsal interosseous, FDI). Low-frequency TENS is completely inert in affecting motor performance. Nonetheless, the experimental group was instructed that the treatment would have induced a reduction of force. To condition the subjects about the effects of TENS a visual feedback on their force level was provided and surreptitiously reduced after the treatment. At the end of the instructive nocebo procedure we found that the subjects of the experimental group had lower levels of force ($p < 0.001$), felt to be weaker ($p < 0.001$) and expected to perform worse ($p = 0.009$) compared to the control group, who was not suggested about TENS. Moreover, by delivering the TMS pulse when all the subjects exerted the same amount of force (thus ruling out bottom-up

influences), we recorded the amplitude of the motor evoked potentials (MEP) from the FDI muscle and from the abductor digiti minimi (as control), and the duration of the cortical silent period (CSP) from the FDI. We found that the experimental group presented a modulation of corticospinal excitability, as shown by decreased duration of the CSP across the baseline and final sessions ($p < 0.001$). MEP amplitude, instead, did not change across sessions and between groups. The change of CSP duration, and not of MEP amplitude, would suggest that the nocebo procedure may impact more on inhibitory circuits rather than on excitatory circuits. These findings hint at a top-down modulation of corticospinal excitability, as a neural signature of nocebo modulations in motor performance.

Motor imagery, movement observation and movement execution: cerebral hemodynamic patterns in fNIRS

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Previous studies have shown congruent cerebral activation during motor imagery, movement observation and movement execution. Moreover, recent neuroimaging studies have reveled similarities in hemodynamic patterns between motor imagery and movement execution as well as motor imagery and movement observation. The aim of this study was to investigate differences in hemodynamic responses among these three conditions, pointing out the contribution of motor areas. We used a fNIRS event related paradigm in co-registration with EEG. Healthy right-handed participants were asked either to imagine, observe or execute right hand movements. During the tasks, changes in oxygenated and deoxygenated hemoglobin were recorded in the left fronto-central, central and parietal areas with fNIRS (24 channel - 8 detectors and 8 injectors). Cerebral activity was simultaneously recorded by EEG. Data analyses showed variations in hemodynamic responses across the conditions, with significant similarities between motor imagery and movement observation. Therefore, the present results showed that differences in hemodynamic profiles are congruent with the type of motor task. Specifically changes in hemodynamic responses within motor areas mirror the specific role of cortical areas underpinning the tasks. Moreover, there are preliminary evidences of a congruent modulation of EEG data in relation with hemodynamic data.

Neuromodulation (tDCS) effect on executive functions in healthy aging: clinical and EEG evidences

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Physiological aging is a dynamic process that, despite an increase in physical and cognitive frailty, gives opportunities for maintaining and strengthening the quality of physiological, cognitive and emotional processes. As suggested by research on cortical plasticity, the re-activation of networks mediating cognitive functions by means of cognitive and electrophysiological interventions may lead to an improvement of function-specific and global functioning. In particular, brain stimulation techniques proved to efficaciously increase performances and functional profile of patients affected by neurodegenerative disorders, but their potential contribution in the empowerment of healthy elderly and prevention of cognitive decline is understudied. Moreover, traditional neuromodulation protocols usually measure treatment outcomes in terms of behavioural performances, while the integration with psychophysiological measures might help in depicting a clearer picture. The present research aims at investigating the efficacy of a non-invasive brain stimulation protocol (tDCS) applied to prefrontal areas in empowering executive functions and automatic attention responses (ERPs) in healthy elderly people. 22 volunteers took part to the study and were assigned to the treatment (11 participants) or control (11 participants) group. Both groups were tested at T_0 and re-tested after three months (T_1). The assessment procedure included both a series of standardized neuropsychological tests aimed at sketching a complete picture of individual cognitive profile and the recording of electroencephalographic responses during a challenging computerized attentional task. The tDCS intervention protocol lasted 8 weeks and included three stimulation sessions per week (15 minutes, 1.5 mA, anodal placement over right dlPFC with cephalic reference), with twice-weekly administration of tasks tapping on non-verbal executive functions. Analyses comparing T_0 and T_1 data of the experimental and control groups showed a significant increase in post-intervention performances for participants undergoing the tDCS protocol, in particular with respect to non-verbal and verbal executive functions – i.e. Raven's Progressive Matrices total score, errors at the Stroop's test, and verbal associative fluency. At the end of the empowerment protocol, the neuromodulation group also showed early differences in attention-related ERPs for incongruent stimuli in a computerized Stroop-like task. Present evidences suggest that a non-intensive neuromodulation protocol may mediate the empowerment of specific cognitive functions in healthy aging people by capitalizing on brain and cognitive reserve, and hint at interesting practical implication for prevention and early intervention.

The effect of the rubber hand illusion on motor cortex excitability

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During the rubber hand illusion (RHI), subjects experience an artificial hand as a part of their own body; furthermore, subjects misjudge the position of their real hand and show a proprioceptive drift toward the RH. It has been proposed that during the illusion the subject's hand-centered reference frame shifts to the RH, entailing a disembodiment of the real hand. Indeed, previous studies suggest that inducing the RHI produces a decrease in the disembodied hand temperature; moreover, cooling down the subject's hand increases the strength of the RHI, while warming decreases it. Here, we investigate the modulation of the real hand parameters during RHI from a motor point of view, hypothesizing that the excitability of motor pathways to the disembodied hand will also be decreased during RHI. If the real hand disembodiment decreases the excitability of the hand area in the primary motor cortex (M1), we expect an amplitude decrease of Motor Evoked Potentials (MEPs) recorded in a muscle of the subject's hand during RHI, compared to a control condition. During the experiment all subjects (N = 14) were tested in two conditions: synchronous visuo-tactile stimulation of the right index finger (RHI condition) and asynchronous stimulation of the same (control condition). MEPs were elicited by a single transcranial magnetic stimulation (TMS) of the hand area in the left M1 and recorded from the right first dorsal interosseus muscle (FDI). In each subject 20 MEPs were recorded in both conditions 2s after the end of each visuo-tactile stimulation, which lasted 12s. The illusory experience was evaluated by a standardized questionnaire and the proprioceptive drift by perceptual judgement. Behavioural results show a significant effect of the RHI, i.e. significantly greater values, for both questionnaire and proprioceptive drift, in the synchronous versus the asynchronous condition, and a positive correlation between questionnaire and proprioceptive drift. Physiological results show that MEP amplitude is significantly reduced in the synchronous condition with respect to asynchronous control, in which no MEP modulation was measured; in fact in each subject MEP amplitude in the asynchronous condition was comparable to that of MEPs recorded without any hand stimulation. Furthermore, a significant negative correlation between MEP amplitude and strength of the illusion, reported in the questionnaire, was found. This study provides the first physiological evidence that the real hand disembodiment during the RHI is accompanied by a significant drop of motor excitability recorded in M1, and shows that MEP amplitude

decrease is directly related to the strength of the subjective experience of the RHI. Furthermore, these results contribute to the theoretical understanding of the link between body and movement, suggesting that motor readiness and sense of body ownership are strongly linked, i.e. that the bodily self-awareness depends on the possibility of movement.

Attentional dysfunction after cerebellar stroke: a P300 case report

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The functional domain of the cerebellum extends beyond its traditional role in motor control. In recent years this structure has increasingly been seen as playing a crucial role also in cognitive processes, supported by observations of cerebellar activation demonstrated by functional imaging studies performed during cognitive tasks, as well as by findings showing that cerebellar lesions produced impairment in cognitive tasks. We investigated the psychophysiological profile of attentional processing of the stimulus in a patient with a cerebellar stroke using P300 component both during the acute phase and during four weeks of follow-up. A 55-year-old man with a history of diabetes mellitus presented with headache in the occipital region and generalized asthenia. At admission, neurological examination revealed a deviation to the left of the index test and of gait star. Diffusion-weighted imaging showed an acute ischemic lesion in the left posterior cerebellar hemispheric cortex, supplied by the posterior inferior cerebellar artery. MMSE, BDI and STAY1-2 and MICARS were administered to assess cognitive, neuropsychiatric and motor status; moreover, patient underwent a psychophysiological evaluation consisting of a classical auditory P300 oddball paradigm at 24 hours from stroke (T_0), after two weeks (T_1) and after four weeks (T_2). The patient correctly performed required tasks during each ERPs recording. Measurements of P300 component at T_0 and T_1 revealed lower amplitude in the patient than in the group of 10 controls matched for age and gender (T_0: Cz $p = 0.05$, Pz $p = 0.01$; T_1: Cz $p = 0.07$, Pz $p = 0.01$). Latency and amplitude of P300 component were comparable to the controls only at the third ERPs evaluation (T_2). The MICARS score improved after two weeks and then remained stable ($T_0 = 11$, $T_1 = 3$, $T_2 = 3$). The early abnormality of the P300 component after stroke suggests a dysfunction in the attentional processing of the stimulus as a result of a focal cerebellar lesion. This ERP component, in fact, reflects activation of a complex neural network involved in attention and memory processes. P300 amplitude seems to normalize progressively after stroke thus indicating a recovery of the cognitive

functioning that was preceded and paralleled by improvement in skilled movements (as indexed by MICARS scores), suggesting that the functional recovery of the cerebellum played a pathophysiological role in both motor and cognitive performances. Reasonably, reduced P300 amplitude results from dysfunction of the cerebellar projections towards prefrontal and posterior-parietal cortices that are crucial for attentional processes. Thus, after a cerebellar stroke, a cerebello-cerebral diaschisis may be the pathophysiological cause transiently inducing a failure in engaging the networks responsible of the attentional and discrimination process of the stimuli.

Psychophysiological aspects in DiGeorge syndrome: psychotic risk and ERPs correlates

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The 22q11.2 deletion syndrome (Velocardiofacial/DiGeorge syndrome; 22qDS) is a neurogenetic disorder resulting from a hemizygous deletion. Individuals with 22q11DS present with a wide range of clinical manifestations (congenital cardiac and palate defects, calcium deficiencies, immune problems); an increased risk of behavioral and neurocognitive *sequelae* throughout development have been reported. Approximately 30% of individuals develops a psychotic disorder in adolescence or early adulthood, making this syndrome one of the largest known genetic risk factors for schizophrenia. Attentional deficits and anxiety disorder are core symptoms of schizophrenia. ERPs could represent an useful approach to detect psychophysiological changes over the course of the disease. The aim of this study is to evaluate some psychophysiological aspects in patients with DiGeorge syndrome in the attempt to recognize earlier specific features able to provide pre-clinic evidence predictive of a possible evolution towards schizophrenia. Eight subjects with 22q11DS (median age 28.6-29.8 ± 2.3 yrs), eight psychotic patients and eight matched healthy controls underwent a psychophysiological assessment. CNV and P300 (oddball and Novel paradigm) were recorded. CNV amplitude (total area and two temporal windows, W1 and W2), and P3 parameters were measured. A total CNV area decrease was found in 22q11DS patients with respect to psychotic and healthy controls (p = 0.04 and p = 0.07 respectively). A slight difference was evident at W1 in 22q11DS patients and psychotics vs controls. A N1 latency reduction was observed in 22q11DS patients during Novelty P3 paradigm (p = 0.03). Psychophysiological changes in CNV and P3 latency and amplitude have been repeatedly found in schizophrenic patients and interpreted as a deficit in attentional processes. Data related to our DiGeorge subjects suggest a possible frontal involvement of attentional processes in absence of a psychiatric symptoms. A follow-up study could confirm a predictive role of these ERPs findings in this syndrome.

Nociceptive blink reflex habituation biofeedback in migraine: a randomized control trial

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Reduced habituation of the Nociceptive Blink Reflex (NBR) is considered a trait marker for the genetic predisposition to migraine. In this open-label randomized controlled study, we aimed to test the efficacy of a biofeedback training based on the learning of habituation of NBR compared with no treated patients in a cohort of migraine without aura patients eligible for prophylaxis. Thirty-two migraine patients were randomly assigned to three months treatment by (1) NBR biofeedback, (2) no preventive treatment. Frequency of headache, disability, anxiety, depression, sleep, fatigue, quality of life, allodynia and pericranial tenderness were evaluated. NBR biofeedback reduced R2 area and restored R2 habituation. It was able to reduce frequency of headache and disability, and to ameliorate physical features of quality of life. This study confirms the usefulness of methods of autogenic training and behavioral stress coping on cortical mechanisms predisposing to migraine attack. Further long term trials may clarify the duration of clinical effects and the best treatment design.

A no-stimulus/no-response P3: fMRI meets EEG. A preliminary report

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Aim of the present study was to investigate the cerebral sources of the visual P300 event-related potential (ERP) analyzed with simultaneous recording of electroencephalographic signal and functional magnetic resonance (fMRI). Both techniques supply a functional exploration of the brain, but with different perspectives. The combination of the high temporal resolution of EEG with the high spatial localization provided by fMRI makes it possible to map with great accuracy the neural circuitries subserving cognitive processes. We used a standard visual "oddball" paradigm, in which target

stimuli were unpredictably intermingled with frequent stimuli. In addition to this, we applied a similar paradigm, in which the stimulus was randomly omitted (target) in a sequence of regularly presented visual stimuli. Both conditions were preceded by a trial in which the subject gave no attention to the stimuli (passive condition). The rationale for such protocol was to detect the neural generators of P300 excluding from fMRI analysis the cerebral sites specifically responding to visual stimuli. The EEG data showed a clear N1/P3 complex during the standard "oddball" paradigm, whereas during the "omitted stimulus oddball" only a P300 component, with reduced amplitude and increased latency (about 700 ms, compared to 400 ms in the standard paradigm) was observed. fMRI showed, during the standard "oddball", prevalent activations in lateral frontal, fronto-operculum, anterior insula regions, prevalently on the right side. Minor activations were observed bilaterally in the parietal cortex near the infraparietal sulcus and in posterior temporal regions, always prevailing on the right hemisphere. During the "omitted stimuli" paradigm, fMRI showed activations in the very same positions but with a greater intensity. During the standard "oddball", but not during the "omitted" paradigm, there was a further activation in fronto-mesial regions with extension to medium cingulate. Our fMRI data show and confirm activation in frontal and parietal brain regions often referred to as the attention network. Interestingly, this network proved to be active also during the "omitted stimuli" paradigm, establishing its endogenous nature. The combined use of EEG and fMRI is a powerful tool for research in neuroscience: a short comment on the technical and methodological challenge it presents will be provided in the platform presentation.

Beyond the "Bereitschaftspotential": action anticipation and cognitive functions

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The "Bereitschaftspotential" (BP or readiness potential), discovered exactly 50 years ago by Kornhuber and Deecke, identifies the negative electrocortical activity preceding motor acts. This response-locked activity is now termed as motor-related cortical potential (MRCP). For self-initiated movements the earliest MRCP component, the BP, initiates 1-3 s before the movement onset over the fronto-central areas of the scalp: it reflects the slow increasing cortical excitability and subconscious readiness for the

forthcoming movement. Starting 400-500 ms before movement onset, the excitability increases more rapidly showing a steeper negative slope (NS' component) reflecting stages of movement preparation often associated with conscious decision of movement. The MRCP is influenced by factors such as movement complexity and timing. The BP originates from the supplementary and cingulated motor areas, while the premotor and motor areas are the main sources of the NS'. The present review aims to update the MRCP literature presenting our recent results in studies investigating complex self-initiated actions as praxic, virtual, fatiguing or incompatible movements, also including self-administration of emotional pictures. Discriminative responses to external stimuli are also considered. These studies show that the MRCP does not reflect a mere "motor" preparation in premotor brain areas and does not only depend by the kinematic complexity of the upcoming action. We have shown that at least two additional associative areas, i.e. the prefrontal cortex (PFC) and the posterior parietal cortex (PPC), are engaged when the actions to be enact are cognitively demanding. Early positivity in the PFC was associated to: (a) awareness of inability to accomplish an action; (b) expectancy of self-administrated arousing pictures; (c) bimanual incompatible actions and (d) action perceived as fatiguing. Otherwise, early negativity in the PFC was associated to top-down control in a discriminative response task; fast polarity inversion of this activity was related to disengagement of this control. The PPC activity showed the earliest pre-movement activity (earlier than premotor areas activity) for pantomimed praxic movements, real grasping actions, virtual grasping actions triggered by key-presses and even for observed actions. These works extend the literature on the neural basis of action planning and contributes to clarify interactions between prefrontal, frontal and parietal cortices. Concluding, the action preparation phase is deeply affected by cognitive factors as task complexity, action meaning and its consequences (practical and emotional) and by the awareness of being fatigued or unable to act. Therefore, beyond the Bereitschaftspotential, during action anticipation, we can catch glimpses of the foundation of cognitive functions.

Are negative emotions the key for everyday beauty appreciation? A subliminal emotional prime study

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Emotions seem to be an essential part of the phenomenology of aesthetic experiences. Recent studies, using affective priming procedures, have shown that the emotional state of an individual contributes to his aesthetic judgments of abstract, ambiguous images. However, in our daily life, we evaluate a series of non-abstract, representational stimuli among which the body is particularly relevant for socio-emotional behaviour. The present study aimed at addressing the possibility to modulate the

aesthetic judgment of body images through the subliminal presentation of emotionally charged images. Twenty-two participants (10 males, average age 23.7 ± 2.8), non-experts in visual arts, took part in the experiment. They were asked to evaluate a set of target stimuli, preceded by arousal-matched positive or negative primes selected from the International Affective Picture System. Neutral emotional primes were used as controls. Target stimuli were either body or abstract images, half static and half dynamic, matched for their basic visual features. Primes were presented subliminally, and were preceded and followed by their scrambled versions so as to be masked. Participants were requested to evaluate (along a visual analogue scale) the beauty and the emotion evoked by the target stimuli. Emotional and beauty judgments reported by participants were considered as dependent variables. At the end of the priming experiment, in order to be sure that the primes were actually subliminal, we included a recognition task in which the masked primes were presented again and the participants were asked to report if they saw anything between the two masks, and if so, to provide details on what they had seen. Subjects who recognized more than 1/5 of the total number of primes were excluded from the analysis. Results showed higher beauty ratings for both abstract and body images when primed with negative emotional images, rather than when primed with positive emotional images. The neutral prime left the aesthetic judgement between the positive and the negative ones. This influence of the prime was specific for the beauty judgment, while being absent for the emotional one. Our result of a rebound from negative emotions to positive evaluations (and vice versa) expands a previous study in which participants evaluated abstract artworks in a significantly more positive way after watching scaring videos. Thus, inducing a given emotional state (in particular a negative one) influences the subsequent aesthetic evaluation of body images. Therefore we show a clear link between emotions and aesthetic evaluation and extend previous research on abstract work by investigating the effect on body images.

A report of transcranial electrical stimulation induced sensations

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Transcranial electric stimulation (tES) is described as a safe and not-painful technique. Nevertheless, in literature there are few reports describing in detail the sensations reported during the stimulation, with different type of currents and different parameters of stimulation. The aim of this work is to clarify if different types of currents (direct-tDCS vs alternating-tACS vs random noise-tRNS) induce different sensations, and to study if the modulation of parameters such as the timing of application and the level of current density and intensity influence these reports. We here

analysed the data of 493 young subjects relating to 598 different sessions of stimulation, collected over the last years in our laboratory (sensations questionnaire published in Fertonani et al., 2010). We first analysed a general annoyance index including all the perceived sensations (e.g., pain, irritation, heath, iron taste, fatigue), then we looked at the more perceived sensations in the different stimulation conditions. A generalized linear model (Poisson distribution for dependent variable with log link) was adopted for evaluating the effects of different factors: *type of current* (three levels: tDCS, tACS, tRNS), *polarity/frequency* (anodal, cathodal, 6 Hz, 10 Hz, 25 Hz, high frequency, low frequency, placebo), *timing* (online, offline) and *density* (four levels: from 0.050 mA/cm^2 to 0.200 mA/cm^2), on the annoyance index. tRNS and tACS seems less perceivable than anodal and cathodal tDCS, regardless of their timing of application. Interestingly, placebo stimulations are not differently perceived from real ones. The effect of the density of the current on the perceived sensations is not linear. The densities of 0.070 and 0.200 appears more perceived than 0.050 and 0.100. Moreover, identification of any patterns in annoyance data in order to highlight their similarity or differences was performed through the principal component analysis. A strong correlation detected by a common pattern, also under different stimulation conditions, was found for heath, irritation and itch. Quite different from the others annoyances appear iron taste and fatigue that seems to suggest two different patterns. In conclusion, our results shown that tDCS is more perceived than tACS and tRNS. Therefore, tRNS and tACS seem ideal to design experimental trials because of their imperceptibility. The sham stimulation is a good placebo method, and is indistinguishable from real stimulation. The most commonly reported sensations are in all cases itching, burning and pinching, with a mild level of intensity.

Reward system, metacognitive control and ERP effect in gambling behavior

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Recent studies showed that pathological gambling is associated with deficits in frontal lobe function and that pathological gambler subjects used to opt in favour of immediate reward, without considering the long-term outcomes like patients with bilateral VMPFC lesions or addictive disorders. Many previous researches tested the ability to distinguish between high- and low-risk decisions and the learning effect based on previous experiences by a typical decisional task such as the Iowa Gambling Task (IGT). Considering specific ERP effects like the feedback negativity (FRN) and the P300, frequently used to explore the impairment of the executive functions in decisional processing, the aim of this study was to analyze behavioral responses, meta-cognitive strategies, and ERP (FRN and P300) effects which are supposed to

be predictive markers of gambling behavior. It was also supposed that high-BAS (high Behavioral Activation System) subjects, who generally are more reward-related, should show inability in monitoring reward predictor errors mainly in case of loss options: specifically we expected the absence of FRN increased amplitude in response to negative outcomes and a substantial equivalence of the P300 amplitude in response to gains and losses. BAS-reward measure was applied to distinguish between high-BAS and low-BAS traits in twenty-two healthy subjects (ten women, age range 19-25, M = 23.78). They were instructed to IGT and the EEG was recorded during the task, measuring left, central and right frontal (F3, Fz, F4), middle-central (Cz, C3, C4), temporo-parietal (P3/T7, Pz, P4/T8) and occipital (Oz, O1, O2) brain activity. After this session a questionnaire was applied to test the general self- knowledge of the cognitive strategy adopted. Results showed a significant decreased IGT rI Index for high-BAS than low-BAS, since the former were focused on the immediate reward (losing long-term strategies). Moreover the high-BAS group showed a significant decreased self-representation of a planned strategy, flexibility, and efficacy. According to the ERP effect related to feedback monitoring (FRN) and attentional mechanisms (P300), the high-BAS group in comparison with the low-BAS showed a significant reduction of the classical "enhanced effect" in response to unattended feedback. Moreover, sLORETA analysis showed that the cortical source for FRN effect was localized over the Dorsolateral Prefrontal Cortex and the ACC, while for P300 the effect was on the Superior Temporal Gyrus. Thus, deficiencies concerning feedback mechanisms were apparent in those individuals extremely focalized on reward (reward bias) if compared to individuals who did not base their decisions on immediate reward. In conclusion it is possible to consider reward salience as an important aspect in feedback processes in subjects with high-risky attitudes.

Defensive responses in brain-damage patients with pathological embodiment of someone else's body part

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Our research focused on a monothematic delusion of body ownership, in which brain-damaged patients systematically claim that the examiner's hand is their own hand (E+ patients). Previous studies have shown that this delusion of ownership is not merely a verbal confabulation, but reflects an embodiment mechanism able to alter the patients' motor and somato-sensory behaviors. In the present study, we explored, in 4 E+ patients and in healthy controls, how defensive responses are modulated by the sense of body ownership. To this aim, we took advantage of the hand-blink reflex (HBR), a subcortical defensive response enhanced when the threated hand is

located close to the face, inside the defensive peripersonal space (DPPS). Here, we investigated weather in E+ patients the magnitude of the HBR is enhanced irrespective of whether the threat is brought by the own or the alien (embedded) hand. This paradigm, applied to E+ patients, can provide evidence of how top-down processes (i.e., the delusional belief that an alien hand is a part of the own body) can modulate physiological reactions. Electromyographic activity (EMG) was recorded from the orbicularis oculi bilaterallyand the HBR was elicited by delivering electrical stimuli to the median nerve at the wrist, in two different conditions. In the "own hand" condition the participant's hand was located either outside (far) or inside (near) the DPPS of the face; in the "alien hand" condition the examiner's hand was located outside or inside the participant's DPPS. Two separate sessions of the experiment investigated, either the "affected side" where the pathological embodiment occurred or the "intact side" where the pathological embodiment did not occur. In our results no difference between the E+ patients' intact side and the healthy controls was found: in both groups the far-near modulation (i.e. the HBR increase in the near with respect to the far position) was significantly higher in the own than in the alien condition. On the contrary, a significant difference between the E+ patients' affected side and controls was found, suggesting that, when the pathological embodiment occurs, the far-near modulation is the same for the own and the alien hand. The crucial aspect of this experiment is that, in the affected side, during the alien hand condition, E+ patients were convinced that the examiner's hand was their own hand moving close to their face. This altered sense of body ownership modulates the patients' defensive response: they showed the same HBR enhancement as that induced by the own hand. The key finding of the present study is that an alien hand that becomes a part of the own body triggers the same defensive physiological response as the real hand.

Hand blink reflex modulation during a voluntary movement

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In the context of motor cognition, the crucial role of intentional motor programs has been described within the predictive model of motor control. According to this model, once the motor commands are selected and sent to the periphery, a forward model is formed to predict the sensory consequences of the movement. Based on this predictive model, we investigated the role of the motor intention in modulating a defensive physiological response. To this aim, we took advantage from the Hand Blink Reflex (HBR), which is a subcortical response at the brainstem level, elicited by the

electrical stimulation of the wrist. We know that the HBR is modulated by the hand position: the response dramatically increases when the hand is located close to the face, inside the defensive peripersonal space. Here, we asked whether, on equal hand positions, the intentional direction of the hand movements (either up to the face or down from the face) can modulate the HBR. Electromyographic activity (EMG) was recorded from the orbicularis oculi bilaterallyin three different conditions, in which the subjects were asked a) to stay still ("static hand"), to move their arm close to the face ("up-moving hand") or far from the face ("down-moving hand"). In each condition, the HBR was elicited by delivering electrical stimuli to the median nerve at the wrist in three hand positions, depending on the amplitude of the elbow angle: with the arm frontally extended at ~180° ($\alpha 1$; far from the face); tilted at ~90° ($\alpha 2$; intermediate position); tilted at ~45° ($\alpha 3$; close to the face). We extracted the area under the curve (AUC) of each HBR average waveforms and we entered the obtained values in a repeated measure ANOVA with two between factors "condition" (three levels: static, up, down) and "angle" (three levels: $\alpha 1$, $\alpha 2$, $\alpha 3$). Our results showed a significant interaction angle*condition ($p = 0.0003$), suggesting that the same angle amplitude induces different HBR modulation, depending on the condition. In particular, in the "static hand" condition, we replicated the previously described HBR increase in $\alpha 3$ (near-position) with respect to the $\alpha 1$ (far-position). In the "up-moving hand" condition, the HBR increase in $\alpha 3$ was found with respect to both $\alpha 1$ and $\alpha 2$. Note that, on equal $\alpha 3$ angle (when the hand was close to the face), compared to the "static hand" condition, the HBR was significantly greater in the "up-moving hand" and significantly lower in "down-moving hand". Crucially, in the "down-moving hand", no difference between the three angles was found. This strongly suggest that, when the hand was close to the face but the subject is planning to go down, the predictive system can anticipate the final state of the movement: the "near" becomes "far".

Transcranial direct current stimulation (tDCS) and cognitive training in traumatic brain injured patients: focus on divided attention and its neural correlates

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Divided attention is defined as the ability to distribute cognitive resources among two or more simultaneous tasks. Following severe traumatic brain injury (TBI) such

a function could be compromised, resulting in problems in numerous activities of daily living. So far, there have been few studies aimed to analyze the effect of cognitive rehabilitation on attention improvement. In particular, no research has investigated whether the use of non-invasive brain stimulation associated with neuropsychological rehabilitation might contribute to a better and faster recovery of divided attention. Main purpose of this research is to assess the effectiveness of 10 tDCS sessions combined with a computerised training, aimed at improving divided attention in brain injured subjects. Specifically, we focused on the neural modifications induced by such a treatment. Sixteen subjects with a severe traumatic brain injury (Glasgow Coma Scale < 8) participated in the study. All participants were submitted to a neuropsychological evaluation one month prior to the beginning of the experiment (T_0). Such an evaluation was repeated the day before the training (T_1). In this occasion, each subject was also submitted to an fMRI session (MRI + divided attention paradigm). The training was characterised by 20' of tDCS, administered twice a day for 5 days. The electrodes were placed on the dorso-lateral prefrontal cortex, with the anode on the ipsilesional area and the cathode on the contralesional one. However, the specific electrode placement could vary for each patient depending on the location of the injury. After each session, the patient received 40' of a computerized cognitive training on divided attention. At the end of the treatment (T_2) TBI subjects were submitted to a third neuropsychological assessment, followed by a second fMRI session. Outcomes of the study highlighted an improvement of divided attention only between T_1 and T_2, resulting in faster reaction times (p = .0001), associated with decreased omissions (p = .0001). Furthermore, neuroimaging data resulted in a cerebral reorganization, associated with a lower cerebral activation following the training. In particular, a significantly lower activation in T_2 compared to T_1 was observed in right superior temporal gyrus (BA 42), right and left middle frontal gyrus (BA 6), right postcentral gyrus (BA 3) and left inferior frontal gyrus (BA 9). It follows that the cognitive and behavioral changes observed after our treatment may be related to modulations of neural plasticity. This neural reorganization may be explained as a sort of "balance mechanism": neural activations, which were wider and more generalized before the training, became more focal and task-specific after it.

Phantom learning: intermanual transfer of sequence learning in an amputee with phantom limb

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Amputees who experience a phantom limb sometimes report that their phantom has certain sensory properties, like touch and pain, as well as kinesthetic properties,

like being able to perform voluntary movements. Here, we focused on the motor domain and recruited one left upper-limb amputee (patient FC), who reported a vivid phantom limb and the ability to move it in a volitional manner. We asked whether the phantom movement go so far as leading to a motor learning, that, in turn, can be able to be transferred to the intact limb. To this aim, we took advantage from the intermanual transfer mechanism, that occurs when healthy subjects learn a motor skill with one hand and this results in performance improvement of the other hand as well. We tested patient FC and 10 aged-matched healthy controls, by using a sequence-learning task, in which the duration of the sequence execution was recorded with a sensor-engineered glove. The sequence duration was assumed as dependent variable to evaluate the ability to perform a fingers-thumb opposition sequence whit the right (intact) hand, before (naïve condition) and after a training with the left (phantom) hand. In the training phase, participants were asked either to actually execute the sequence (real condition) or to imagine it (imagery condition). The crucial aspect of this paradigm is that FC reported to be able to discriminate between the real and imagery training with her phantom. In healthy controls, results showed that, after a real training with the left hand, the ability to perform the sequence with the right hand was significantly improved with respect to the naïve condition (i.e., the sequence duration was significantly reduced). After the imagery training, no performance improvement was found (although the presence of a not significant tendency). Crucially, in FC, we found a significant performance improvement only after a "real" training with her phantom, suggesting the presence of an intermanual transfer. The first finding of the present study is that, in healthy subjects, an imagery training is not sufficient in order for the intermanual transfer to occur; a real motor learning seems to be necessary. In FC, we demonstrated that (a) volitional movements with a phantom limb can induce an intermanual transfer comparable to that evident in real movements; (b) motor execution and motor imagery with a phantom limb are functionally disentangled; (c) neural mechanisms underpinning the intermanual transfer continue to operate despite the prolonged absence of any proprioceptive or visual feedbacks. Converging evidence show that phantom limb is not "imaginary", but arises from physiological changes that occur after amputation. Here, we provided the first evidence that phantom limb can learn a motor skill and transfer it, through the callosal connections, to the intact limb.

Motor cortex excitability during linguistic and non-linguistic tasks in spasmodic dysphonia

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Adductor-type spasmodic dysphonia (ASD) is an adult-onset focal dystonia affecting laryngeal muscles during speech and other linguistic tasks. Its pathophysiology is largely unknown. In healthy subjects (HS), transcranial magnetic stimulation (TMS) applied during linguistic tasks discloses excitability changes in the dominant hemisphere primary motor cortex (M1). We investigated whether linguistic task-related M1 excitability modulation is altered in ASD. We studied 10 patients with ASD (4 drug-naïve and 6 patients chronically-treated with botulinum neurotoxin-type A-BoNT-A injections) and 10 age-matched healthy subjects. All participants were right handed. Speech examination included voice cepstral analysis. Single-pulse TMS was used to investigate excitability in the dominant and non-dominant M1 hand area at baseline and during various "linguistic" and "non-linguistic" tasks: (1) reading aloud of single words; (2) silent reading; (3) looking at meaningless non-letter strings; (4) oral movements without vocalization; (5) producing simple syllabic phonation. In healthy controls, the motor evoked potential (MEP) elicited by TMS of the dominant M1 were significantly larger during reading aloud. In ASD patients, MEP enhancement in the dominant hand emerged not only during reading aloud but also during syllabic phonation. BoNT-A improved speech as tested by cepstral analysis and restored the neurophysiologic abnormalities. We conclude that ASD is characterized by an abnormal excitability of the hand area of the dominant M1 during specific linguistic tasks. This likely reflects an altered functional connectivity between cortical speech network and M1. BoNT-A returns these excitability changes to normal.

Event-related potential correlates of word recognition memory in patients with coronary artery disease

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The relationship between left ventricular ejection fraction (LVEF) and cognitive performance in patients with coronary artery disease (CAD) without overt heart failure is still under debate. In the present study we combine behavioral measures and event-related potentials (ERPs) to verify whether electrophysiological correlates of recognition memory (old/new effect) is modulate differently as a function of LVEF. Twenty-five male patients with CAD (13 without [LVEF > 55%] and 12 with [LVEF < 40%] left ventricular dysfunction), and a Mini Mental State Examination score > 25 were enrolled. ERPs were recorded while participants performed a visual word recognition task consisting of a test phase in which they were asked to judge whether visual stimuli were previously presented in a learning phase ("old") or not ("new"). ERPs responses from the test phase were analyzed. A late positive ERP component between 300-500 ms was differentially modulated in the two groups: a clear old/new effect (enhanced mean amplitude for old respect to new items) was observed in patients without LVEF dysfunction; whereas patients with overt LVEF dysfunction did not show such old/new effect. These data suggest that ERPs may reveal possible functional brain abnormalities that might be not observed at behavioral levels.

Hemodynamic responses (fNIRS) and EEG modulation of prefrontal cortex during emotion processing

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The investigation of neural networks underlying emotion perception and recognition has received considerable attention during the past few years within the affective neu-

roscience domain. Neuroimaging studies revealed that the prefrontal cortex (PFC) is involved during emotional stimuli comprehension and evaluation, based on stimulus valence and arousal. Nevertheless, the way in which these emotional parameters affect hemodynamic variations has to be clarified. The present study investigated the changes in prefrontal hemodynamic activation by means of an event-related near-infrared spectroscopy (fNIRS) paradigm during the presentation of emotional patterns taken from the International Affective Picture System (IAPS). During the task, 20 subjects (12 females and 8 males) passively viewed neutral, positive and negative emotional images, which could also be low or high arousing (20 stimuli for each category). Stimuli were presented for 6 s in a randomized order, with 12s interstimulus interval. Hemodynamic and electrocortical (EEG) activities were simultaneously recorded from 6 NIRS and 16 EEG channels, in the same session. Changes in oxygenated (oxyHb) and deoxygenated (deoxyHb) hemoglobin were measured with respect to the different experimental conditions. Results showed that the emotional valence of the picture modulates the activation of the PFC, with increased activity for negative patterns and decreased activity for positive ones, if compared to neutral condition. Moreover, preliminary analyses revealed a consonance between EEG (frequency band oscillations) and hemodynamic responses. In conclusion, the present study revealed that prefrontal blood oxygenation and brain oscillations are differently modulated by the emotional content mainly related to the stimulus valence, and demonstrated that the PFC is involved in emotional processing.

Spatial attention effect on SEP components and their dipole sources differentiates migraine children with imploding pain from those with exploding pain

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Different physiopathological mechanisms are supposed to work in young migraineurs with either imploding (IP) or exploding (EP) pain (Iacovelli et al., 2013). A previous study demonstrated that in migraine children the N140 SEP amplitude increases during spatial attention as compared to a neutral condition, while in healthy subjects it does not. In the present study we aimed to: (1) extract the dipole source of the middle-latency SEP components, and (2) to compare the effect of spatial attention on SEP source strength between migraine children with either IP or EP. We studied 10 migraineurs with IP and 9 migraine children with EP. SEPs to median nerve stimulation were recorded from 31 scalp electrodes in a neutral condition (NC) and in a spatial attention condition (SAC), in which the subjects had to count tactile

stimuli delivered on the stimulated hand. Dipole sources of SEP components ranging from the central P40 to the vertex N140 potentials were calculated by using the Brain Electrical Source Analysis (BESA). Raw data analysis showed that the N140 amplitude increase during SAC was higher in EP than in IP patients, especially in the frontal region. In all our subjects, the scalp topography of SEPs recorded in NC was explained by a four-dipole model, including 2 dipoles in the perirolandic region contralateral to the stimulation and a bilateral opercular source. In EP migrainers, the tangential perirolandic source was more superficial during SAC than during NC. In IP migraine children, no reliable source location change was observed between NC and SAC. Our results suggest that the psychophysiological mechanisms underlying spatial attention are different in migraine children with imploding or exploding pain.

Virtual reality and planktonic elements: cognitive preference and 3D perceptions in marine biology students

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New Technologies are the news interaction and learning tools for new generation. In particular Virtual and Augmented Reality are highly relevant because are involved in embodied cognition. But there are very few study about how our brain percepts a 3D anaglyph object or a 3D immersive object and if the level of perceptions are conditioned by cognitive preference and by stimuli recognition. We worked about this field of application to understand the perceptual processing in Immersive Virtual Reality and 3D anaglyph perception, and to understand how to build a virtual reality movie based on Brain Computer Interface. The aim of this study was to understand how to build a neuroergonomic movie creating interfaces between the brain and the computer and investigating the modulation of ERP component P3 during a virtual reality task. For the construction of a Virtual Reality Movie with Planktonic Elements, for MAUS, a University Museum, we analyzed a set of images in 2D, and 3D active stereoscopic glasses (Maus objects 2D, Tarbosaurus 3D, Plankton 3D, Plankton 2D, colored screens 2D). The images have been presented with E-prime presentation, in the context of the museum. The images were presented with a Go-no Go paradigm (with E-prime 2.0 presentation) during an EEG and GSR recording.

Participants were instructed to press a computer key when they recognize an element living in the sea during a presentation of a set of random images in 2D, anaglyph and stereo active 3D. The task was in 3D immersive environment presentation. We recruited 8 university students of Marine Biology, and 11 University Students of Cultural Heritage (both groups were age and gender matched). All the subjects were volunteers and had normal hearing, normal or corrected to normal vision and had a right manual dominance. A GLM repeated measures analysis was computed on the amplitude and latency of the P300 component, RT and GSR. Main results of statistical analyses showed significant value in Group Condition and in the type of objects in perceptual modality and an effect Group x Image. Analyses for Lateralization showed a significant Value in Left Amplitude in direction of an increased amplitude in Left Hemisphere in group of Marine Biology students. In Image Condition we found an increased amplitude in Left Hemisphere for 3D picture too. In agreement with these results, we could say that an immersive 3D processing, is really different from a 2D or a 3D non-immersive. Also we can observe a different kind of arousal, in left side when the subject is competent, in right side when the analysis of the stimulus plankton is devoid from a semantic knowledge of the image. It can be concluded that the stimulus in virtual reality can be analyzed and studied in a much more precise 3D nature of a stimulus, the perception criteria of a 3D immersive normally are very different and that a neuroergonomic and neuroaestethic approach and must interface also with these perceptive products.

Advertising and consumer preference in Neuromarketing: rTMS and individual trait effects on decision-making

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The present neuromarketing research aimed at detecting changes in brain activity in response to commercial stimuli and goods to understand the impact of neurophysiological measures on marketing efficacy. This study explored the effects of subjective evaluation (self-report measures) and personality attitudes (BIS/BAS: Behavioural Inhibition and Activation System) on brain oscillation (Alpha, Beta, Theta, Gamma), in response to some consumer goods relative to different commercial sectors (alimentary, pharmaceutical, electronic, financial, clothing). Greater attention was given to the left DLPFC, an important area in decision-making processes. We adopted a combined rTMS (low-frequency 1 Hz on left and right DLPFC) and elettroencepalography (EEG) approach to determine the consumers' (N = twenty-four)

response during the vision of five commercials. Two control conditions were included in the experimental design to control both the simple inhibition effect (SHAM condition with absence of TMS stimulation) and the localization effect (control site condition, with the two half of the sample receiving either F3 or F4 stimulation). After the stimulation (TMS/SHAM) subjects evaluated goods and they were required to express their preferences by using semantic differential. The results showed higher left DLPFC theta activity in relationship to subjects with higher rewarding trait (BAS-Reward) during the vision of emotionally involving commercials independently from the valence of the good (more preferred and rejected goods). Moreover, some commercials engaged consumers and induced them to choose and prefer their goods, if compared to others. Specifically, theta modulation supported consumer's engagement, showing significant differences between some commercials (i.e. "Samsung", "Barilla"). Probably these brands were able to engage consumers, by inducing them to choose and prefer their products. Emotional and rewarding condition effects were adduced to explain the preference formation and the prefrontal cortical activity.

Preference, reward mechanisms and prefrontal cortex activation in multimedial artefacts

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The present research aims to explore the impact of reward mechanisms and their prefrontal (left dorsolateral prefrontal cortex, DLPFC) correlates to support cognitive and emotive processes in evaluating some multimedial artefacts. Implicit (brain oscillations and hemispheric lateralization effect) and explicit (subject evaluation) measures were considered in order to define the cortical network related to this reward mechanisms. These mechanisms were supposed to be frontally left-lateralized. Indeed, brain oscillations (delta, theta, alpha, beta) and lateralization effect (Log-Transformed-Asymmetry, LTA) were monitored within the prefrontal area, when subjects (N = 34) observed some brief commercial videotapes. Subjects were also required to explicitly evaluate each good (on eleven dimensions) and to express their preference on them. It was observed a more left DLPFC increased activity in response to videos evaluated as more emotionally involving and interesting. Moreover, as shown by regression analysis, left DLPFC was responsive to high rewarding condition, predicting the preferred artifacts. Therefore, a strong relationship was revealed between explicit and implicit measures based on reward mechanisms.

Responsiveness to the emotion and autonomic measures in syncopal profile: a preliminary study

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"E caddi come corpo morto cade" (And fell, even as a dead body falls). So in the fifth canto of Dante Alighieri's *Divine Comedy*, in what is probably the first literary description of an emotional syncope in the world literature. The neurally mediated syncope (NMS) known as neurocardiogenic syncope, or vasovagal syncope (VVS), or simply "fainting" is by far the most common cause, with 60% of the total prevalence of cases of syncope found. It is a common clinical problem in all age groups and affects 40% of people during their lifetime. Major lines of evidence suggest that NMS is not a disease, but a "characteristic" of the individual. Given that this reflex is sporadically displayed, the most likely hypothesis is a "heart protection mechanism" during particularly stressful and dangerous conditions. In fact, the slowing of heart rate induced by the vasovagal reflex may constitute a beneficial pause of cardiac pump. The purpose of this study is to explore the hypothesis of a psychogenic etiopathogenesis at the base of the NMS. Therefore, according to several studies' suggestions, we investigated the autonomic response to emotional stimuli with negative valence and high arousal that could be related to the mechanisms of anxiety, phobia and depression. For this reason, we examined a preliminary sample of healthy subjects to verify there is a significant increase in autonomic activity when people watch to these stimuli. Seven subjects took part to the experiment. The partecipants were requested to look to some images (IAPS pictures). The task was composed by four blocks of images interspersed by a brief pause; images were displayed on a computer screen. Images were divided into five categories, obtained by crossing of two emotion's dimensions: valence and arousal. The five categories, thus, were: positive valence and low arousal; positive valence and high arousal; negative valence and low arousal; negative valence and high arousal; neutral images. For the duration of the task, physiological measures were recorded through a biofeedback. At the end of the task subjects were asked to answer to some psychometric tests: Big Five Questionnaire (BFQ-2) for personality, STAI-Y for anxiety traits, Back's Depression Inventory (BDI-2) for depression traits and BIS BAS (Behavioral Approach System - Behavioral Avoidance/Inhibition System) for the role of behavioral inhibition and activation systems in relations to stimulus-situations. The results showed an increase in skin conductance (SCR) and pulse (PULS) values for the negative valence and high arousal stimulus category, also supported by psychometric indexes. The fact that this trend is impaired in subjects with a history of recurrent NMS has to be tested in a second phase. Indeed we supposed that this increasing of the autonomic measures is higher in NMS and it is followed by a sharp decline of these parameters, in agreement with the dominant theory on the NMS.

Cognitive vulnerability to levodopa therapy in ataxia-telangiectasia patients: a psychophysiological study

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Ataxia-telangiectasia (AT) is a human disease caused by mutations in the ATM gene. The neural phenotype of AT includes progressive cerebellar neurodegeneration, which results in ataxia, oculocutaneous telangiectasias, immunodeficiency, recurrent infections, radiosensitivity and proneness to cancer. No therapies are available for this disease. Experimental studies on mice showed severe degeneration of tyrosine hydroxylase-positive, dopaminergic nigro-striatal neurons, and their terminals in the striatum. The aim of the current study was to investigate the effects of the levodopa therapy on psychomotor performance and motor scores in AT patients using clinical and psychophysiological evaluation. 3 young AT-patients (age: 12 years) underwent a neurological evaluation and a CNV recording in basal condition (T_0) and at two times points after levodopa therapy (at 4 weeks – T_1 and 8 weeks – T_2). MICARS and UPDRS III scales were administered in order to assess clinical performance and disability. CNV amplitude (total and in two different temporal windows – W1, W2) was evaluated. Reaction times were also obtained. Total CNV amplitude (T_0 vs. T_2: Fz $p = 0.03$; T_1 vs. T_2: Fz $p = 0.05$, Cz $p = 0.07$), W1 (T_0 vs. T_2: Fz $p = 0.06$; T_1 vs. T_2: Fz $p = 0.08$) and W2-CNV areas (T_0 vs. T_2: Fz $p = 0.05$, Cz $p = 0.05$, Pz $p = 0.05$; T_1 vs. T_2: Fz $p = 0.01$, Cz $p = 0.04$) were significantly higher after 8 weeks of levodopa therapy than during basal condition and at 4 weeks of levodopa therapy. UPDRSIII values significantly improved after 8 weeks of L-dopa therapy (T_0 vs. T_2: $p = 0.004$). Our data suggest that levodopa treatment led to a significant improvement in motor performance in AT patients. Additionally, the ability to sustain attention during a double choice motor task appears to ameliorate after levodopa therapy. These results induce us to hypothesize the presence of a dopaminergic dysfunction likely related to a possible involvement of the subcortical networks in AT subjects as suggested by experimental studies.

Prefronto-cerebellar tDCS improves cognition in euthymic bipolar patients: preliminary neuropsychological and neurophysiological (P300) findings

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Bipolar Disorder Type I (BDI) and Bipolar Disorder Type II (BDII) are chronic and disabling conditions characterized by manic/hypomanic and depressive episodes. Cognitive disturbances seem to affect both the subtypes of BD, specifically in frontal executive functioning and verbal learning working memory. The aim of the current study was to verify whether the transcranial tDCS applied to cerebellar and prefrontal cortices could improve the cognitive functioning of euthymic patients with bipolar disorder or not, and assess the variation of the cognitive functioning and the global information processing stream through neuropsychological, neurophysiological and neurological measures. 25 BD outpatients underwent prefrontal (anodal) and cerebellar (cathodal) tDCS for 3 consecutive weeks. All participants were clinically assessed through neuropsychological and neurophysiological (P300) examinations at baseline and after tDCS therapy. Neuropsychological tests in the domains of visuo-spatial memory and attention improved significantly ($p < 0.05$) or showed a favourable statistical trend ($p < 0.07$) after the treatment. The patients who had worse baseline cognitive performances showed a more relevant improvement in all the neuropsychological domains investigated. After tDCS treatment the P3b component revealed a significant higher amplitude and shorter latency (Latency: Fz $p = 0.02$, Cz $p = 0.03$, Pz $p = 0.04$; Amplitude: Fz $p = 0.24$, Cz $p = 0.02$, Pz $p = 0.35$). In our study, prefrontal-excitatory and cerebellar-inhibitory stimulations lead to better global cognitive performances quantified through neuropsychological, neurophysiological and neurological assessments. This improvement could result from the normalization of prefrontal-talamic-cerebellum circuit activity pattern, that has been proven to be altered in BD. Prefronto-cerebellar tDCS may represent a useful therapeutic tools to increase the efficiency of standard treatment used for BD.

The many faces of attractiveness: one-night stand or a long-term relationship? Insights from ERPs

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Facial attractiveness plays a key role in emotional and social behavior. In addition to its purely aesthetic aspects, it is important to consider also those aspects of attractiveness that are related to emotional and motivational processes such as sexual attraction or mate choice. The goal of the present study was to characterize, by using event-related potentials (ERPs), the timing of the neural responses elicited by different levels of attractiveness as a function of gender. Female and male participants (10 males and 10 females) were shown faces of the opposite sex and different attractiveness (during the task EEG and behavioral responses were recorded). First, they were to judge attractiveness with a binary choice and, second, for faces judged as attractive, to motivate their decision by choosing one of these alternatives: Attractive: (i) for a one-night date or short-term relationship, (ii) for a long-term relationship and (iii) just for friendship. The behavioral results highlighted significant gender differences with men showing higher preference for the short-term relation than women who, on the contrary, privileged the long-term relationship. These gender differences were confirmed by the electrophysiological responses: Faces rated as attractive for short-term relation elicited overall larger amplitude in males compared to females. This difference was found beginning from the early P100 component throughout the entire time course of the evoked response, including components involved in structural encoding (N170), extraction of specific face features (P2), and, from 400 to 800 ms, the Late Positive Potential (LPP) that index emotional and motivational evaluation. Women, compared to men, showed an enhanced LPP for the long-term relation. The effects found on the early components are likely to reflect the attention-grabbing power of attractive faces, given their emotional significance, while the later responses might index more deliberative and motivational decisional processes. The remarkable gender difference found suggests that attractive faces of the opposite sex have different emotional and reward value for men and women. Overall, men showed a higher sensibility to physical attractiveness cues and a greater responsiveness to sexually arousing faces. These gender differences are probably rooted in the adaptive significance of attractiveness according to which a short-term relationship has a higher cost-to-benefit ratio for women than for men. All in all, these findings suggest that in men and women attractiveness influences differential neural processing stages related to attentional, perceptual and emotional responses.

Personality and fear learning: a correlation study with healthy human participants

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The aim of this work is to investigate the relations between the characteristics of personality and the modalities of acquisition and extinction of fear in a Pavlovian conditioning paradigm. The experiment collects data on a large amount of parameters of personality, being configured in some ways as an exploratory study on aspects poorly studied in the literature. The experiment is performed on 23 right-handed male university students between 20 and 30 years. We used three batteries of personality tests (CBA 2.0, 16PF-5 and COPE-NVI) in order to have as much information as possible on the psychological characteristics of the subjects participating in the experiment. Fear learning and extinction have been processed through a classic Pavlovian conditioning paradigm where the participants were subjected to the vision of geometric figures (the conditioned stimuli CS+, CS-, and neutral control stimuli) on the screen of a computer. Some of them, in the fear acquisition phase, were associated with administration of unconditioned stimulus (US) (electric shocks to the index finger of their right hand and an annoying sound) previously calibrated on the subjects to be unpleasant. To measure occurred acquisition and extinction of fear conditioning, one index of physiological response was detected, known to be sign of reaction to aversive stimuli: skin conductance. The fear extinction was created with the administration of the same stimuli without association with annoying stimuli. Through correlation analysis, significant relationships between fear conditioning and personality characteristics emerged: in particular, the fluctuation of anxiety was positively correlated with high physiological activation in response to innocuous stimuli in aversive contexts, the coping strategy of Positive Attitude was recorded with high activations to conditioned stimuli in the acquisition phase, while the Transcendent Orientation was negatively correlated with high levels of physiological arousal to all stimuli in the acquisition phase of conditioning. In the extinction phase, high levels of depressive or phobic manifestations were related to a greater difficulty in extinguishing the fear previously associated with aversive and neutral stimuli. On the contrary, there were no coping strategies significantly related to the extinction of fear conditioning. In the correlation analysis between 16PF-5 factors and conditioning tests, more specific personality factors were found to be correlated in the two experimental phases; moreover, only the global factor Independence was statistically correlated with high levels of activation in the process of extinction of fear conditioning. These results contradicts some evidence reported in the literature, where both Extraversion and anxious states and traits are presented as significantly important in the acquisition and extinction of conditioned fear.

Bursts of high frequency random noise stimulation (tRNS) increase arousal in a discriminative reaction time task

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Arousal reflects a state of generalized physiological activation, and different neuronal nuclei are responsible for its regulation through widespread projections to the cortex. Reaction times (RTs) have been used as a behavioral measure of arousal, and in a condition of increased arousal it has been showed a reduction of RTs, denoting a performance improvement. Recent modeling studies on transcranial electrical stimulation (tES) suggest a wide diffusion of the current across different regions of the cortex. On this basis it has been suggested that, sometimes, the effect of the tES might not be specific for the stimulated site but it might induces a general arousal. In the light of these results, the aim of the present study was to increase arousal using tES during a discriminative RTs task, in order to improve the performance. 16 healthy volunteers (8 F, mean age 25) participated to the experiment. The task was a continuative quasi-random visual presentation, for 100 ms, of digits from 1 to 9, with a variable inter-trial interval of 800-2000 ms. Subjects had to press response buttons for target digits (8-9) which were presented after a warning digit (1). We evaluated RTs using a paradigm that has been showed to be sensitive to the modulation of the arousal. Skin conductance response was recorded during the experiment to have also a physiological index of arousal. The experiment was divided in 6 blocks. During blocks 2, 3 and 4, bursts of high frequency random noise stimulation (tRNS) were administered to the subjects concurrently to the presentation of the warning digit, with the aim to increase the endogenous activation related to the preparation of the response. Each burst (2 mA) lasted for 900 ms. We used a pair of circular electrodes (22.8 cm^2) placed with a fronto-occipital montage (FPz-Oz). Real and sham stimulation was balanced in a within subjects design. Results showed a significant reduction of RTs during the second block of stimulation (interaction between condition and block, $p \leq .001$) denoting a performance improvement. Concerning skin conductance, analyses showed a main effect of condition ($p \leq .001$) with a higher phasic activation during the real stimulation session, which was maintained over time. During the sham session, instead, the phasic activation decreased in a faster way, according to a physiological habituation to the repetitive stimuli. These results support the effectiveness of bursts of tRNS to increase arousal over time, measured both with a physiological (skin conductance) and a behavioral (RTs) index. Modulations over the behavioral performance, however, are weaker in comparison to the physiological ones, probably due to the less sensitivity of the behavioral measure used in the present research. The study of the tES effects on other behavioral tasks through the

use of additional physiological measures of arousal (e.g., pupil dilation, EEG) are the future steps needed to support this promising research line.

Spatiotemporal neurodynamics underlying internally- and externally-driven temporal prediction: a high spatial resolution ERPs study

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Temporal prediction (TP) is a flexible and dynamic cognitive ability. Depending on the internal or external nature of information exploited to generate TP, distinct cognitive and brain mechanisms are engaged with the same final goal of reducing uncertainty about the future. In this study, we investigated the specific brain mechanisms involved in internally- and externally-driven TP. To this end, we employed an experimental paradigm purposely designed to elicit and compare externally- and internally-driven TP and a combined approach based on the application of a distributed source reconstruction modeling on a high spatial resolution electrophysiological data array (128 sensors). Specific spatiotemporal ERP signatures were identified, with significant modulation of Contingent Negative Variation (CNV) and frontal Late Sustained Positivity (LSP) in external and internal TP contexts, respectively. These different electrophysiological patterns were supported by the engagement of distinct neural networks, including a left sensorimotor and a right prefrontal circuit for externally- and internally-driven TP, respectively.

Laser evoked potentials habituation in irritable bowel syndrome

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The mechanisms of most chronic pain syndromes are only partially understood. Intense and/or long-lasting afferent barrage can strongly contribute to central sensitization and often seems to be associated with abnormal endogenous pain modulation.

Many patients with chronic pain disorders show evidence of increased facilitation and decreased or absent inhibition of pain. Majority of Irritable Bowel Syndrome (IBS) patients have both rectal and somatic hypersensitivity. Local rectal anesthesia reduces rectal and somatic pain in irritable bowel syndrome patients, supporting the possibility that visceral hyperalgesia and secondary cutaneous hyperalgesia is the result of central sensitization dynamically maintained by input from the Gastrointestinal Tract (GIT). The aim of this study is to evaluate the cortical responses to laser stimuli and pain modulation in patient with IBS. 22 out-patients (17 F, 5 M) with a IBS diagnosis and 15 controls subjects were examined. We registered 62 channels Laser Evoked Potentials while patients received three trains of 21 laser stimuli at 10-12 sec ISI delivered on the right hand and right periunbilical region. We evaluated habituation by comparing the average of the first group of seven stimuli with the last group of the same series. Psychopathological assessment was performed with Stai I, Stai II, BDI, MAF, MOS, SF36, BPI and Dn4 scales. We found a normal N2-P2 amplitude and latency after stimulation of periunbilical region with a reduction of habituation in both sites. These results can be expression of a central sensitization that appears to involve this pain hypersensitivity syndrome which may share the same mechanism underling Fibromyalgia and other chronic pain conditions.

Dance expertise modulates the visuomotor processing of complex body movements

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In the present electrophysiological study the effect motor expertise (acquired by professional dancers in years of performance) on the neural processing of relatively common actions, belonging to the typical human repertoire was investigated. Eighteen right-handed volunteers took part to the experiment: nine were professional contemporary dancers with at least 10 years of formal training, the other nine had no experience whatsoever with dance. 212 videos in which a professional dancer performing a motor action lasting 3 seconds were presented to participants while their event-related brain potentials (ERPs) were recorded. Each video was followed by a second one (named "post") which might be either the repetition of the previous one (named "same"), or a slight variation (named "different") along 3 main dimensions (time, space and body). Participants were required to respond to static images of dancer's body by pressing a button. A N400-like component was identified at fronto-central sites (F3-F4, FC1-FC2) at about 700/900 ms, which was enhanced in amplitude by "different" videos in the dancers group, thus indexing the automatic detection of a visuomotor deviance between pre and post video modulated by motor expertise. At frontal sites (AAF1-AFF2, FFC1h-FFC2h) a Late Positivity component was identified at about 600/1000 ms, which was reduced in amplitude by "same" videos only in dancers,

therefore possibly reflecting action coding. The lack of a significant modulation of brain responses to deviant or same stimuli in the control group indicates a strong effect of neural plasticity in professional dancers. swLORETA source reconstruction was performed on the difference waves obtained by subtracting ERPs to "same" from those elicited by "different" videos in the N400 time window. In dancers it was observed the engagement of a widespread network devoted to the processing of spatially and temporally complex actions, including fronto-parietal system areas (BA 40, 45, 3), biological motion areas (BA 22, 38), face and body related visual areas (BA 18, 19, 37). As a whole, the results provide evidence of the role of motor expertise in modulating the ability of processing complex biological movements, allowing only professional dancers to detect subtle differences in body movements.

Neural correlates of multiple object processing in healthy aging

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The ability to enumerate multiple items is crucial in our everyday life and it may undergo age-related decline. Previous studies suggest that in order to enumerate objects we first need to individuate them as separate entities and then to maintain those representations active in visual working memory (VWM). However, so far it is unknown whether the changes in enumeration performances associated to aging are due to a diminished ability to individuate items as separate individuals or to a decline in VWM capacity. In order to address this question in the present electrophysiological study we compared a group of young (M = 24.8) and old (M = 69.7) adults while counting a varying number of targets (1-6) presented among distractors. We measured two posterior ERP components, N2pc and CDA, that have been associated respectively to individuation and VWM. To further characterize the age-related changes in enumeration we computed theta (4-7 Hz) and alpha (8-12 Hz) synchronization, a measure associated to memory encoding. Our results show that old participants performed worse than the younger in the enumeration task. Electrophysiological data showed that both components were modulated by target numerosities independently of age. However, N2pc was suppressed in the old group over the whole numerosity range (1-6) while CDA showed a suppression only for the largest set (4-6), suggesting that aging influences individuation and simultaneously diminishes the capacity of VMW. Finally, older adults showed higher theta and alpha synchronization over frontal electrodes than the younger, suggesting that to enumerate successfully the aged group required more memory resources that were recruited from frontal sites.

Fast-muscle contraction as a proxy to embodiment and BCI-control in tetraplegia: an EEG study in immersive virtual reality

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Allowing humans, particularly when they suffer from somatosensory and motor disability (e.g. after spinal cord injury), to control through their brain artificial virtual or physical agents is a fundamental challenge for both neuroscience and engineering. A crucial process for achieving optimal control may be the induction of embodiment, i.e. the feeling that an artificial agent is part of our body (ownership) and we are responsible of its movement (agency). Combining EEG recording and immersion in a virtual environment (Cave System) we had demonstrated that observing, either in first (1pp) or third person perspective (3pp), wrong movements performed by an avatar activated the onlookers' error monitoring brain systems. More specifically, subjective reports of higher embodiment paralleled higher Medial-Frontal Theta band synchronization and larger Error Related Negativity deflection in reaction to the erroneous grasping of an avatar seen in 1pp condition. In the present study, we tested a tetraplegic patient in a modified version of the original paradigm task in which the request performs a short and rapid contraction (monitored through ElectroMiografic-EMG burst activation) of an axial muscle before passive observation movements of the avatar seen in first-person perspective. The contraction triggered the start of the avatar's action and activated a cascade of events ultimately leading to increased sense of agency and ownership of the acting virtual arm. We confirmed that increase of embodiment paralleled Medial-Frontal Theta activity suggesting oscillations in this frequency band may represent a signature of embodiment that may be crucial for improving the flexibility of current brain computer interface devices.

Directed forgetting for faces: the role of inhibition and contextual information

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The present study aims to examine the electrophysiological correlates of voluntary memory control. The novelty of the study concerns the influence of emotional contextual information over conscious memory control for facial stimuli. Another objec-

tive of this study is to provide evidence regarding the hypothesis of active/passive inhibition relative to the modulation of long-term memory storing. Sixteen healthy volunteers (8 male and 8 female, mean age 25.7) were tested using an item-method directed forgetting paradigm where they studied a series of neutral faces embedded in a scene with emotional valence (positive, negative or neutral). Experimental stimuli were neutral faces from NimStim database and emotive (positive or negative) and neutral images from I.A.P.S. database (all the images were validated for valence and arousal). Each screen (item face and contextual information) was presented randomly followed by either a "remember" cue (TBR) or a "forget" cue (TBF); subsequently the participants undertook an old/new memory test for which they were requested to classify studied items regardless of original remember/forget status. EEG was recorded during the paradigm trough a Neuroscan NuAmp amplifier from 28 Ag/AgCl electrodes (10-20 system) with a linked-mastoides reference. Impedance was reduced to less than 5 kΩ. Electrical activity was amplified from 0.01 to 100 Hz at a sampling rate of 1000 Hz. Event related potentials (ERPs) time locked to the cues were averaged (-200 – 1000 ms) separately for each channel as a function of both the remember/forget instruction and the scene emotional valence. Results showed that TBR and TBF cues elicited an activation that differs in scalp distribution and polarity, suggesting activation of fundamentally different operations during the cue presentation. In particular the electrical pattern elicited by TBF cues implied a frontal inhibition mechanism that is engaged to stop the intentional memory formation process. Additionally, our data showed different electrical modulation between TBR and TBF items as a function of emotional contexts. In this vein our main results were: (1) a different modulation in N200 and P300 for TBF and TBR faces embedded in neutral scenes compared to faces embedded in emotional scenes. (2) Later on in the time course we observed a different pattern of activation for faces embedded in positive and negative contexts that might reflect differences in the capacity of directed forgetting task execution. In case of positive emotional context we observed a reverse electrical pattern compared to neutral and negative context. This effect may be related to the emergence of different attentional effects relative to the contextual emotional valence. In conclusion this study provides evidence about the active inhibition account for TBF items and also about the influence of contextual information over the voluntary control of memory for human faces.

Effects of un-neurotic psychotherapy sessions in electroencephalographic synchrony

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A therapeutic approach has recently appeared in monographic literature. This approach reveals characteristics which are presently being evaluated and offers the

possibility for successful results and expanding interests in the various epistemological aspects. This intervention is based upon a theoretical framework which requires an in-depth study capable of explaining the obtained results. For this reason it is necessary to study the above indicated subject. This study considers the value of synchrony between the different couples of electrodes following the sittings carried out in conformity with the course model in question. Twenty normally intelligent people, affected by psychopathological disturbances of a neurotic nature but without being subjected to any pharmacological therapy, participate in the experimentation. This group is composed of 10 females and 10 males between the ages of 20 and 50. Between the fifth and the fifteenth sitting of the psychotherapeutic treatments, registrations were carried out on each patient for three consecutive sessions. Before each session a registration of 240 seconds with eyes opened and 240 seconds with eyes closed was performed followed by another using the same modality. The data relevant to the average values of synchrony in the various couples of electrodes in the pre and post sittings by means of the t-test, were successively compared in the sample. This test evaluated a statistically significant difference in the sample between the two moments of therapeutical activity and verified the reduction in the values of synchrony before and after the sitting. The decrease in the registered values is noticeable in many couples of electrodes. These values present extremely interesting images of individual activity which correlate with the results registered during the clinical session. In connection with this, the major differences are singled out and the values and relevant statistics are indicated. The particular characteristics of the study render necessary a qualitative analysis which permits one to isolate the variables in question in the execution of the above activity. Moreover it marks the various aspects which led to the final results of the clinical evaluation. The unequivocalness of the data allows us to understand the elements which provocate the various results obtained.

Sensory memory in physiological and pathological aging indexed by the mismatch negativity

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The Mismatch Negativity (MMN) is a neurophysiological marker of sensory memory. MMN is elicited when an auditory discriminable change occurs in a sequence of frequent standard stimuli. It reflects an automatic change detection mechanism, supported by the perception of the incoming stimulus and by the maintenance of its trace in memory. Therefore, MMN is a good index for studying memory trace decay in physiological and pathological aging. Several studies reported that MMN

amplitude is reduced and its peak latency prolonged with ageing. In comparison with other indices the MMN seems particularly suited to study sensory memory in mild cognitive impairment (MCI) and Alzheimer's disease (AD) patients, because it can be recorded without compliance of the subject. Aim of the present study is to evaluate sensory memory in elderly subjects, MCI and AD by means of MMN. Specifically, our aim is to evaluate if the MMN response could differentiate AD from MCI patients. We used different inter-stimulus intervals (ISIs) to explore the integrity of the auditory sensory memory trace in these patients. Sequences of three tones (standard vs. deviant) were presented binaurally with earphones. The deviant tone had the same frequency and intensity as the standard tone, but a different duration. Every participant completed two separate sessions, each one having a short (0.4s) and a long (4s) ISI. EEG signal was recorded from 19 electrodes. Forty-eight subjects took part in the experiment. They were divided into 3 groups, matched for age: 15 elderly (68.1 ± 5.7 years), 12 MCI (71.5 ± 6.5 years) and 11 AD (73.64 ± 6.80 years). The MMN component was quantified by measuring mean amplitude of responses evoked by standard and deviant tones in the 150-180 ms time window. Four electrode locations were considered in the analyses, which allowed to discriminate between frontal (F3, F4) and temporal (M1, M2) MMN. The results shown a significant differentiation between the two clinical pathologies. At short ISI no difference in the MMN amplitude was present between groups in frontal area. While in temporal areas, MMN was not elicited only in MCI group. At long ISI, nor frontal neither temporal MMN were present in elderly and MCI, whereas AD show a reliable temporal MMN. These data indicate that the encoding of acoustic tones was preserved in AD patients as in the elderly. While in MCI was possible to identify a difficulty already in the first phase of encoding of sound properties. Moreover, the maintenance of sensory memory was impaired in elderly and MCI, while unexpectedly it was present in AD patients. It might be possible that a compensatory mechanism in the early stage of AD results in an optimization of the temporal feature analysis, but no change detection (frontal) information process is evident. Another possible explanation of data could be related to the cholinergic system and the pharmacological treatment of AD patients which may have enabled a recovery mechanism.

Short-latency somatosensory evoked potentials to median and tibial stimulation recorded by intracerebral electrodes

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Preoperative evaluation, by means of intracerebral electrodes, in patients presenting with symptomatic drug resistant epilepsy, provides an opportunity to explore the S1

area in depth. We studied 7 pediatric patients with drug resistant epilepsy. Intracerebral electrodes were implanted in frontal, temporal and parietal lobes at different sites, depending on seizure types. SEPs were recorded to median and tibial nerve stimulation from the intracerebral electrode contacts referred to the earlobe ipsilateral to the stimulation. The analysis was addressed to the electrode contacts where an inversion of SEP component polarity was observed. A part from the median nerve N20 origin from the anterior bank of the postcentral gyrus, in 3 patients having electrode contacts close to medial surface of the parietal lobe, an inversion of polarity of the tibial nerve P40 component was observed. This is the first study demonstrating the origin of the tibial nerve P40 component from the medial surface of the S1 area by using intracerebral SEP recording.

Correlation between abnormal brain excitability, anger management and anxiety in migraine children

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To analyze the possible correlation between abnormal brain excitability and psychological factors in migraine children. We studied 12 migraine children. P300 response was recorded in three successive blocks to test EP habituation. Psychological profile was assessed by Picture Frustration Study test for anger management (PFS) and Psychiatric scales for self-administration for youths and adolescents (SAFA-A scale for anxiety). In migraineurs, all the EP component (N1, P2, and P300) showed a reduced habituation, as compared to healthy children. In both the second and third blocks, a significant correlation between P300 deficit habituation and SAFA-A (social anxiety subscale) was found. Moreover, the P300 habituation was also correlated with PFS-I (intraggressive anger) in the second block and with the total SAFA-A score in the third block. To our knowledge, this is the first study showing a correlation between abnormal brain excitability, intraggressive anger and anxiety, suggesting a possible role of the latters in producing the migraine phenotype.

Sound-induced flash illusion in migraine patients

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The sound-induced flash illusion (SIFI) is a multisensory perceptual phenomenon in which the number of brief visual stimuli perceived by an observer is influenced by

the number of concurrently presented sounds. The brain potentials for the illusory flash appear qualitatively very similar to those for a physical flash, suggesting that the same mechanism underlies the percept of both illusory and physical flashes. These results suggest that the activity in the visual cortex can be modulated by sound. Migraine is a neurological condition characterized by abnormal central processing of sensory stimuli and particularly by an increased responsivity of the primary visual cortex. In this study we investigated SIFI susceptibility in 16 migraine patients and 10 controls and we evaluated event related potentials (ERPs) associated with this phenomenon. We measured trial-by-trial ERP to isolate neural activity associated with the visual stimulus. In an analysis time of 0-500 ms, we found a positive component (P100) with a greater amplitude on the migraineurs occipital cortex. A verbal responses analysis showed that migraine patients were less susceptible to the multisensory illusion than controls. Both data confirm that migraine patients have a greater responsivity of the primary visual cortex.

Alpha-rhythm signs of time-related inhibition of visual attention orienting during cue-target spatial processing as indexed by EEG Wavelet analysis

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Previous research has indicated that visuospatial orienting of attention is related to brain EEG α-frequency band. The most recent evidence points to a determining role of occipito-parietal α-band activity (8-14 Hz) in anticipatory orienting facilitation (α-power decreases) vs. inhibition (α-power increases). Yet, while such α-modulations are a common finding, the direction of modulation and its timing varies to a great extent across studies implying dependence on task demands. Furthermore, scarce knowledge is available about the power of this EEG oscillatory band in the diverse endogenous and exogenous orienting modalities and about its trend in time. In this study, nineteen students were recruited to investigate these matters. They were administered a modified version of Posner's ANT (Attention Network Test) made up of diverse spatial cueing tasks priming the presentation of a target. The cue provides diverse spatial information as a function of task: namely, a CC (Central Cue) task, a NC (No Cue) task, and a LC (Local Cue) task. On each trial, the EEG was recorded from 128 scalp sites going from 100 ms before the cue to 1300 ms after it, a target being presented 500 ms after the cue, to which the participants had to respond motorically. We computed LC-CC and CC-NC differ-

ence waves to get access to the orienting system and the alerting system functionality, respectively. Wavelet analysis was used to measure event-related α-band oscillations power (in uV^2/Hz) between 8-12 Hz, so to investigate its functional role and its effects on the Attention Networks, at 20 parietal-occipital (PO5h/PPO6h, POO9h/POO10h, PPO9h/PPO10h, PO9/PO10, PO7/PO8) and frontal (F5/F6, FCC5h/FCC6h, AFF5h/AFF6h, FC5/FC6 and FFC5h/FFC6h) sites. EEG time span was divided into four ranges: 0-240 ms, 240-500 ms, 500-800 ms, and 800-1300 ms. Interestingly, CC-NC condition showed the alerting system efficiency and, once the target was delivered, also the orienting system functions. This also provided us information on differences on target processing modes in time. The results pointed out thatα-band gradually decreased, reaching the lowest peak power in the 800-1300 ms latency range. A greater α-band power was measured at parietal-occipital electrodes and for the CC-NC condition, in the left hemisphere both before and after the target (0-240 ms, 240-500 ms, 500-800 ms) delivery, and in the right hemisphere after the target appearance only (800 ms to 1300 ms). In conclusion, our findings provide support to an active facilitative versus inhibitory role of α-power decreases and increases and suggests that these attention-related changes are differentially deployed during anticipatory attention orienting to prepare versus maintain the cortex for optimal target processing.

Reduced current spread by concentric round electrodes in transcranial direct current stimulation (tDCS)

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Transcranial direct current stimulation (tDCS) is a non-invasive technique widely used in neuroscience research, which is able to modulate brain activity, acting on cortical polarization. In this way it is possible to increase or decrease cortical excitability of the stimulated area. In the literature, the most common montage consists of two square or rectangular electrodes from 25 to 100 cm^2, one placed over the target area and the other on a different site that could be cephalic or extracephalic. Nevertheless these montages present limitations, in terms of stimulation focality. The purpose of the present study is to develop a new method consisting of two small concentric electrodes that can help to solve these problems. The main goal was to replicate the results on cortical excitability changes achieved by standard rectangular electrodes, and to obtain a more precise and focal stimulation by manipulating a limited population of neurons. To test the efficacy of these electrodes, three types of stimulation (anodal, cathodal and sham) were delivered to a group of participants for

10 minutes. The electrodes were positioned on the left primary motor cortex (M1), over the first dorsal interosseous (FDI) hotspot. In order to localize the stimulation site and to check the effect of tDCS on motor evoked potentials (MEPs) amplitude, single pulse TMS has been used. 20 MEPs of two muscles (target muscle: FDI; control muscle: ADM – abductor digiti minimi) were recorded before and after the stimulation to compare the excitability of the cortex at baseline and after the application of the tDCS. In line with previous studies, the results showed that anodal-tDCS increases MEPs amplitude of FDI, while cathodal-tDCS decreases it. There were no changes in the sham condition. Moreover the focality of stimulation was reflected by no significant effects on MEP amplitude for the ADM. These data suggest that these concentric round electrodes lead to an effective and focal modulation of neural activity by limiting the current spread on the cortex. This ensures better control during the stimulation and can represent a novel tool which is able to offer important advantages to those who use tDCS, or transcranial electrical stimulation in general, in their research activity.

The smarter, the stronger: intelligence level correlates with brain resilience to systematic insults

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Neuroimaging evidences posit human intelligence as tightly coupled with several structural and functional brain properties, also suggesting its potential protective role against aging and neurodegenerative conditions. However, whether higher-order cognition might in fact lead to a more resilient brain has not been quantitatively demonstrated yet. Here we document definite relationships between individual intelligence quotient (IQ) and brain resilience to targeted and random attacks, as measured through resting-state fMRI graph-theoretical analysis in 102 healthy individuals. In this context, enhanced brain robustness to targeted attacks in individuals with higher IQ is supported by an increased distributed processing capacity despite the systematic loss of the most important node(s) of the system. Moreover, brain resilience in individuals with higher IQ is supported by a set of regions mainly belonging to language and memory processing network(s), whereas regions related to emotional processing are mostly responsible for lower IQ individuals. Results quantitatively confirm intelligence level among the predictors of post-lesional or neurodegenerative recovery in the context of the cognitive reserve theory, also promoting the evolutionary role of higher order cognition and simultaneously suggesting a new framework for brain stimulation interventions aimed at counteract brain deterioration over time.

The role of extrastriate area V5/MT in aesthetic appreciation of visual art

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To explain the biological foundations of art appreciation is to explain one of our species' distinctive traits. In the last decade, neuroimaging experiments have provided insight into the cognitive and neural correlates of aesthetic appreciation. It has become clear that aesthetic appreciation relies on the activity in a number of different brain regions. In addition to cortical and subcortical regions associated with pleasure and reward, frontal cortical areas involved in decision-making and evaluation, as well as various cortical areas related to perception, have been identified as key neural substrates of aesthetic appreciation. In this study we focused on the role of extrastriate visual area V5/MT in aesthetic appreciation of paintings. V5/MT is known to respond to both real and implied motion. Since dynamism of an image is a key factor in determining how much it is liked, our aim was to investigate whether interfering with V5/MT activity while observing paintings would have affected their aesthetic appreciation. To clarify this issue we applied triple-pulse online transcranial magnetic stimulation (TMS) over (left) V5/MT or over a control site (vertex) while participants were evaluating a set of figurative (Experiment 1) or abstract (Experiment 2) paintings. In each experiment the participants (with no specific background in fine arts, N = 20 in Experiment 1, and N = 18 in Experiment 2) were asked to indicate whether they liked each of the paintings (I like it / I do not like it, yes/no fast response required) and whether they regarded the painting as dynamic or not (I see it as dynamic / I see it as static, yes/no fast response required). Order of tasks and order of TMS sites was counterbalanced across participants. Repeated-measures ANOVA showed that TMS over area V5/MT significantly reduced the motion perceived in both abstract and figurative images compared to stimulation of the control site (vertex). In turn, the effects of V5/MT TMS on aesthetic appreciation varied depending on the type of art considered. Stimulation of V5/MT did not affect aesthetic appreciation of figurative artworks, but did reduce to a significant extent appreciation of abstract artworks. Overall, our data suggest that area V5/MT plays a critical role in the network mediating aesthetic appreciation of artworks, although this seems to be limited to abstract artworks in which dynamism was related more to the painter's likely painting-moves rather than to the content itself.

Treatment with Epigallocatechin Gallate rescues neurogenesis and neuron maturation in the Ts65Dn mouse model of Down syndrome

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Severe neurogenesis reduction and dendritic pathology starting from early developmental stages are the major determinants of cognitive disability in Down syndrome (DS), a genetic condition due to triplication of chromosome 21. Thus, therapies aimed at rescuing behavior should be targeted to both these defects and administered during early phases of brain development. In the current study we examined the effect of Epigallocatechin Gallate (EGCG), a phytochemical found in green tea, on neurogenesis and neuron maturation taking advantage of the Ts65Dn mouse, a widely used model of DS. Using cultures of neural precursor cells (NPCs) from the subventricular zone of Ts65Dn mice we found that treatment with EGCG restored defective proliferation, increased the number of new neurons and rescued neurite development. Analysis of the phosphorylation levels of GSK3beta, a crucial regulator of neurogenesis and neuron differentiation, showed that in treated trisomic cultures the reduced phosphorylation (i.e. increased activity) of GSK3beta was fully normalized, suggesting that the positive impact of EGCG on trisomic cells may be mediated through an increase in GSK3beta phosphorylation. In order to establish the impact of EGCG in vivo we treated neonatal Ts65Dn mice during the first two postnatal weeks, the period of maximum hippocampal neurogenesis. We found that treatment fully restored neurogenesis in the dentate gyrus and that this effect led to restoration of total granule cell number. Moreover, treatment restored proliferation of NPCs in the subventricular zone of the lateral ventricle, a neurogenic niche crucial for corticogenesis. Results show that EGCG restores the major defects of the trisomic brain and suggest that early treatment with EGCG may be a suitable therapy for the prevention of cognitive disability in DS.

Brain activity during mental imagery in Multiple Sclerosis

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Mental Imagery (MI) is defined as mental execution without any actual movement and involves neural networks overlapped with those activated during actual actions. Isochrony between mental and actual motor performance is usual in healthy subjects, whereasanisochrony is typically correlated to neurological deficit. Although widely investigated in stroke, very little is known about MI in Multiple Sclerosis (MS). A recent behavioral study showed that MI is anisochronous in patients with MS (PwMS) with relapsing-remitting MS course (RRMS). However we need more knowledge about MI in MS. Here, we propose to better investigate the neural correlates of MI in PwMS using fMRI and behavioral tasks and to assess whether MI deficit is associated with disease severity. We recruited 24right-handed subjects, 8 RRMS (32.6 ± 6.4 yrs; EDSS: 1.5, 1-3.5), 8 clinically isolated syndrome (CIS) patients (31.88 ± 6.10 yrs; EDSS: 1, 0-1.5), 8 healthy control subjects CTRL (29.6 ± 3.4 yrs) undergoing MRI (1.5T GE scanner) with the following sequences: (a) T2-W spin-echo; (b) 3D-T1-W FSPGR; (c) EPI for fMRI. Two tasks were performed during fMRI acquisition: (1) motor execution (ME) with subjects squeezing a ball with the dominant/non-dominant hand; (2) MI with subjects imagining to squeeze the ball with the dominant/non-dominant hand. The same tasks were performed before the MRI scan to record ball squeezes executed/imagined ratio evaluating anisochrony in dominant and non-dominant hand. RRMS and CIS showed an increased ratio compared to CTRL: RRMS = 1.76 ± 0.69; CIS = 1.41 ± 0.17; CTRL = 1.17 ± 0.12. Regarding fMRI, ME showed a gradient of increased activity in MS (RRMS > CIS) than CTRL; intra-group comparison between MI and ME showed decreased activation in MI compared to ME in all the groups. Compared to CTRL, CISwere not significantly different in brain activation during MI, whereas RRMS showed increased activation with the non-dominant hand in the Thalamus bilaterally, right Precentral, right Fusiform gyrus, right Cingulum and left Inferior Parietal Lobule. Compared to CIS, RRMS showed increased activation with dominant hand in the left Postcentral, right Thalamus and left SMA and with non-dominant hand in right Pre- and Postcentral, right and left IPL, left Cingulum. No significant association was found between areas of brain activations and T2-LV in patients. Results showed

that brain activity during MI is higher in RRMS than in CTRL and CIS and that is associated with increasing asynchrony on the behavioral task. Interestingly, the strongest association is found with increased activity of left Cingulum connecting sites implicated in cognitive control. Following evidences on other neurological pathologies, this pilot study is aimed to better clarify neural correlates of MI in MS in order to possibly identify basis for new rehabilitative strategies towards a better QoL for PwMS.

The role of high-gamma motor cortex oscillations on visuomotor coordination chronometry: a tACS study

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While the role of beta (~20 Hz), theta (~5 Hz) and "mu" oscillations in the motor areas have been repeatedly associated with motor performance, the investigation of gamma oscillatory activity during motor tasks constitutes a more recent and still not fully understood component of motor control physiology. In order to better understand the role of gamma activity during visuo-motor coordination chronometry, here we implemented an online neuromodulation paradigm based on transcranial alternating current stimulation (tACS) of the dominant motor cortex. We tested, in fourteen healthy volunteers, the effects of 5 Hz, 20 Hz, 60 Hz and 80 Hz, and sham tACS on their performance during a custom-made unimanual tracking task addressing several components of visuo-motor coordination of the contralateral hand. Results showed a significant enhancement of motor performance during tACS at high gamma, 80 Hz stimulation – as well as a trending effect for 60 Hz –, with the effect being prominent between 400 and 700 milliseconds after the onset of a new motor program. tACS did not produce significant effects in other frequencies, neither during steady-tracking, acceleration or continuous pattern motion. Our findings posit a specific role for high-frequency motor cortex oscillations during complex visuo-motor tasks involving the sudden rearrangement of motor plans. Results might be of relevance for planning rehabilitation strategies in motor disorders, like Parkinson's disease, where the switching from a motor program to another involving the same limb is impaired.

Prolonged inhibitory effect of 1 Hz rTMS of the motor cortex on the nociceptive evoked potentials to contralateral hand stimulation

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While the inhibitory effect of high frequency motor cortex rTMS on pain is well known (O'Connell et al., 2014), there are only few data about the effect of the low frequency motor cortex rTMS on both clinical and experimental pain. Theoretically, since low frequency rTMS should have an inhibitory effect on motor cortex, whose activation is known to reduce experimental pain, one could expect that 1 Hz motor cortex rTMS increases an objective pain measure, such as laser evoked potentials (LEPs). In 8 healthy subjects, we investigated the effect of 1 Hz rTMS of the left motor cortex on LEPs to stimulation of both right and left hand dorsum. LEPs were recorded at 4 different times: baseline, Time 0 (immediately after 20 minutes of 1 Hz rTMS), Time +20 (20 minutes after 1 Hz rTMS), and Time +40 (40 minutes after 1 Hz rTMS). We found that rTMS modified the amplitude of the N2/P2 LEP component only to right hand stimulation ($F = 12.06$, $p < 0.001$), while there was no effect on left hand LEPs ($F = 0.7$, $p = 0.56$). Post-hoc analysis showed that the N2/P2 amplitude was reduced at Time 0, Time +20, and Time +40, as compared to baseline ($p < 0.01$). Instead of the expected facilitatory action of low frequency motor cortex rTMS on pain, our results show that 1 Hz rTMS of the motor cortex inhibits contralateral pain and that this effects last up to 40 minutes after the cortical stimulation. Moreover, they suggest that the functional network connecting the motor cortex with the pain matrix areas is complex and cannot be trivialized to mere reciprocal inhibitory/facilitatory actions.

Rule-dependent and stimulus-dependent visuomotor mappings: combined repetitive TMS/fMRI studies of functional connectivity of the lateral prefrontal and parietal cortices

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In our recent work we demonstrated a biphasic time-course of motor cortical excitability during a counter-imitative task: early bottom-up automatic activation and a

late top-down executive activation. We showed a double-dissociation between the effects of offline rTMS to the lateral prefrontal and parietal cortices on the early and late components. This allowed us to hypothesize the presence of two different anatomo-functional pathways: a parieto-(premotor) network mediating early stimulus-based responses and a (temporo)-prefrontal network producing late rule-based responses. These two visuomotor mapping systems converge necessarily at some point prior to movement production. Our next step is to investigate specifically at what cortical level they converge. According to the literature, the three most likely candidates are the premotor cortex, the motor cortex or the caudate nucleus. We are testing this hypothesis by combining offline (real or sham) 1 Hz rTMS to the prefrontal or parietal cortices with a whole-brain measure such as fMRI. During scanning participants are challenged with a visuomotor imitative task and a visuomotor counter-imitative task in a blocked-design. The analysis that is expected to provide informative results is the presence of voxels with activity showing an interaction between type of stimulation (real vs. sham) and task (imitative vs. counter-imitative). The results from localizer scans without rTMS (N = 10) showed that the counter-imitative task engaged more activity in the lateral prefrontal cortex and vice versa the imitative task elicited stronger signal in the posterior parietal cortex. These functional data guided individually rTMS in the main rTMS-fMRI experiment (N = 7). The preliminary results of the main experiment showed a spot of interaction between the two stimulations and the tasks in the dorsal premotor cortex.

Functional reorganization of brain networks in patients with painful chronic pancreatitis

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The study aimed to investigate the organization of brain networks involved in nociceptive processing in patients with painful CP. Contact heat-evoked potentials (CHEPs) were recorded in 15 CP patients and in 15 healthy volunteers. The upper abdominal area (sharing spinal innervation with the pancreatic gland) was used as a proxy of "pancreatic stimulation", while stimulation of the right forearm was used as a control. The brain source organization of CHEPs components were analysed. After abdominal stimulation, brain source analysis revealed abnormalities in the cingulate/operculo-insular network. A posterior shift of the operculo-insular source ($p = 0.004$) and an anterior shift of the cingulate source ($p < 0.001$) were seen in CP patients, along with a decreased strength of the cingulate source ($p = 0.01$). The operculo-insular shift was positively correlated with the severity of pain ($r = 0.61$,

p = 0.03). CP patients showed abnormal cerebral processing after stimulation of the upper abdominal area. These changes correlated with the severity of pain, probably reflecting maladaptive neuroplastic changes.

Reward mechanisms in processing highly emotional artifacts: a multi-method study by fNIRS, EEG and autonomic measures

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The experience of viewing and processing artifacts is influenced by the emotional external features of the stimulus (e.g. valence and arousal), together with the subject's internal dispositions and feelings. Indeed, emotionally relevant visual pictures can capture attention because of their motivational significance, their emotional appealing and their rewarding features. Moreover, the way in which we select and process these visual cues varies according to our personal attitudes and produces different psychophysiological patterns. Such complex relationships need to be clarified and can be better understood within a multi-method approach. Therefore, the aim of this study was to investigate a possible relation between hemodynamic (functional Near-Infrared Spectroscopy, fNIRS), electrophysiological (EEG) and autonomic variations while viewing visual scenes selected to induce pleasant and unpleasant emotional experiences, with respect to personality attitudes and reward mechanisms. NIRS is a relatively new optical method to investigate the oxygenation of brain tissue and it is very suitable for environmental contexts. Highly emotional stimuli varying in valence (positive vs. negative) and arousal (high vs. low) were presented to the participants for 6s in a randomized order, with 12s inter-stimulus interval. Hemodynamic measures were recorded from 6 NIRS channels placed over the prefrontal region as changes in oxygenated (oxyHb) and deoxygenated (deoxyHb) hemoglobin levels. Electrocortical measures were simultaneously recorded from 16 channels, while cardiovascular indexes were measured as biomarkers of arousal. After the experimental session participants were required to complete BIS/BAS questionnaire to assess motivational components related to the behavioral inhibition (BIS) and activation systems (BAS). Specifically, BAS-reward subscale was considered. Results showed that, depending upon the emotional content and arousing power of the scenes, the prefrontal cortex was differently activated during the fruition of pleasant and unpleasant affective stimuli. These results were strengthened if considered together with the personality correlates and the stimulus rewarding features. In conclusion, this study suggests a possible relationship between motivational, hemodynamic, psychophysiological and autonomic measures and proposes a multi-measures technique as a promising approach to study artifacts fruition during the contemplation of emotional pictures.

Electroencephalographic signatures of aesthetic experience during the perception of interior designs in a virtual reality CAVE system

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Nowadays there is the hope that neuroscientific findings will contribute to improvements in the design of buildings and help to create environments satisfying man's demands. In order to map the brain activity related to the aesthetic experience of architectural environments, we recorded the electroencephalographic (EEG) signals in an immersive virtual reality during the perception of interior designs. We hypothesize appreciated environments involve embodied simulation mechanisms and circuits mediating approaching stimuli. Three-dimensional environments have been simulated in a CAVE system formed by three back-projected active stereo screens and a front-projected screen on the floor surrounding the subject. Three rooms have been designed in real size (5 × 5 m) and tested with different interior design: empty, modern and cutting edge furniture. EEG recordings (10-20 I.S.) of 12 healthy subjects (26.8 ± 2.4 yrs) have been performed during the perception of each room, randomly presented for 4 minutes. Afterwards, the enrolled volunteers expressed judgments about Familiarity, Novelty, Comfort, Pleasantness and Arousal on a 9-points Likert scales for each virtual scenario. Principal Component Analysis (PCA) have been performed on behavioral data to identify principal dimensions describing the subjects' aesthetic experience. These scores have been exploited to analyze the Power Spectral Density (PSD) of the EEG in the theta, alpha and mu bands by topographic statistical maps (Student's t- test, $p < 0.05$, False Discovery Rate corrected). The PCA resulted in three behavioral dimensions (principal components, PCs; % of explained variance): pleasant-novel-related (PC1, ~50%), familiarity-related (PC2, ~24%) and comfort-related (PC3, ~15). Spectral statistical maps of Pleasantness, Novelty and Familiarity revealed the activation of left frontal areas (theta and alpha bands) during the perception of environments judged more pleasant, more novel and less familiar. In addition, Pleasantness, Novelty and Comfort are correlated with a desynchronization of the mu rhythm over the left sensorimotor areas. An increase of Comfort also returns an enhance of the theta frontal midline activity. Such as results show how the perception of pleasant and novel/familiar architectural environments activate cerebral areas regulating approach/withdrawal. Moreover, the activation of motor areas suggest the involvement of the embodied simulation in perception of

pleasant, novel and comfortably rooms, whereas the activity of the frontal midline is related to internalized attention. The present experiment provides evidence of the asymmetrical involvement of the prefrontal cortical areas and embodied simulation mechanisms during the aesthetic appreciation of architectonical stimuli in a virtual reality CAVE system. These observations may allow to develop quantifiable neural markers for testing how the design process of architectonical environments matches the changing needs of man.

Brain network analysis during verbal suggestion of placebo and nocebo effect in migraine

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In previous studies migraine patients seemed not influenced by verbal suggestion of nocebo and placebo effect on laser pain. Pain modulation under verbal suggestion may be better examined applying connectivity analysis to laser evoked responses. Thirty-one migraine without aura outpatients (MIGR) were evaluated and compared to 19 controls (CONT). The right hand was stimulated during a conditioned task, where CO2 laser stimuli were delivered after a verbal cue of decreased (D), increased (I) or basal (B) intensity, which was left unmodified during the entire task. EEG signal was examined by means of Morlet wavelet, synchronization entropy, Granger causality and graph theory analysis. Pain rating changed in accord with stimulus cue in CONT, remaining unchanged in MIGR. In the pre-stimulus phase enhanced synchronization entropy in the 0.5-30 Hz range was present in MIGR in the D and I conditions on the bilateral temporo-parietal regions, which were more connected in the post-stimulus phase compared to controls, who displayed increased connections across the midline. A different pattern of cortical activation under verbal suggestion of pain intensity was present in migraine. Brain network analysis may give an aid in understanding subtle changes of pain processing under laser stimuli. Effects of primary motor area and left dorsolateral prefrontal cortex transcranial direct current stimulation on laser evoked potentials in migraine patients and normal subjects.

Effects of primary motor area and left dorsolateral prefrontal cortex transcranial direct current stimulation on laser evoked potentials in migraine patients and normal subjects

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Non-invasive brain stimulation techniques induce an electrical stimulation of the brain in an attempt to reduce chronic pain by directly altering brain activity. In this case-control study we compared the effects of transcranial direct current stimulation (tDCS) of the left primary motor cortex (M1) and left dorsolateral prefrontal cortex (DLPFC) both on subjective pain and on evoked responses induced by laser stimulation (LEPs). The study was conducted in a cohort of thirty-one migraine without aura patients during the inter-critical phase, and twelve age and sex-matched non-migraine healthy controls. Among migraine patients, we stimulated left DLPFC area in 16 cases and M1 area in 15 cases. Evoked laser potentials were recorded in basal, sham and after tDCS, by stimulating the contralateral hand and supraorbital zone. For tDCS a constant current of 2 mA intensity was applied for 20 minutes. For sham stimulation, the electrodes were placed in the same positions as for real stimulation, but the stimulator was turned off after 30s and thereafter received no stimulation for 10 minutes. The one-way ANOVA was used to analyze the data where the LEP latency, amplitude, N2-P2 amplitude, and the laser pain rating were variables, the session (baseline, TDCS and sham) within subject factor. To compare the variables across the three different sessions, a post hoc multiple comparison Bonferroni test was applied to single groups. We didn't find significant acute changes in any LEPs parameters and pain perception among subjects who received tDCS of both left M1 and DLPFC. After tDCS of DLPFC we noticed a more significant reduction, compared with sham stimulation, of habituation of N2P2 component in migraine patients and controls. Only few studies with small sample size examined the effects of tDCS on chronic pain and gave conflicting results. Our study doesn't confirm the result of our previous study of rTMS stimulation of M1 that showed a reduced amplitude of the N2P2. The increase of habituation induced by tDCS of DLPC confirms his modulating effect on cortical excitability. Our results could suggest a different modulatory mechanism of tDCS due to a long-term effect. Further studies with chronic application are needed to clarify the possible role of tDCS in the management of migraine.

Hedonic experience of musical artifacts and relaxation affect pain perception: an example applied to Fibromyalgia

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Fibromyalgic Syndrome is characterized by chronic musculoskeletal pain associated with mood and sleep disorders and weakness. Classical analgesic therapies are often uneffective, for this reason we are interested in studying the effects of an alternative non-pharmacological treatment: psychoacoustic stimulation through binaural beats. In particular we aim at investigating cortical activation in fibromyalgic patients (electroencephalography, EEG) and self-report measures of pain intensity. Five participants affected by fibromyalgia took part to the study and were asked to listen to four music tracks composed according to the binaural beats technique. Musical tracks were interspersed with two minutes of silence and have been calibrated to the frequencies corresponding to delta, theta, alpha and beta bands. EEG was recordered during the experimental sessions. The experimental design included five recording blocks: an initial baseline and four blocks relative to the tracks. Before and after the psychoacoustic stimulation, subjects were asked to report the intensity of their pain perception trough a Visual Analogue Scale (VAS) and a Numeric Rating Scale (NRS). The VAS is a segment of 10 cm on which subjects indicate a position along the continuous line between two end-points: "no pain" and "severe pain". NRS is a 11-point scale through which the subject can locate himself on a scale of 0 to 10, with 0 being no pain at all and 10 severe pain ever felt. This procedure was repeated once a week for 4 consecutive weeks. Data were analysed by repeated-measures ANOVA. The results of the analysis showed a generalized relaxation effect mirrored by an increase in delta frequency, particularly in fronto-central area, and by an increase of alpha frequency power over occipital areas. Consistently, we observed also a decrease of beta band power. The overall prevalence of delta during listening to the music tracks is made even more evident during the acoustic stimulation frequencies focusing on that frequency band. Electrophysiological evidences are supported by a substantial decrease of VAS scores and NRS scores after subjects exposition to psychoacoustic musical stimuli. The hedonic experience combined with relaxation has an effect on pain perception and EEG activity associated to binaural stimulation through music tracks suggests that those alternative method may have an extended efficacy in fibromyalgic pain treatment.

Neurostimulation and pain perception: a TMS/EEG study

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In the present research we investigated the potential role of neurostimulation (transcranial magnetic stimulation, rTMS) in pain perception, studying the effect of rTMS (10-minutes 5 Hz applied to left dorsolateral prefrontal cortex, DLPFC) on acute pain experience. A sample of healthy participants took part to the study. We used a capsaicin-based gel to induce acute but progressive experimentally-controlled pain and recorded self-report Visual-Analogue Scales (VAS) for pain intensity each 5 minutes and EEG measures over time. The experimental design included five 5-minutes recording blocks: a pre- rTMS stimulation baseline and four consecutive post-stimulation blocks. The capsaicin gel was applied to the back of the non-dominant hand at the beginning of the first post-stimulation recording block and removed at the beginning of the last one. The results showed a greater frontal cortical activation involving Theta frequency increasing after rTMS stimulation. These data were supported by VAS scores that showed increased values and a long-lasting time perception after capsaicin gel application compared to subjects who did not receive rTMS stimulation. DLPFC is usually related to sustaining attention, monitoring and control function. We supposed, compared with previous research, that these results may represent a significant modulation effect on the monitoring and control experiences, pain-related, after 5 Hz rTMS applied on the left DLPFC. The use of TMS paradigm may suggest a relevant role of DLPFC in monitoring and inhibition processes in pain experience. Nonetheless, they may hint at clinical interventions to relieve pain in chronic patients where non-invasive techniques may complement pharmacological treatment.

A method for automatic REM sleep segmentation

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A basic property of REM sleep is that it is not a uniform stage. Two kinds of variations are particularly significant. First, a remarkable amount of literature, based

on polygraphic signals, fMRI images, and psychophysiological data, has shown that "phasic" epochs, presenting distinct oculomotor activity, should be distinguished from "tonic" epochs. Second, recent literature has provided interesting data about slow eye movements (SEMs), which are present during REM sleep in addition to rapid eye movements (REMs), although, according to Rechtschaffen and Kales (1968), during REM sleep SEMs "do not approach the abundance, magnitude, and pendular pattern of the slow eye movements during stage 1". Our research has aimed to propose a method for segmenting REM sleep into three substages, respectively characterized by (a) enhancement of REMs; (b) selective enhancement of SEMs; (c) no enhancement of either REMs or SEMs. A wireless digital polygraph (SOMNOScreen) was used for recording polygraphic signals from healthy subjects while they were sleeping in their houses. Twelve EEG traces were recorded from electrodes placed over the scalp according to the 10-20 System, together with two EOG traces, EMG, and EKG. Our method consisted of the following stages: (a) band-pass filtering in order to extract a slower component (0.2-0.6 Hz) and a faster (1-3 Hz) component from the original EOG signal; (b) recognition of events consisting in a transient increase of either of these components; (c) calculation of parameters characterizing these events; (d) insertion of these parameters into a relational database; (e) final segmentation provided by queries to this database. This method allowed quantitative parameters to be calculated connected to the amplitude variations of REMs and SEMs during each REM sleep epoch in the course of the night. The study of the oscillating properties of eye movements can lead to a better knowledge of the thalamocortical intrinsic loop active during REM sleep and of the interaction between unimodal sensorimotor areas and higher-order association cortices. Furthermore, an investigation of the properties of the REM substages in patients affected by REM sleep Behavior Disorder can shed light on the mechanisms of this disease, thus helping clinicians with the diagnosis and the treatment. Other currently debated issues connected with the study of REMs and SEMs regard vulnerability during REM sleep, the homeostatic process of sleep regulation, and the features of mentation in the course of sleep.