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Abstracts

Mental imagery disintegration in dementia

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Mental imagery is an internal representation based on information stored in memory that gives rise to the experience of viewing a stimulus in the absence of appropriate sensory input ("seeing with the mind's eye, hearing with the mind's ear"). Mental imagery has played a central role in the theories of mental function. John B. Watson (1913), the founder of Behaviourism, denied that mental images existed. According to Dual Coding Theory, Allan Paivio (1971) argued that mental representations, underlying the experience of mental imagery, involve the activity of two distinct subsystems, verbal (logogens) and non verbal systems (imagens). Conversely, different view was supported by Zenon Pylysyn (1973, 1981) who suggested that mental images are the same type as those used in language and that the pictorial aspects of imagery are epiphenomenal. The emergence of cognitive neuroscience has opened a new era in the study of imagery and a large amount of information has been learned about neural architecture of visual perception, memory and motor control. New neuroimaging technologies (ERPs, PET, fMRI) have allowed researchers to verify new theories in humans contributing to provide electrophysiological and correlational neural approach in exploring mental imagery. Mental imagery, similarly to all other cognitive functions, is not a single ability but it comes from the interaction of distributed networks of sensory and motor systems engaging brain mechanisms that are used in perception and action. Mental images can also be created by combining and modifying stored information (visual, auditory, motor, kinesthetic) in a novel way. Visual mental imagery is the most used modality. A theory of subsystem components of visual mental imagery has been developed by Kosslyn: he describes six major components (visual buffer, attention window, object properties processing and spatial properties processing, associative memory, information shunting, attention shifting) that are hypothesized to be implemented in different regions of the brain. The majority of degenerative dementias are focal or multifocal but never global, except for the terminal stages. They are characterized by a wide range of cognitive and behaviourally abnormalities whose neuropsychological profile may have implications for predicting the nature of the underlying neuropathology. The theory of visual mental imagery developed by Kosslyn suggests that the above mentioned subsystem works to create, generate and transform images. This theory may be useful in studying the visual mental imagery disintegration in dementia providing new hypotheses about which brain structures support each component process. We discuss particular profiles of visual imagery disintegration in Alzheimer disease and in other degenerative dementias to better understand the nature of mental imagery and how it is generated in the brain.

Creativity and dementia

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In these last years, creativity was found to play an important role for dementia patients in terms of rehabilitation strategies. Thus, the understanding of how dimensions of creativity change in the setting of dementia is extremely important in order to better implement stimulation programs. The present study investigated the extent to which dementia affects creativity and divergent thinking, which is an important cognitive process associated with future creative achievement. At the aim a group of dementia patients (mostly affected by Alzheimer's disease) was compared to a group of normal aged people at the performance on two different types of tasks: the Alternative Uses Task (AUT), which measures divergent thinking, and the Creative Mental Synthesis Task (CMST), which involves the ability to create original and functional objects. In the AUT participants were asked to describe as many different uses of common objects as they could within five minutes. Stimuli to work out were: brick and newspaper. In the CMST participants were asked to mentally combine three visual components in order to assemble a creative object belonging to a specific category. Six triads of components were used (e.g., cube, bracket and cone). In the combination process, components could be changed in position, rotation, and size, but not in their general structure. For each triads, participants sketched their invention and provided a short definition of it. The AUT was scored according to fluency (the number of relevant ideas), originality (the number of statistically infrequent ideas), flexibility (the number of categories or shifts in responses), and elaboration (the number of details provided along with the ideas). Regarding the CSMT, two independent judges evaluated all drawings on originality, defined as a drawing being new and not derived from something else, and on functionality, defined as an item involving an actual use in a specific context, rather than a hypothetical use. A Likert scale ranging from 1 (very poor originality/functionality) to 5 (very high originality/functionality) was used to evaluate the drawings. Results showed slight differences between the two group in terms of divergent thinking, whereas non-dementia participants were markedly better than dementia participants at the creative mental synthesis task, both in terms of originality and functionality. These results showed that dementia affects divergent thinking and mainly the ability to create objects when visuo-spatial processing is required. However, these results do not contrast with the idea that dementia patients are sporadically capable to come up with original ideas. In conclusion, the present study supports the possibility that divergent thinking can enhance copying abilities in the setting of dementia, and that the rehabilitation of dementia patients should include the enhancement of creativity that relies on visuo-spatial processing.

Brain plasticity in dyslexia after phonological rehabilitation

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In the present research, we investigated language lateralization in Italian children affected by developmental dyslexia before and after they underwent 6-month phonological training. To measure linguistic reorganisation, we analyzed an early wave – the recognition potential (or N150) – elicited by automatic word recognition and peaking over left temporo-occipital cortex. N150 elicited by written words was measured in a sample of 14 normal readers and in group of 14 dyslexic children (before and after training), during Phonological, Semantic and Orthographic tasks. Normal readers exhibited the typical left posterior N150, whereas dyslexic children showed, before training, a pattern of bilateral activation. After training, dyslexic children increased their reading speed and their N150 was shifted to left posterior sites. In addition, after the training, dyslexics' left posterior N150 asymmetry to the Phonological task was significantly correlated with reading speed improvement (Pearson's r = 0.56): that is, those children who showed the greatest left shift in the phonological N150 also had the greatest reading speed improvement. Source localization of the N150 component was localized in the left occipito-temporal cortex (Brodmann Areas 39, 37 and 19) in good readers, but in right homologous areas in dyslexic children before training. After the treatment, the dyslexics' main N150 generator shifted to the left occipito-infero-temporal cortex (namely, BAs 37 and 19) with small differences between tasks. Results add to current literature on the phonological hypothesis of dyslexia by showing plastic, hemispheric reorganisation of linguistic networks at the level of early word recognition potential in a regular/transparent language like Italian.

Role of audio/visuomotor neurons in music learning

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The discovery of audiovisual mirror neurons supports the hypothesis that they encode visual and sensorymotor information about musical gestures in association with the sounds they produce. These neurons may underlie the ability to learn how to play an instrument, which is a rather long and expensive process that takes place through imitation and exercise, under the guide of visuomotor, audiomotor and proprioceptive feedbacks. Arguably, learning to play a musical instrument will stimulate the formation of new synaptic connections between audiomotor neurons and IP, motor, premotor, SI, SII somatosensory cortices, cerebellum, corpus callosum, basal ganglia, and extra-striate visual areas. However the neural mechanism supporting music ability and learning remains relatively unexplored. To address this matter we investigated the temporal dynamics of brain activation during audio-visual perception of congruent vs incongruent sound/gesture movie clips in 30 musicians of Milan Conservatory (15 clarinetists and 15 violinists) and healthy controls, while listening and watching violin and clarinet executions. To this aim 200 audiovisual clips were recorded in which a clarinetist and a violinist played the same pieces of music with their instruments. The sounds produced were similar in pitch, intensity, rhythm and duration (across instruments). In one condition the clips were presented as recorded, whereas in another condition the visual information was accompanied by a discording soundtrack. This manipulation was aimed at stimulating the recognition of an incongruence between sound and action in musicians (hence, in violinists for the violin but not the clarinet and vice versa). ERP were recorded from 128 scalp sites and swLORETA inverse solution was applied to ERP responses. Only in musicians it was noted a N400 response elicited by incongruent audiovisual information. Musicians' ERPs were also sensitive to violations relative to the non-familiar instrument, with a gradient in the response, while the naïve brain was unaffected. The results showed when and how in the brain is coded the relationship between finger/hand/arm/orobuccal muscles activity and corresponding sounds produced, as a result of musical learning.

Cross-modal perception: sensory interactions and cortical excitability

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Multisensory integration refers to the mechanisms whereby sensory inputs from different modalities are combined into a unified percept. At the perceptual level, multisensory integration can express itself in two main ways: it can improve the processing of sensory-specific stimuli when coherent information is provided by different senses, or it can bring out crossmodal illusory percepts when incoherent information in different modalities is presented. Crossmodal illusions are of great value for testing hypotheses on mechanisms of multisensory integration, and in particular for exploring the perceptual consequences of disrupting the normal relationships among sensory cues. In this framework, a new line of investigation has taken advantage of the non-invasive brain stimulation technique of transcranial Direct Current Stimulation (tDCS). With this technique, it was shown that cortical excitability shifts in heteromodal, association, areas (e.g., superior temporal sulcus), as well as in primary sensory cortices (e.g., primary visual cortex), can greatly impact the interaction between vision and audition, in turn modulating crossmodal illusions resulting from audio-visual functional links. This was first shown in the temporal domain, where audition is the dominat modality, and it can especially affect vision, as shown by the "sound-induced flash illusion". But even in speech perception, a function that is generally considered to be an auditory function, vision has been shown to strongly alter the quality of the auditory percept, as shown by the "McGurk illusion". Both these audio-visual illusions can be augmented or diminished by up- or down-regulating cortical excitability by means of tDCS. These modulatory effects are highly specific, being dependent on the stimulation parameters (i.e., the current polarity), the stimulated area, and the type of evoked illusory percept. Overall, tDCS studies of crossmodal illusions show that sensory-specific perceptual judgments concerning one sense, and their interactions with other senses, depend on the level of excitability of unisensory and multisensory cortical areas. This novel evidence elucidates the causal association between neural activity and the conscious perceptual experience brought about sensory interactions, and it highlights the effectiviness of tDCS for altering multisensory processing in the human brain.

The role of ocular movements induced by endogenous and exogenous attentional signals on motor programming

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In natural conditions gaze and arm movements, via visuospatial attention, are commonly aimed at the same target and their accuracy is considerably enhanced if both effectors move together. It has been well established that oculomotor system and visuospatial attention share a common neural substrate. On the other hand, data suggest that arm and saccadic motor systems are at least partially driven by a common command, but no direct evidence for this has been so far provided. To investigate whether fast eye movements induce excitability changes in the upper-limb Corticospinal System (CSS) even in the absence of an overt manual response, we applied single-pulse TMS to the left motor cortex of right-handed subjects and recorded Motor Evoked Potentials (MEPs) induced in relaxed hand and wrist muscles of the contralateral arm while different ocular tasks were executed. In Experiment 1 (19 participants), a visually-guided saccade was made to one of 6 positions along the horizontal meridian (±5°, ±10° or ±15°) and TMS was randomly delivered at one of 3 different time delays after saccade onset. On top of a change in the overall CSS excitability, MEPs were specifically modulated in the recorded muscles, depending on target position and TMS delay. Modulations clearly showed a subthreshold motor coupling of the resting hand with gaze. We investigated the nature of this coupling by conducting two experiments to assess whether CSS changes are triggered whenever a shift of spatial attention occurs, or are tied to the actual execution of an eye movement. In Experiment 2 (27 participants), the effects of overt and covert shifts of attention were tested by making the subjects discriminate whether a peripheral cue had to be targeted or not by gaze. TMS was delivered randomly before the cue onset or within 1 s from it. An overall inhibition of CSS excitability and a subthreshold motor pattern compatible with a hand pointing were found, but only after overt shifts of visuospatial attention. In Experiment 3 (29 participants), the effect of eye movements towards peripheral cues (prosaccades) was compared with that of saccades executed towards a location endogenously computed by subjects, placed in the opposite hemi-field of the visual cue (antisaccades). Again, TMS was delivered randomly within about 1 s from the stimulus onset. In this case, no modulations of CSS excitability followed overt shifts of attention driven by endogenous signals, i.e. by cognitive factors. Altogether, these evidences demonstrate for the first time that eye and hand motor systems are coupled even when only one effector is overtly recruited. Moreover, the motor nature of the signal coupling hand control system and saccadic eye movements (i.e., visuospatial attention) was disclosed. However, this coupling requires that visuospatial attention is overtly shifted towards a peripheral stimulus and is not elicited by endogenous attention shifts (antisaccades).

Psychophysiology of eye-movements and "attentional gradient effect" in unilateral spatial neglect

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Neglect patients generally fail to respond appropriately toward stimuli located in the contralesional space and may ignore stimuli or reduce the extent eye and hand movement to objects occurring within this space. Thus, systematic spatial biases in the visually guided actions were observed for patients with right-hemisphere damage. As it was found in previous studies, in addition to the behavioral response, it is important to monitor the eye behavior during a visual search task to analyze the difficulties related to the exploration of the visual space by neglect patients. The present study analyzed behavioral and eye-movement measures in unilateral neglect patients in response to online bisection task (unfilled gap lines). Two different tasks were used to test the bisection performance, a pointing and a grasping strategy. Indeed, we hypothesized that neglect patients may be more directly impaired in task execution (online bisection) in case of pointing than of grasping strategy. Therefore, it was explored whether these different strategies may influence subjects' behavioral and eye-movement measures. Secondly, segment length (from shorter to longer) and its spatial position (from right to left spatial location) were monitored, to verify the consistency of rightward bias increasing as a function of left-side more than right-side dislocation and of longer more than shorter segments. Eleven neglect patients and ten control subjects were included into the study. The subjects could give their response pointing the perceived midpoint starting from stimuli onset (pointing condition). In the grasping condition, subjects were required to imagine they had to grasp an object localized on the midpoint of the segment, instead of only perceptually visualize and point the midline of the segment itself. Eye movements were recorded using an infrared-based video tracking (Tobii X120), including the total number of fixations, fixations length, and direction of the first fixations during bisection task execution. Consistent spatial biases were found for both bisection responses, fixation count, and duration, as well as for the first fixation count in case of pointing task. The spatial gradient effect was found only in response to specific "leftward" positions. In addition, bisection task was affected by the cognitive strategy of patients, with a more consistent rightward response bias in case of a representation finalized to pointing more than grasping. Eye-movement behavior supported and confirmed this behavioral trend. An "extreme-left" gradient effect was suggested and discussed, with patients' behavioral and eye measures more impaired. On the contrary, the patients' performance was similar to the controls' one in case the grasping task. The direct link of visual pointing and grasping strategy with two distinct cortical pathways was adduced to explain these results.

Eye movements and semantic priming analysis for a differential diagnosis between hemianopia and neglect

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The difficulty in exploring the surrounding space after a brain damage could be caused by an attentional deficit (neglect) or by a reduction of visual field width (hemianopia). Even though there are different anatomical substrates between neglect and hemianopia, the performances of the patients may provide confounding results at the specific examinations. In particular it is not yet clear if the observation at the neuropsychological tests is a unique expression of neglect nor if the result at the visual-field exam is exclusively dependent by hemianopia. In the last twenty years only few studies tried to disentangle neglect from hemianopia. Besides these contributions, scientific literature provides lot of results concerning an implicit information processing for patients with neglect which is not present in patients with hemianopia. We then hypothesize that a prime-word in the neglected field should determine a semantic activation effect; whilst, if the prime-word occurs in a blind hemifield, the stimulus should not determine any activation effect. Considering this hypothesis, we studied the performance of a patient with a bilateral brain lesion causing left visual neglect and right homonymous hemianopia. The experimental procedure consisted in a fixation point in the centre of the screen for 150 ms; after that, a prime word occurred in six possible positions on the central horizontal line of the screen corresponding to three positions on the left and three on the right. At that point, a target word appeared in the centre of the screen. The patient was required to press the space-bar only when the target word belonged to a living category. Noteworthy, the primed word could be defined as related, unrelated or neutral (namely, an "x" string) with the target word. During the experimental session, eye movements were recorded by means of an infrared-based video tracking that provided further details in describing how patients explored the space. A significant semantic activation was observed when prime-words occurred in neglect hemifield (left) but no activation was found when they appeared in blind hemifield (right). Eye movement analysis showed the presence of saccades towards neglect hemifield when prime occurred in extreme-left positions and fixations when prime occurred in central-left position. We did not observe any saccade nor fixation when prime occurred in hemianopic field. Our results are in line with the hypothesis concerning semantic activation in the space affected by neglect but not in hemianoptic field. In addition, eye-movement analysis supports evidences concerning a spared automatic orientation of attention towards neglect space. In conclusion, even thought our data concern a single case study and further observations are needed, our findings seem to confirm the importance of a comparison between behavioural and visual exploration data to differentiate between neglect and hemianopia.

Anticipatory postural adjustments in children with balance disorders: research and clinical perspectives

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Anticipatory Postural Adjustments (APA) are postural muscle activities that occur approximately 150 ms prior to predictable postural perturbation (i.e., voluntary movement) and accompanying biomechanical effects and is hypothesized to minimize the effects of the forthcoming postural perturbation in a feedforward manner. Research in adults show that APAs accompany learned voluntary movement or prior to some predictable externally induced perturbations. APA patterns are modified not only to the direction of body perturbation but also context of the task. For example, timing of onset of APAs can be altered depending on time-accuracy constraints, available sensory cues, balance demands t, etc. Much less about organization of APAs in children are known. In this talk, recent results comparing APA patterns in children with typical development, children with diplegic Cerebral Palsy (CP) and hemiplegic CP will be presented. Three groups of children performed series of upper extremity tasks while standing on a force platform. Electromyographic activity of six trunk and leg muscles and displacement of Center of Pressure (COP) were recorded. Children between 7-16 year old with typical development can generate typical APA patterns similar to that of adults when performing different upper extremity tasks while standing. Children with CP, can also generate APAs but are generally much smaller in magnitude, especially in children with diplegic CP. Translation of APA research findings into clinical practice to improve balance strategies for children with CP as well as postural control disorders will be discussed.

Anticipatory postural adjustments in patients with balance disorders

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Anticipatory Postural Adjustments (APAs) can be evoked not only before a voluntary movement during upright stance but also during platform-administered, repeated, and therefore predictable, balance perturbations in the Anterior-Posterior (A-P) direction. During predictable perturbations, patients with Parkinson's Disease (PD)-fallers show larger body oscillations than PD-non-fallers. Body displacement increases with the levodopa dose, indicating a trend for medication to worsen balancing capacity. Patients with peripheral neuropathy show better performance when tested on the continuously moving platform than during quiet stance. This paradoxical phenomenon might be connected with the preserved capacity of these patients to exploit APAs. Patients with unilateral vestibular deficit show larger body oscillations than normal subjects. In spite of this, the basic coordination strategy for maintaining equilibrium is not overthrown, pointing to a major role of APAs in this task. Overall, the results suggest that predictable perturbations are a useful tool for assessing the capability to produce APAs and for detecting instability in patients with balance disorders.

Do anticipatory postural adjustments follow Fitts' law in pre-planning elite dancers' actions?

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Despite the wealth of studies on APAs and modulations for executing movement, very few have investigated the distinct role APA magnitude and duration play in actions that include a trade-off between speed and accuracy and none to our knowledge have investigated their behavior on a Fitts' law paradigm considering both different target distances and widths. The beauty of testing APAs in a Fitts' task resides in taking advantage of the model's predictions about task parameters over performance as indicated by the ID. Here we present analysis of APAs behavior to reveal how the CNS tunes the timing and the magnitude of anticipatory muscle activity with respect to task parameters for successfully accomplishing an action. Both APA magnitude and duration are considered; here we show that APA magnitude is involved in preparing mainly for movement speed, while APA duration modulate to the ID, thus including movement accuracy as well. The action considered very closely resembles "battement tendu", a basic ballet move. Here we tested experienced/elite professional dancers to ensure optimal performance in the trade-off between movement speed and movement accuracy.

Functional brain networks and empathy for pain

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Successful interpersonal relationships require people to appropriately represent and understand actions, intentions and feelings of their conspecifics. Neuroscientific evidence suggests that a large expanse of the human cortex shows stimulus-driven activity when subjects observe other individuals displaying actions, intentions and emotions. These regions largely overlap with the cortical regions activated during the first-hand experience. This shared resonance system firstly hypothesized for the domain of action it has been now proposed also for our comprehension of sensations and emotions of others, including touch, pain, disgust and gustatory emotions. In the domain of empathy for pain, the vicarious experience of pain does not only recruit the affective node of the pain matrix, as evident through seminal fMRI works, but also elicits the stimulus-driven activity of the somatomotor cortex coding the basic sensory dimension of the experience. Using the high temporal resolution of MEG, we expanded this finding demonstrating that the empathic reactivity to other's pain is linked to a functional network mediated by the gamma-band synchronization in the sensorimotor cortex. Importantly, this sensorimotor synchronization is significantly correlated with the intensity and the unpleasantness derived from the observation of other's pain. Overall, these results suggest that empathy like other complex cognitive processes is inherently linked to the activation of a task-dependent functional network, more than of single areas. Interestingly, recent works in human functional neuroimaging suggest that networks of the brain maintain even at rest, i.e. in absence of any external stimulus or task, a high degree of temporal correlation. Although the topography of these Resting State Networks (RSNs) is similar to that of task networks and is resilient to behavioural manipulations, a recent fMRI study suggests that the spontaneous intrinsic neural activity predicts our ability to empathize with others' pain. To conclude, understanding the neural mechanisms underlying the large-scale interaction between spatially separated brain areas not only provides important clues on the functional brain networks involved in observation of pain in others but also suggests that our disposition to react to other's emotions and feelings is driven by the intrinsic neural activity, which is thought to reflect a prior for task-driven patterns of activity.

Olfactory perception: from molecules to psyconeurophysiological response

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The olfactory perception return a heteromodal response characterized by the integration of information carried by the chemophysical characteristics of the odorant molecules such as volatility, molar concentration and density, and biological features e.g. consciousness, pleasantness and mind recall. This complex system in order to be investigated must be decomposed in basic parameters. The aim of this study is to evaluate the complete olfactory function, in large population sample, by dissecting into its principal components: threshold; discrimination, identification, associative and short term memory. Ad hoc psyconeurophysiological tests, modified for Italian population, coupled to new generation of sensor are used for this purpose. The recording system used in these experiments was an iAQ-2000 equipped with a Metal Oxide Semiconductor (MOS), which is able to detect a broad range of Volatile Organic Compounds (VOCs). Six hundred (age = 29.3 ± 15.3 SD) healthy individuals were enrolled in the study establishing the Italian Database for the Olfactory Function Evaluation (IDOFE, Neuroscience Institute, CNR-Pisa) release 1.0. The database provided 193 male (age = 32.68 ± 17.8 SD, interquartile range [Q3-Q1] = 27, minimum age = 5, maximum age = 76) and 407 female (age = 27.65 ± 13.6 SD, interquartile range [Q3-Q1] = 12, minimum age = 5, maximum age = 86) single data sets of age and gender. The test reliability coefficients is 0.82, the one way ANOVA between test and re-test returned no significant differences. In particular, regard as the threshold the MOS sensor revealed that the theoretical threshold curve based on molar concentration of the stimuli dramatically diverge from the measured ones. The threshold curves per sexes show a trend inversion in the age cluster 40 for the whole population. The one way ANOVA report a significant effect of the ageing process in both sexes $p < .001$. Moreover, the cluster 40 comparison between sexes report a significant difference, such as for cluster 50, $p < .03$. A comparison within no-ovulatory, ovulatory, pills taker and menopause show significant differences. Furthermore, a three peak distribution is found in the whole population, and in sexes separately, threshold frequencies. The results shown that age cluster 40 is a critical limit in the population ageing process for the olfactory threshold. Furthermore, in the healthy population the distribution of the threshold frequencies suggests three phenotypes: juvenile, adult and ageing. In healthy women the hormonal statuses

influence the olfactory capability. In conclusion, this work release the first Italian database of the complete olfactory function, based on real perceived ppm. In particular, the olfactory threshold is a key parameter in the evaluation of the complete olfactory function.

Olfactory system dysfunction as an early sign of neurodegeneration

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The olfactory system has attracted much attention among researchers in the field of brain aging and age-related neurodegenerative diseases. The human olfactory bulb undergo apparent age related degeneration that might be more prominent in Alzheimer's Disease (AD) cases. This could be due either to neuronal loss or reduced neurogenesis in the subventricular zone or olfactory epithelium as a result of impaired trophic support. Thus, the relevance of olfactory deficits have been discussed for AD patients as regard its etiology, pathogenesis, diagnosis and potential prevention/therapy. Olfactory functional impairments in AD include deficits in odor detection threshold, discrimination, identification, memory and associated behaviors. Moreover, histopathological markers as neuritic dystrophy, amyloid deposition and tau pathology are reported in the olfactory epithelium, olfactory bulb, anterior olfactory nucleus, and olfactory high cortical centers. Morphological changes in AD patients are associated with reduced resting neuronal activity and blood supply as well as with altered evoked responses in olfactory centers. This complex neurodegenerative pattern raise the important issue of whether olfactory impairment represents an early sign of neurodegeneration that can be detected in subjects at risk of developing AD. We have designed a pilot study in a small group of Mild Cognitively Impaired subjects (MCI, n = 9, mean age 75.5 ± 2 SE, max age = 83, min age = 63). The aim was to evaluate the olfactory function in MCI evaluating its principal components: threshold; discrimination, identification, associative and short term memory. Ad hoc psychoneurophysiological tests, modified for Italian population, coupled to new generation of sensor was used for this purpose. In addition different biomarkers for neurodegeneration and the levels of BDNF, a trophic factor that promotes neuronal survival, were evaluated in plasma and CSF of MCI subjects and compared to Non Cognitively Impaired age matched individuals (NCI, n = 17). We found that olfactory threshold was significantly higher in MCI subjects respect to the average threshold of healthy population in the same cluster of age (7.3 ± 0.5 vs 6.39 ± 0.58 SE, one-way ANOVA, $p < 0.05$). Moreover in MCI subjects olfactory discrimination was significantly impaired and both associative and short-term olfactory memory were severely compromised. Interestingly, BDNF levels in CSF of

MCI patients were significantly reduced ($p < 0.001$, Mann-Whitney Rank Sum Test) respect to NCI individuals and differently correlates with the specific components of olfactory function. In conclusion, in agreement with previous studies our data suggest that olfactory impairment might represent an early sign of neurodegeneration that could be useful in association with other biomarkers to identify people at risk of developing AD.

The clinical evaluation of olfactory deficits in Alzheimer disease and idiopathic Parkinson's disease

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A complete and appropriate medical investigation of the olfactory deficits relies on the combination of a number of elements: the patient's personal history, clinical findings collected from otorhinolaryngological and neurological examinations, psychophysical assessment of olfactory performance, structural assessment of the olfactory apparatus with imaging techniques, and functional assessment of the olfactory system with electrophysiology such as Olfacto-Electroencephalography (Olphacto-EEG) and Olfactory Event-Related Potentials (OERP). Psyconeurophysiological testing allows a semiobjective evaluation of the olfactory function. In particular, orthonasal testing involves presenting different smells through the nose during inspiration or sniffing, or both; while retronasal testing involves presenting different odors through the mouth, the odorant molecules reaching the olfactory neuroepithelium through the retrovelopharyngeal pathway. In the present study we investigated a sample of Alzheimer Disease (AD; n = 10, age = 74.6 ± 11.18 SD, minimum age = 50, maximum age = 92) and Idiopathic Parkinson's Disease (IPD; n = 9, age = 73.89 ± 9.58 SD, minimum age = 52, maximum age = 84) psychophysiologically. We found in AD patients a threshold of 7.43 ± 2.49 SD, discrimination 3.7 ± 1.17 SD, identification 1.6 ± 0.69 SD, associative memory 0.3 ± 0.48 SD and short term memory 1.8 ± 1.39 SD. In IDP patients the outcome is a threshold of 6.45 ± 1.82 SD, discrimination 4.22 ± 0.67 SD, identification 1.78 ± 1.2 SD, associative memory 1.44 ± 0.88 SD and short term memory 2.78 ± 0.83 SD. The threshold, identification, short term memory evaluation prove a severe hyposmia for AD and IDP patients respectively. However, the olfactory associative memory is dramatically impaired in AD patients. Furthermore, this component is a key parameter to distinguish between the two pathologies, the one way ANOVA yielding a significant difference $F(1.17) = 12.7$, $p < .01$. Furthermore, we already recorded OERP from orthonasal stimulation induced by a prototype of the olfactometer in some cases. The olfactometer is essential for synchronizing the stimulation to the OERP response which is the critical aspect in such technique. The prototype of the olfactometer allowed stimulating by using isolate pulses of controlled duration and/or train of pulses. Moreover, it is suitable for molecule dilution and combination for both unimodal and heteromodal stimulation. In conclusion, even if the study

is still in progress we may conclude that evaluation of olfactory system represent a useful tool to investigate and quantify olfactory impairments in these diseases and to follow up their time evolution; furthermore a specific device, like that implemented by our lab, could represent a significant improvement to detect and quantify such involvement.

Changes of EEG topography during sleep as biological markers of Alzheimer diseases and major depression

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Sleep disorders or changes in normal sleep pattern commonly affect neurodegenerative and psychiatric disorders. The interest in studying cortical EEG topography during sleep in these diseases may potentially affect our knowledge of basic mechanism of sleep and, especially, may provide some neurophysiological early markers of these diseases. For this reason, we are involved in projects aimed to assess how EEG topography of sleep (1) discriminates Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD) patients from healthy elderly; (2) predicts clinical outcome in Major Depression Disorder (MDD), as a consequence of rTMS of Dorsolateral Prefrontal Cortex (DLPFC). The main results point to that: (1) a diurnal slowing of EEG in most of frequency bands of AD and MCI patients, compared to healty elderly people, is paralleled by similar EEG changes during NREM sleep; (2) the bilateral rTMS treatment in MDD patients over the DLPFC induces topographical-specific decrease of the alpha activity during REM sleep over left-DLPFC, significantly associated to the clinical outcome. These preliminary findings strengthen the view that neurophysiological changes during sleep in neurodegenerative and psychiatric disorders negatively affect the life of these patients, but may also be potentially useful in indentifying new biological markers of these diseases.

Cortical reactivity to transcranial magnetic stimulation in Alzheimer's disease and severe major depression

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Electroencephalography (EEG) combined with navigated Transcranial Magnetic Stimulation (TMS) provides a direct and non-invasive measure of cortical excitability in humans. Hence, our group has employed TMS/EEG to measure pathological alterations of cortical circuits and to track over time therapy-induced modifications of neural activity. Here we summarize the main results of researches on two different diseases, namely Alzheimer's disease and severe major depression. In a first study we explored how frontal cortex excitability (i.e. the early and local cortical response to TMS) changes during healthy and pathological aging. In particular, we compared the TMS-evoked EEG potentials collected in healthy elderly individuals (n = 10) with the ones collected in healthy young individuals (n = 10), and in patients with Alzheimer's disease (n = 10) characterized by a considerable impairment of cognitive functions. We observed that frontal cortex excitability was not significantly different between healthy young and elderly individuals, and was clearly reduced in elderly patients with Alzheimer's disease. In a second study we applied TMS/EEG to evaluate the electrophysiological effects of Electroconvulsive Therapy (ECT). From a clinical perspective, ECT has significant short-term antidepressant effects on drug-resistant patients with severe major depression. We compared the EEG responses to TMS collected before and after a course of ECT in a group of patients (n = 8) with severe major depression. Clinical assessment confirmed the beneficial effects of ECT on depressive symptoms at the group level. TMS/EEG measurements revealed a clear-cut increase of frontal cortical excitability after ECT as compared to baseline, that was significant in each and every patient. These results agree with previous animal studies showing potentiation-like synaptic remodeling after electroconvulsive seizures, thus corroborating the idea that ECT may produce synaptic potentiation in humans. Overall, we can conclude that TMS/EEG may be effectively used to noninvasively detect pathological changes in the state of cortical circuits across the lifespan as well as to monitor longitudinally the electrophysiological effects of different therapeutic neuromodulators.

Neurophysiological phenotypes of schizophrenia

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Studies that aim to find diagnostic markers for schizophrenia through pathological images and morphological abnormalities of the brain have been conducted for over a century, but most of them were fruitless. The diagnostic process in schizophrenia is syndromal, based on a collection of symptoms, including delusions, hallucinations, flattened affect, and thought disorder: these symptoms have heterogeneous presentation in different patients and may vary over time within the same individual. Thus, biological markers can not be used to diagnose schizophrenia. With the progress in brain imaging technology, several lines of research have tried to characterize the differences in brain structure associated with the clinical diagnosis of schizophrenia. Some evidences, such as lateral ventricular enlargement and decreased cortical volume in medial temporal lobe and frontal lobe, have been consistently replicated. Although these studies are interesting, they are essentially descriptive and do not provide specific information about the etiopathophysiology of schizophrenia. In the last decade, a more hypothesis-driven strategy has being increasingly adopted, involving the use of quantitative measures, within more specific neurobiological mechanisms. These variables, the so-called "intermediate phenotypes", are phenotypic variables, easily quantifiable, independent from the state of the illness and involved in a biologically plausible mechanism of pathogenesis. More relevantly, an intermediate phenotype should be heritable, and be found in non affected family members of patients with schizophrenia, at higher rate than in the population. In other words it should be strictly linked to the genetic of the illness. In the recent past, a large effort has been spent in evaluating Working Memory (WM) deficits in schizophrenia. Performance at WM tasks has been considered a good intermediate phenotype for schizophrenia, and a potential diagnostic and prognostic value has been suggested. More recently it has been selected a brain phenotype related to working memory (i.e., the prefrontal activity during WM tasks as measured with functional magnetic resonance) that could be considered physically closer and more causally linked to gene expression. In the present talk it will be described how an intermediate phenotype such as WM brain activity has helped to show the impact of genetic variants putatively involved in the pathophisiology of schizophrenia (such as the variants in the COMT gene, in the dopamine D2 receptor gene, in the AKT1 and GSK3b gene) and their interactions, in healthy subject and in schizophrenia patients. To date, we are far from a complete understanding of the pathophysiology of schizophrenia, but focusing on intermediate phenotype may allow more accurate exploration of the neurobiology underlying the symptoms of schizophrenia and the response to treatment.

SELECTED ABSTRACTS
FOR ORAL AND POSTER PRESENTATIONS

Effects of rTMS of left inferior frontal gyrus on human movement responses to the Rorschach test

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Suppression of the 8-13 Hz (Mu) frequency EEG band recorded over sensorimotor cortex has been postulated as an index of mirroring activity in the brain. Using repetitive Transcranial Magnetic Stimulation (rTMS), recent research has also shown that temporary disruption of activity in the Left Inferior Frontal Gyrus (LIFG; presumably implicated in mirroring activity) eliminates Mu suppression during social perception tasks, while also decreasing performances. Based on these, and also other evidences showing that EEG Mu suppression is reduced during exposure to ambiguous, Rorschach inkblot designs eliciting "feeling of movement", we aimed at further investigating the link between mirroring activity in the brain and exposure to the Rorschach, ambiguous stimuli. Sixteen right-handed healthy volunteers took part in the experiment. Each was first examined with a self-report screening tool (so as to exclude overt psychopathology), and then exposed to the static, ambiguous Rorschach inkblot designs. For each inkblot design, participants were asked to answer the question "what might this be?" and responses were transcribed verbatim by the experimenter. The number of spontaneous attributions of human movement reported during exposure to the Rorschach stimuli (i.e., the number of human movement [M] responses) was our dependent variable. All participants underwent rTMS: half of the sample was stimulated over the LIFG (experimental condition) and the other half over the vertex (control condition). Also, all participants were exposed to the stimuli twice, i.e., during a baseline and soon after rTMS, with the time range being 4 weeks. Thus, a crossover, 2 (Between Sample: Vertex, LIFG) × 2 (Within Sample: Baseline, rTMS) design was adopted. Consistent with the hypothesis that the attribution of human movement to ambiguous stimuli is associated with mirroring activity in the brain and embodied simulation, disrupting LIFG, but not vertex, decreased the number of M responses produced by the participants. These findings provide additional support for the hypothesis that internal representation of the "feeling of movement" may be sufficient to trigger mirroring activity even when minimal external cues are present. Also, the study of the neurological and psychophysiological correlates of the Rorschach responses provides an unique opportunity to broaden our understanding of the psychological processes associated with the test.

Classification proposal of polysomnographic patterns in children and adolescents awakening from coma: a neurorehabilitation cohort study

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There is an increasing interest in the sleep patterns of patients with disorders of consciousness both in the acute and post-acute phases. Factors such as the presence of a sleep-wake cycle and the sequential alternation of the different sleep stages with physiological elements reflect the global integrity of the central nervous system and are known to be of critical importance for brain maturation and plasticity. The present study aims: (1) to evaluate the importance of prolonged polysomnography recordings in children and adolescents with sub-acute severe disorders of consciousness due to an acquired brain damage; (2) to characterize their sleep-wake patterns looking for neurophysiological markers of prognostic relevance. We performed a polysomnographic cohort study in 20 pediatric patients with acquired brain damage in the post-acute phase. Patients received a full neurological examination and a clinical assessment with standardized scales. We performed a prolonged PSG recording (24 hours) and a brain MRI. Outcome was assessed after 36 months. The presence of an organized sleep pattern as well as REM sleep and sleep spindles in the PSG recordings in the post-acute stage appeared to be highly predictive of a more favourable outcome. We developed a new classification proposal for PSG patterns which can be applied to children and adolescents in a vegetative state in the post-acute phase and appears to correlate with the possibility of recovery. Our study confirms that PSG recordings can help determine the ability to recover from a vegetative state and can be used as prognostic markers in young patients.

Motor cortical plasticity induced by motor learning through mental practice

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The general aim of this study is to better understand the neurophysiological mechanisms underlying the motor learning process in healthy humans, and more precisely learning by motor imagery. We studied the effect of physical and mental motor learning by examining cortical plasticity induced of the neural sensorimotor system. Paired-Associative Stimulation (PAS25) has been used to reveal Long-Term Potentiation (LTP)-like plasticity induced by motor imagery training. Nine subjects (5 males, mean age 23.3 ± 3.5) participated at three different experiments, performed in three separate days. The baseline experiment was designed to the test the effect of PAS25 on Motor Evoked Potentials (MEPs). PAS25 consisted of 200 electrical stimuli of the right median nerve at the wrist paired with a single TMS pulse over the hotspot of the Abductor Pollicis Brevis (APB) muscle area of the left hemisphere at a rate of 0.25 Hz and with an inter-stimulus interval between peripheral and TMS stimuli of 25 ms. 15 MEPs from APB, were collected with a TMS intensity able to evoke a 1 mV MEP amplitude on APB before and after PAS protocol. Then, subjects participated to other two experiments, separated by at least one week, where, the effect of PAS25 on cortical excitability was evaluated after the session of motor practice or motor imagery training. On the motor practice and motor imagery experiment days the MEPs were measured before and after the motor practice (or imagery). This was immediately followed by the PAS protocol and subsequent measurement of the MEPs. Motor practice consisted in executing 15 times a block of 5 finger sequences (opposition of thumb to index, medium, ring and little fingers), at individual maximum speed, with 10 s rest between the blocks (total number of finger movements: 375). The motor imagery training consisted in imagining the same task. For the motor imagery task, subjects were asked to imagine themselves executing the movement ("kinesthetic imagery"). Results showed that, similarly to motor practice, motor imagery training induced a marked inhibition of PAS-induced LTP. At baseline the PAS protocols produced the expected effects of MEP facilitation ($p < 0.05$). After motor practice and motor imagery training, the effect of PAS25 was opposite to that observed at baseline; instead of increasing MEPs, PAS25 reduced MEP amplitudes ($p < 0.05$). Further, a significant increase in movement speed was observed after both mental and motor training. These results expand the concept of

similarity between neural mechanisms involved in motor imagery and motor practice. Indeed, the concept of temporary suppression of associative cortical plasticity by neuronal mechanisms involved in motor practice training seems to be shared also by motor imagery training. As suggested by animal models dynamic properties of LTP formation are likely to play a crucial role in human motor memory formation induced by both motor and mental training.

rTMS stimulation improves the facial mimicry and detection response in an empathic emotional task

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Facial expression detection and facial mimicry in response to an empathic situation were analyzed in the present research. Recent studies on emotions have revealed a wide range of areas activated in response to emotional cues, specifically the premotor cortex and the sensorimotor cortex, when a subject "mirrors" the perceived emotions. We supposed a "simulation mechanism" may be related to empathic response, and that it could be supported by some specific prefrontal cortical structures. High frequency (10 Hz) rTMS (repeated Transcranial Magnetic Stimulation) was applied to premotor area to induce an increased response to facial expression of emotions when subjects (n = 26) were required to empathize with the emotional stimuli. The stimulus emotional valence was also varied (negative vs positive vs neutral faces) to explore the emotional content effect on empathic behavior. Autonomic (facial zygomatic and corrugator EMG subjective response) and detection (Correct Recognitions, CRs; Response Times, RTs,) measures were found to be modulated by the premotor cortex activity. Specifically, when prefrontal structures were activated (in comparison with sham effect and control site stimulation, parietal area) an increased performance was observed in terms of increased CRs and reduced RTs for face recognition from one hand; of increased emotion-specific EMG response from the other hand. In fact, zygomatic muscle was more responsive in case of positive emotion (happiness), whereas corrugator activity was related to negative emotions (fear, anger, disgust). A more significant effect was revealed for negative, and potentially aversive, faces in comparison respectively with positive (happiness) and neutral faces. Finally, a direct correlation was found between the autonomic and detection measures. Taken together, these results suggest a "simulation mechanism" and "embodied behavior" underlying empathic situations that includes both EMG and behavioral responses. This mechanism appears to be supported and regulated by the premotor area.

What kind of relationship between CNC, DRS scales and ERP measure in DOC (Disorders of Consciousness) patients? A semantic association task

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A diagnosis of Disorders of Consciousness (DOC) is difficult to provide, because clinical examination is limited in these unresponsive DOC patients. Available standardized tools specifically developed for the evaluation of patients with severe impairment are very limited and mostly relatively insensitive to minor changes in level of consciousness. Based on the evidence to-date, electroencephalographic assessments of consciousness provide valuable information for evaluation of residual functions, formation of differential diagnoses, and estimation of prognosis. Specifically, ERPs (Event-Related Potentials) might be used to assess consciousness, providing an on-line monitoring of information processing in the brain. The present research explored the relationship between different measures of DOC, that is electrophysiological measures (ERP N400 effect) and clinical measures (Coma Near Coma, CNC; Disability Rating Scale, DRS). This analysis aimed to verify the preservation of semantic linguistic processes in eighteen DOC patients. MCS (Minimally Conscious State) and VS (Vegetative State) patients were compared with respect of N400 amplitude and latency measures. They were submitted to an associative auditory task that included congruous (related final words) or incongruous (unrelated final words) word sequences. Firstly, an increased N400 peak amplitude within the fronto-central cortical areas was revealed in response to incongruous sequences for all patients. Moreover, this peak was temporally delayed in response to incongruous conditions in these cortical sites. In addition, VS patients showed a delayed N400 in comparison with MCS patients in incongruous condition. Moreover, a direct correlation was found between the clinical scales (both CNC and DRS) and the ERP modulation, in term of peak amplitude and latency. Thus the present results were discussed taking into account the significance of N400 as a marker of semantic processes in DOC patients. Secondly, it was underlined that this semantic cognitive covert process may be demonstrated also in patients that show significant impairment in overt behavior (as in VS or MCS). Finally it was suggested to use ERP measure to improve the diagnostic profile in case of DOC patients.

Left hemispheric unbalance and reward mechanisms affect gambling behavior. The contribution of the metacognition, SCR and cortical brain oscillations

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In general subjects choose their decisional strategy based on the estimated outcomes, in many cases mainly taking into account the long-term effects, since they learn to select the advantageous strategy across time. It was shown that pathological gambling is associated with deficits in frontal lobe functioning, and that this dysfunctional decisional strategy shows features similar of patients with bilateral VMPFC (Ventromedial Prefrontal Cortex) lesions since they prefer choices that bring immediate reward, although they are losing. The present research tested the effect of reward-sensitivity (BAS-Reward, Behavioral Activation System) construct on the ability to distinguish between high- and low-risk decisions by using IOWA Gambling Task. In order to elucidate the individual differences which influence the decisional processes, making them more or less advantageous, we considered the impact of BAS-Reward, of the frontal left and right cortical activity, of the SCR (Skin Conductance Response) and of the metacognitive skills, on subjects' decisions. More specifically, the lateralization effect, related to the increased activation of the left (BAS-Reward-related) hemisphere, was explored by using frequency band analysis. Thirty subjects were grouped in high-BAS and low-BAS group. Behavioral responses (gain/loss options, response Index, rI), pshychophysiological measure of SCR, and delta, theta, alpha and beta band modulation (asymmetry index) were considered. Moreover, sLORETA method was used to localise the source of neural activity in response to gain/loss options. It was found that high-BAS group increased the tendency to opt in favour of the immediate reward (losing strategy) more than the long-term option (winning strategy), and that high-BAS subjects showed an increased left-hemisphere activation when they responded to losing choices in comparison with low-BAS subjects. Dorsolateral prefrontal cortex and anterior cingulate cortex were found to differentiate the high-BAS vs low-BAS brain activity. In addition, no significant SCR modulation was observed for high-BAS group in response to losing strategy, in contrast to the low-BAS group. Finally, high-BAS subjects were unable to adequately represent their cognitive strategy. A "reward bias" effect was supposed to act for high-BAS, based on a left-hemisphere over-activation.

DLPFC and left supramarginal gyrus activation increases the recognition of instrumental and functional violations in action representation

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The correct outcome of many actions depends on the objects use, considering both the instrumental and functional features. Evidence that people have a dedicated system that links objects to possible uses or functions comes from lesion studies and experimental research on normal subjects. Indeed, object-related actions are blind to both the correct instrumental use of the object and to the functional use of the object. We directly compared two different object-related semantic violations, that is the incorrect object-action relationship (i.e., instrumental incongruence), in which the object was incorrectly used to perform the action in violation of the instrumental object-related features (grasping a bat upside-down), and an unusual object-action relationship (i.e., functional incongruence), in which the object was incompatible with the goal-related and intention-related requirements to perform that action (using a bat to mince meat). The contribution of frontal (Experiment 1) and posterior (Experiment 2) areas to process semantic violations (instrumental vs functional) in action representation was explored. The DLPFC and supramarginal gyrus activity was appositely modulated by tDCS (transcranial Direct Current Stimulation). The effect of tDCS (anodal) stimulation when subjects processed congruous/incongruous object-related actions was verified by measuring ERs (Error Rates) and RTs (Response Times) modulation. Forty-three subjects performed the detection task within a dynamic context (video tapes representing a sequence of four action frames ending with a congruous vs incongruous action). A constant current of 2 mA was applied for 13 min. The anode was placed above the DLPFC (with the centre above FCz, Experiment 1), and above the left supramarginal gyrus (with the center above P3, Experiment 2), and the cathode above the right supraorbital region. Significant decreased RTs were observed for incongruous stimuli in the case of DLPFC stimulation in comparison with sham condition. This effect was mainly related to instrumental semantic violations. It was suggested that activation of the DLPFC may increase the ability to analyse the semantic anomaly, limiting the cognitive costs. Moreover, parietal (supramarginal gyrus) stimulation reduced RTs only in response to functional semantic violations: this "reduction effect" was related to a specific mechanism induced by the action observation in case of contextual-constraint violation. Thus, different cortical generators were supposed respectively for the instrumental (more frontally distributed) and the functional (more frontally and parietally distributed) semantic incongruence.

Listening to speech recruit specific tongue motor synergies: a TMS tissue doppler imaging study

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The discovery of mirror neurons triggered several studies on a similar sensori-motor integration system for speech. Activation of the motor system during speech perception was demonstrated via single-pulse Transcranial Magnetic Stimulation (TMS). However, the measurement of cortico-bulbar excitability modulation is technically challenging and enables only a rather coarse measurement of the motor mirroring. In the present study, we applied TMS to the tongue motor area in association with Tissue Doppler Imaging (TDI) to describe fine-grained tongue kinematic synergies evoked by TMS during passive listening of speech sounds. Participants listened to four different syllables (/ki/, /ko/, /ti/, /to/), which are characterized by different patterns of dorso-ventral and antero-posterior movements of the tongue. TMS was delivered 200 msec after sound onset and TDI images were recorded 10 msec after TMS pulse to capture the evoked movement. We analyzed the images to extract information about the overall amount of tongue movement, its mean velocity and direction (raising or lowering of the tongue on the sagittal plane). We show that passive listening to speech sounds evokes a pattern of motor synergies coherent with speech production. In addition, we show that elicited motor synergies were more evident in those subjects showing good performances in discriminating speech in noise. We could observe such specificity only because of the combination of TMS and TDI, thus opening to a whole new series of studies. In fact, our data let us conclude that the motor system, during passive listening, does not simply increase its sensitivity gain to the same effector-related auditory features, but rather implements a specific and detailed simulation of the ongoing speaker motor plan.

Stimulus predictability modulates the timing of pre-motor activity in prefrontal cortex

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The Prefrontal Cortex (PFC) plays a critical role in motor control. The aim of the present study was to compare PFC activity in a Go/No-go task as a function of the predictability of stimulus onset. Twelve healthy participants (mean age 23.7 ± 5.1 years) volunteered. Cortical activity was measured by 64-channels EEG while the subject performed a Go/No-go task in which the visual stimulus (i.e., four-squared figures made by vertical and horizontal bars; two figures were defined as Go and two as No-go stimuli) were randomly displayed with equal probability; the subject had to push a key with his/her right index finger as fast as possible to Go stimuli or to refrain the response to No-go stimuli . Two conditions were considered: unpredictable and predictable. In the unpredictable condition, the Inter-Stimulus Interval (ISI) varied randomly from 1 to 2 s. In the predictable condition, concentric circles (n = 16) with progressively smaller diameters were displayed for 150 ms in sequence on the screen, centered on the fixation point; after the offset of the smallest circle (overlapping the fixation point), either a Go or No-go stimulus was displayed. In the latter condition, the timing of the imperative stimulus could be anticipated. At behavioral level, RTs and accuracy were measured. The Movement-Related Cortical Potentials (MRCPs) were segmented and averaged in 2-s epochs (from 1500 ms before movement to 500 ms after movement onset). The onset latency, peak latency and peak amplitude of the Bereitschaftspotential (BP) and prefrontal activities were analyzed. Repeated measure ANOVAs were used to compare the two conditions. The performance in the two tasks was not different. In the unpredictable condition, the MRCPs showed the typical slow rising negativity at both prefrontal (pN component) and frontal (BP) sites, reflecting inhibitory control and response preparation, respectively. A strong prefrontal Positivity (pP) starting after stimulus onset peaked immediately before the motor response, likely reflecting the disengagement of inhibition. In the predictable condition, the pN component was absent and only the BP was detectable; furthermore, the pP component initiated much earlier and was larger than the unpredictable condition. Thus, while the frontal activity was similar in the two conditions, the PFC and parietal activities were modulated by conditions. Overall, it seems that the PFC regulates executive functions, including motor inhibition and execution. When the ISI is random, there is sustained inhibition of the action plan by PFC; then, when the Go stimulus is recognized, the action plan is released. On the contrary, when the timing of the imperative stimulus and consequently of the motor action is predictable, the PFC does not need to inhibit the action, but it only releases the action plan after stimulus discrimination.

Action representation and tool use: a motor imagery study in expert tennis players

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The present study tested whether and how motor experience with a specific tool influences motor representation of a specific movement. To this aim, we considered as experimental population a group of expert tennis players and as control population a group of athletic individuals without tennis experience. Participants were asked to execute twenty single forehands into the wall with a tennis racket (Movement Execution, ME) and, afterwards, to produce a kinesthetic imagine of themselves while executing the same movements (Motor Imagery, MI). During MI participants handled one of the following tools: a tennis racket, a tennis-like racket and an umbrella. Results showed that the real and the imagined movements were almost synchronous when participants of both groups held the tennis rackets. In contrast, when tennis players handled the tools not specific for tennis the duration of the imagined movements increased significantly compared to the durations of ME and MI with tennis racket. On the opposite, the handled tool did not modulate novices' MI performances. In conclusion, this study showed that motor representation of people who developed motor skills associated to tool-use is reliant on the object used to practice movements. This suggest that, although motor imagery mainly relies on the activity of cortical motor regions, the non-motor information – as the tool used to practice movement – coming from the associative areas strongly affects the motor imagery performance.

Action observation combined with peripheral electrical nerve stimulation induces plasticity in human motor cortex

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Human action observation (AO) is known to affect the activity of the primary motor cortex (M1). 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. Here, we designed a stimulation protocol where the observation of a video showing repetitive finger-tapping movements was paired with electrical stimuli delivered on the right peripheral median nerve (AO-PNS). Left M1 excitability, measured by means of transcranial magnetic stimulation (TMS), was compared with that assessed after AO and peripheral electrical median nerve stimulation (PNS) alone. We showed that left M1 excitability increased only after AO-PNS. In contrast, AO effects on M1 excitability vanished immediately after video observation, and PNS did not evoke plastic modifications. Notably, the increased M1 excitability was still present 45 minutes after the AO-PNS protocol administration and was specific for the stimulated muscle. Finally, we showed 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) opening a general debate on rehabilitative treatments using action observation.

Transcutaneous spinal direct surrent stimulation modulates interhemispheric processing of motor and visual stimuli

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Transcutaneous spinal Direct Current Stimulation (tsDCS) is a noninvasive technique for modulating spinal cord function and consists in delivering a constant electrical field over thoracic spinal cord though a pair of sponge electrodes, one placed over the spinal cord and the other over the right arm. Although tsDCS was shown to focally modulate motor and somatosensory pathways in a polarity-specific manner, little is known about its effects on brain activity. We assessed the effects of tsDCS on interhemispheric processing in healthy volunteers, by evaluating changes in ipsilateral Silent Period (iSP) and hemifield Visual Evoked Potentials (hVEPs). Eight healthy subjects were enrolled; we evaluated changes in iSP duration and hVEPs (N1 and P1) amplitude, latency and interhemispheric delay (e.g. difference between latency of each potential recorded on the right hemisphere and that recorded on the left one), before (baseline, T0) and at a different intervals (immediately after = T1, 60' = T2) after anodal and cathodal tsDCS applied over the thoracic spinal cord (T10-T12 level, 2.0 mA, 20 minutes). iSP was evaluated by recording Motor Evoked Potentials (MEPS) from Abductor Digiti Minimi (ADM) and Abductor Hallucis (AH). VEPs were elicited by reversal (1 Hz) of a horizontal square wave grating (spatial frequency 2 c/deg) and the display was positioned in the right hemifield (with its inner edge at a distance of 1 degree from the fixation point). Stimulation was always monocular. Anodal tsDCS significantly reduced iSP duration for the upper limb (one-way ANOVA, ADM: T0 vs T1: $p = 0.0002$; T0 vs T2: $p = 0.0001$) and shortened the interhemispheric delay for both N1 (T0 vs T1: $p = 0.0006$; T0 vs T2: $p = 0.017$) and P1 potentials (T0 vs T1: $p = 0.0025$; T0 vs T2: $p = 0.0006$), while cathodal stimulation has opposite effects both on upper limb iSP (ADM: T0 vs T1: $p = 0.0001$; T0 vs T2: $p = 0.0006$) and h VEPs (N1: T0 vs T1: $p = 0.04$; T0 vs T2: $p = 0.005$; P1:T0 vs T1: $p = 0.048$; T0 vs T2: $p = 0.019$). tsDCS seems to modulate interhemispheric processing of motor and visual stimuli in a polarity-specific manner: while anodal stimulation facilitates interhemispheric communica-

tion, cathodal one seems to dampen it. Given the well-known inhibitory phenotype of callosal connections in humans, our results fit with recent data showing that, different from transcranial Direct Current Stimulation (tDCS), anodal tsDCS has inhibitory effects on cortical areas. tsDCS could be of particular interest as a new promising therapeutic tool in the managing a number of human diseases characterized by an unpaired interhemispheric balance, such as stroke, parkinsonisms and schizophrenia.

Effects of parietal continuous theta burst stimulation on episodic memory

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Although the parietal lobe is not traditionally thought to support declarative memory, recent fMRI studies and electroencephalography evidence during episodic memory tasks have consistently revealed a range of memory-related influences on activation in lateral Posterior Parietal Cortex (PPC) and Precuneus. Therefore, we aimed at investigating the possible causal role and the specific involvement of PPC and Precuneus in episodic memory. To this aim continuous Theta Burst Stimulation (cTBS) was applied to modulate the activity of these areas between the study phase and the test phase of an episodic memory task. Thirthy healthy right-handed subjects took part in the study and were randomly assigned to one of three groups according to the stimulated target (Precuneus or left PPC; Sham). During the study phase subjects viewed 160 pictures half outlined in green and half in red. During the test phase, 160 previously presented items and 80 new pictures were outlined in black and subjects were asked to indicate for each items if it was an old/Red, old/Green or New item. cTBS was delivered offline over the target regions before the test phase. The data were analyzed in terms of hit; false alarms; source errors and omissions. The main results showed a decrease of source errors after stimulation of Precuneus but not after right parietal posterior cortex and after sham simulation. This result suggests that modulation of Precuneus activity improved the retrieval process and thus supports its role in memory process.

Emotional bodies triggers fast motor reactions and motor resonance: single and paired-pulse TMS studies

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Perceiving and reacting to the emotional body expressions of conspecifics is critical for effective social functioning. Imaging studies suggest that perceiving emotional bodies recruits action-related fronto-parietal regions. However, it is unclear whether motor system involvement reflects "resonance" with the observed body movement or reaction (e.g. fight/flight) to emotional signs. To address this issue we used Transcranial Magnetic Stimulation (TMS) to explore changes in corticospinal (Exp. 1) and cortical (Exp. 2) motor excitability during observation of emotional body expressions. MEPs were recorded from the FDI muscle during active categorization of pictures of joyful and fearful expressions, neutral gestures (i.e., body configurations with implied motion similar to the emotional expressions but no emotional meaning) and static neutral postures. In experiment 1, corticospinal excitability was assessed in both hemispheres at 150 and 300 ms after picture presentation. In the earlier time window, MEPs to TMS of the right motor cortex were reduced for emotional relative to neutral gestures. Conversely, at 300 ms, greater excitability for dynamic emotional and non-emotional relative to static bodies was found in both hemispheres. The magnitude of the early (150 ms) and late (300 ms) motor modulations correlated with distinct personality dispositions, namely the tendency to feel personal-distress and to take the perspective of others, respectively. In experiment 2, using paired-pulse TMS, we further explored early changes in the excitability of the right motor cortex by assessing Short Intracortical Inhibition (SICI) and Facilitation (ICF) at 100-125 ms after picture onset. We found that emotional expressions reduced ICF relative to neutral bodies, and fearful reduced ICF more than joyful expressions. No modulation was seen for SICI or corticospinal excitability. Our findings highlight the temporal dynamics of the motor system during perception of emotional expressions. Seeing emotional – in particular fearful – bodies induced an early reduction in intracortical facilitation (100-125 ms) of the right motor cortex. Then, a reduction of corticospinal excitability for emotion bodies emerged at 150 ms in the right but not left motor cortex. These modulations were independent from "motion" features of the expressions, were greater in participants with higher interpersonal anxiety-related personality traits and likely reflected a freezing-like orienting response toward emotional body cues. An increase in corticospinal excitability occurred at 300 ms in both hemispheres independently from the emotional meaning of the gestures and was greater in participants with higher cognitive empathy. This

later response likely reflected the simulation of the body movement implied in the observed gestures. These findings suggest that fast reactions to emotional cues occur well before motor features of the observed emotional gesture are simulated in the motor system.

Counter-effects of high-intensity long-lasting tDCS on motor learning

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Transcranial Direct Current Stimulation (tDCS) is a non-invasive technique that can induce LTP/LTD-like plasticity and modulate cortical activity according to polarity of the current: Anodal Stimulation (A-tDCS) has been shown to increase cortical excitability and Cathodal Stimulation (C-tDCS) to decrease cortical excitability. Accordingly, the application of anodal tDCS during motor training can improve learning whereas cathodal application can reduce learning. Interestingly, recent studies have shown that increasing stimulation intensity or increasing stimulation duration can result in opposite effects on cortical excitability, which can be due to the triggering of compensatory mechanisms of metaplasticity. In this study, we aimed at investigating the effect of high-intensity long-lasting tDCS stimulation on motor learning to evaluate if A-tDCS may enhance plasticity and learning or may induce counter-effects as consequence of metaplasticity. To this aim, we ran two experiments: in experiment 1, the Motor Practice (MP) task consisted of Fast thumb abduction movements (F-MP) of the left hand, which induce learning. In experiment 2, the motor practice task consisted of Slow thumb abduction movements (S-MP), which do not induce learning. In both experiments, six blocks of MP (corresponding to 20 minutes) were performed while tDCS was delivered at 1.5 mA (electrode surface 25 cm^2; current density 0.06 mA/cm^2) on contralateral M1. Moreover, two blocks with fast thumb abduction were performed, one before and one after tDCS application. Peak acceleration in the fast thumb abduction blocks was used as measure of performance. Results of experiment 1 showed a general learning effect when participants performed the F-MP task. Crucially, A-tDCS reduced learning compared to sham stimulation and C-tDCS. Results of experiment 2 showed the opposite pattern: When participants performed the S-MP task, performance improved after A-tDCS, whereas no learning effect was found in the sham stimulation condition. Our results highlight that tDCS-induced plasticity in the motor cortex is state-dependent: When applied during a MP task that does not induce learning, A-tDCS increased performance; When applied during motor learning, A-tDCS interfered with performance, suggesting that the concurrent combination of tDCS with another plasticity-inducing protocol may trigger compensatory mechanisms of metaplasticity.

Improvement of reactive inhibition and proactive control by means of transcranial direct current stimulation

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Reactive inhibition and proactive control are two key aspects of proper behavior, coming into play when inappropriate or unwanted responses must be suppressed. The former allows restraining an already initiated response, the latter to increase attentional control over selective signals during a long period of time. Both the tasks are sustained by fronto-basal-ganglia circuits partially overlapped, in which the right Inferior Frontal Cortex (rIFC) is a common core area. Previous studies, however, investigated these cognitive processes separately, letting unexplored whether they can be improved simultaneously. In the current study, we modulated the neural excitability of the rIFC by means of transcranial Direct Current Stimulation (tDCS), while twenty-two healthy participants performed a single task in which both reactive and proactive processes were required. The task combined a classic Go/No go task and a Stop-signal task. One of two letters or digits (l and V; 1 and 5) was presented on the left or right side of a permanent fixation cross, asking for left or right hand responses with the corresponding index finger. A stop-signal (i.e., a red square) was presented after a variable delay at the same position of the last Go stimulus, indicating participants to inhibit the Go response in those trials. During the task, all participants received anodal tDCS and sham stimulation (current intensity = 1.5 mA; electrode surface = 9 cm^2; duration = 18 min) in two separated sessions conducted at least one week apart. The order of the stimulation sessions was contrabalanced across participants. The analysis of the data revealed an increase of reaction times for Go stimulus, a reduction of false alarms and a concurrent reduction of the stop signal reaction time, a covert index of the inhibitory process, during the anodal tDCS in comparison with sham condition. These results suggest that the stimulation of the rIFG with anodal tDCS induces both an increase of the attentional control and an improvement of the inhibitory processes. In conclusion, the current study shows a strict interrelation between reactive inhibition and proactive control and their dependence by rIFC.

Interindividual variability in functional connectivity predicts discounting behavior during intertemporal choice

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During Intertemporal choice Tasks (IT), in which individuals are required to choose between an immediate small reward and a larger delayed reward, future outcomes are usually devaluated as a function of the delay until their receipt increases, a phenomenon known as Temporal Discounting (TD). Previous neuroimaging studies have proposed two neural accounts for TD: the first assuming two agonistic neural networks (β and δ systems) for the evaluation of immediate and delayed rewards, respectively; the second assuming a single system for the evaluation of both rewards. Given the great inter-individual variability of TD and its relevance for several disorders such as pathological gambling, one of the currently most critical challenges is to define a specific neural marker able to predict TD independently of task-evoked activity. To address this issue we submitted twenty-five healthy volunteers (mean age: 25.8) to: (1) three fMRI scans (3T) of resting state activity; (2) an IT computer-based task, in which they choose between an immediate amount (10 €) and 7 (amounts: from 15 to 60 €) × 6 (delays: from 7 to 180 days) future outcomes; (3) a BIS II questionnaire measuring trait impulsivity. The main connectivity analysis was conducted using a seed-based approach in which the BOLD time course was first extracted from a set of seed regions identified in previous fMRI studies and then a correlation coefficient was computed between two seeds timecourses or between the timecourse of a seed and those of all other brain voxels. The analysis of the predictive relationship between fc-MRI and behavior was conducted using linear regressions and correlation analyses. We also conducted a leave-one-region-out analysis, which is able to identify the specific weight of each region of such networks. Results showed that TD can be reliably predicted by both the internal correlation of the single system (beta = 0.12) and by its correlation with both β (beta = 0.12) and δ (beta = 0.09) systems. Moreover, all regions of the single and δ systems appeared crucial for the fc-behavior relation, while in the β system only the mPFC appeared crucial. The results suggest an alternative view according to which the δ system, which includes regions involved in cognitive control and episodic future thinking, exerts a modulatory effect on regions of the single valuation system that are more directly involved in reward evaluation, thus influencing the selection between alternatives. Finally, we also found that TD is independent of trait impulsivity, in contrast with the widely held idea that impulsivity has a key role in TD. Overall, our findings indicate that individual variability in functional connectivity within and between critical nodes of task-evoked neural networks associated with IT is able to predict discounting behavior measured a long time afterwards, independently of impulsivity.

Transcranial direct current stimulation increases long-rage fronto-parietal connections in patients with disorder of consciousness: a preliminary study

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The aim of the present study was to assess the effect of transcranial Direct Current Stimulation (tDCS) applied to the Dorso-Lateral Prefrontal cortex (DLPF) on the behavioral responses and brain oscillations in 15 patients in Vegetative (VS) and Minimally Conscious State (MCS). Ten daily sessions of anodal tCDS were applied to the left DLPF. A sham stimulation was used as a control condition. 19-channels EEG was recorded before and after stimulation. The EEG coherence and spectral pattern differences before and after each treatment were analyzed. EEG data analysis showed a significant increase of coherence over the frontal and fronto-parietal areas in Beta and Gamma frequencies after tDCS. No significant effects were observed after sham stimulation. Clinical assessment of patients showed no significant changes. However all caregivers reported a reduction of oscillations of arousal level. Our study suggests that tDCS could influence the EEG coherence of rapid frequencies allowing the interaction between frontal and parietal areas. This interaction represents a fundamental prerequisite for all conscious perception mechanisms. tDCS may represent an useful new tool for cognitive rehabilitation.

Repetitive transcranial magnetic stimulation as an additional treatment to speech therapy in aphasia following sub-acute stroke

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Twenty percent of patients with stroke suffer from aphasia, of which 50% remain in a disabled state, thereby impeding their reintegration to society. Although efficacy of logopedic treatment in post-stroke aphasia is controversial a meta-analysis of 21 studies confirmed its usefulness. Repetitive Transcranial Magnetic Stimulation (rTMS) is able to modify neuronal activity both locally both at distant sites. Results of rTMS for post-stroke aphasia are controversial. Moreover rTMS has scarcely been explored in the acute rehabilitation setting. We assessed the efficacy of inhibitory rTMS with conventional speech therapy to modulate language performance in sub-acute stroke aphasia. In a randomised case-control double-blind study 12 non-fluent aphasic post-stroke were consecutively enrolled. All patients suffered a first-ever stroke in the sub-acute stage defined as time since lesion onset from 1 month post-stroke. Patients were randomized either to receive real (1 Hz on right-hemisphere homologue of Broca's area) or sham rTMS, to a 3-week (5 day in a week) Immediately after each rTMS treatment all patients received speech therapy. The patients' performance was evaluated with Italian version of Aachener Aphasia Test (AAT), before (T0) and after (T1) treatments. Seven patients were treated with real rTMS and 5 patients with sham rTMS. No adverse effect (seizures or cognitive decline) have been reported. Total AAT average score showed a similar improvement in real rTMS and in the sham rTMS groups between T0 and T1 (real rTMS vs sham: Token Test 2.33 vs 4.25; written language 3.8 vs 5.5; naming 6.1 vs 6). Repetition (4.8 vs 1.2) and understanding (7 vs 5.7) seem to improve more in patients treated with real rTMS. Our data are not fully in agreement with those of the literature probably due to strict criteria of patient selection; indeed all patients were affected by medium or severe non-fluent aphasia (AAT: pT < 52) and were treated in early phase of rehabilitation (sub-acute stroke).

Perturbational complexity in chronic patients with disorders of consciousness

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The level of consciousness of patients who survive severe brain injury is assessed clinically from their ability to respond to commands and to communicate with the environment. However, both theoretically and practically, consciousness basically depends on the ability of different cortical regions to effectively interact, and does not require a communication with the external world. Electroencephalographic responses (EEG) to Transcranial Magnetic Stimulation (TMS) can directly and non-invasively measure the integrity of different cortical areas and of their interconnections, also in patients who are unable to communicate. In particular, we have recently observed that the algorithmic complexity of TMS-evoked potentials (labelled as Perturbational Complexity Index, PCI) can discriminate the level of consciousness in wakefulness, sleep, anesthesia and coma. In this study we tested the reliability of PCI to evaluate chronic patients with severe brain injury. Twenty-four chronic in-patients (n = 14 in Vegetative State – VS – and n = 10 in Minimally Conscious State – MCS) with severe brain injury and with stable clinical diagnosis were involved. TMS-evoked potentials were recorded from all patients with a 60-channel EEG during stimulation of the premotor and parietal cortex. Clinical assessment with the Coma Recovery Scale - Revised (CRS-R) was performed on the same day of TMS/EEG recording. After estimation of the cortical sources from scalp recordings, statistical analysis was performed to identify the spatio-temporal distribution of brain activity significantly evoked by TMS pulses, that was used to compute the PCI. The CRS-R score was significantly lower in the VS group as compared to the MCS group. PCI was able to correctly classify between VS and MCS conditions at the single-patient level. In MCS patients at least one stimulating target showed a PCI greater than the maximum value previously observed during sleep and anesthesia. In VS patients PCI was overlapping the range of values obtained during sleep and anesthesia. In one VS patient the PCI was higher than expected: a second evaluation after 7 months confirmed this value and revealed a clinical improvement of the patient, who evolved toward the MCS condition. We conclude that PCI can be considered a promising tool to discriminate VS and MCS chronic patients, who are difficult to evaluate because of a progressive decline of residual sensory and motor abilities. Moreover, PCI might reveal an improvement of the level of consciousness earlier than any behavioral evidence of communication. Future studies should include larger populations of patients to provide a comprehensive validation of PCI for the evaluation of consciousness in chronic patients. Moreover it would be interesting to compare and integrate TMS/EEG results with other brain functional assessments, e.g. event-related potentials, functional magnetic resonance imaging.

The parietal operculum stores the haptic working memory of objects for grasping in humans: a bifocal TMS study

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The human Parietal Operculum (OP) is an heterogeneous cortical region located above the caudal Silvian fissure comprising Brodmann's areas 39, 40, 43, 3, 1 and. We investigated how haptic information is encoded in the OP and may be used for guiding object-directed motor acts. We tested the effects of conditioning single-pulse Transcranial Magnetic Stimulation (spTMS) applied to the left OP on corticospinal excitability assessed by a test spTMS applied to the ipsilateral motor cortex (M1) 5 ms after conditioning spTMS. Participants explored the size of a graspable object visually or haptically and waited for a go-signal to grasp it in the dark. They received TMS during the delay phase. In a separate group of participants performing the same task, conditioning spTMS was applied to the ventral Premotor cortex (vPM) 7 ms before test spTMS. Results showed that conditioning TMS over OP modulated M1 output according to the information on object size that had been acquired haptically but not visually. Vice-versa, conditioning TMS over vPM modulated M1 output according to information on object size acquired by vision but not haptically. Moreover spTMS over OP produced a significant modulation of the upcoming reaching behavior only when the object had been explored haptically. the present study indicates that OP and vPM play a fundamental role in the transformation of short-term memory of object geometry into a coherent pattern of muscle activation for grasping. Each of the two areas is specialized for one sensory modality, the OP contains information acquired haptically and the vPM contains visual information. Despite this segregation, the role of the two cortical stations appears very similar in storing macroscopic sensory information to be used in an open-loop manner for object-directed motor behaviour.

Fronto-parietal EEG coherence in patients with disorders of consciousness after neurosensory stimulation

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Restlessness, movement artefacts and metal implants can completely rule out use of magnetic fields in defining diagnosis and monitoring of unconscious patients. Electroencephalogram represents a suitable choice to overcome small movement artefacts and the presence of surgical metallic clips. In particular, quantitative EEG techniques including coherence analysis allow to measure functional relationships between pairs of neocortical regions and seem to be closely correlated with cognitive or behavioral measures. The aim of the present study was to investigate the remaining cortical information processing and, in particular, the contribution of higher order associative cortices of patients with disorders of consciousness in response to sensory stimuli. We explored the EEG coherence of twenty-four patients with Disorders of Consciousness (DOC) in response to visual, auditory and noxious stimulation. Coherence was split into five frequency bands: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-50 Hz) ranges. In visual and auditory modalities a considerable enhancement of fronto-parietal coherence in slow frequencies was seen in the controls. In contrast, DOC patients showed a local increase of alpha connectivity. Electrical stimulation evoked a widespread increase of gamma coherence in both groups. Our results further confirm the hypothesis that unambiguous vegetative state patients can activate primary somatosensory cortices but not associative cortical networks, suggesting a lack of information integration, and therefore of conscious perception. On the other hands, nerve electrical stimulation seems to act as a peripheral gateway to the central nervous system provided by the synapses between the spinoreticular component of the median nerve pathway and the neurons of the ascending reticular activating system, supported by the diffuse increase of gamma frequencies in all EEG derivations. Again, fronto-parietal networks result to be a necessary prerequisite for consciousness and sensory processing and coherence can represent a powerful tool to measure them.

Gender differences in the visual underpinning of perceiving and appreciating the beauty of the body

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Accumulating evidence suggests potential sex differences in the lateralization of response of Extra-striate Body Area (EBA) to human body images. Although previous studies have found some degree of right hemisphere dominance in body perception, presently it is unknown whether such a functional lateralization may differ between men and women in appreciating the beauty of the body. Here, we applied rTMS over left and right EBA and over vertex to investigate the contribution of visual body representation on esthetic body perception. Female and male healthy volunteers judged how much they liked opposite- and same-gender virtual model bodies that varied in body size. In a further task, volunteers were required to express VAS heaviness judgments about the virtual models, thus allowing us to compare the effects of right and left EBA on evaluative (esthetic) and perceptual (size) judgments of human bodies. In each trial, after a 500 ms fixation cross, the stimuli were presented for 150 ms at the center of the screen and were followed by a mask for 500 ms and, finally, by a 100 mm liking or heaviness VAS. Five 10 Hz rTMS pulses were delivered after 150 ms from stimulus onset. The analysis on the esthetic VAS revealed that in women, but not in men, right EBA-rTMS increased the liking judgments of opposite- vs same-gender models, as compared to vertex and left EBA stimulation. Conversely, in men the liking judgments of opposite-gender models decreased after virtual disruption of both right and left EBA as compared to the vertex; thus suggesting a specific involvement of right EBA in esthetic judgments in women with respect to men. In addition, a negative correlation between a laterality index of the effects of EBA stimulation and the observer's Body Mass Index (BMI) indicated that increased right hemisphere dominance relative to the esthetic preference of opposite-models was associated with lower BMI values. Since such correlation, however, was not find within each gender group, it is likely to be ascribed to the difference in BMI between men and women and the different effects of right vs left hemisphere rTMS in the two genders. Crucially, no significant effect was found for the perceptual task, showing that rTMS over left and right EBA did not affect VAS heaviness judgments of opposite- or same-gender virtual model bodies. Our results provide first evidence of gender difference in the hemispheric asymmetry of EBA in the esthetic processing of human bodies, with women showing right hemisphere dominance in comparison with men. The present results may be useful for designing psychotherapeutic interventions for eating disorders patients using body exposure, highlighting the importance of considering lateralized presentations of body stimuli to the left visual hemifield in women. Furthermore, the more lateralized representation of body aesthetics in women than in men might also help to explain the greater incidence of eating disorders among women.

Interhemispheric transmission of visual information between the intact and the lesioned hemisphere in hemianopic patients

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A unilateral lesion of the human central visual pathways results in a contralesional visual field loss known as homonymous hemianopia, a long-lasting and often permanent impairment. An important open question concerns the role of a commissural cross-talk between the intact and the lesioned hemisphere for recovery of homonymous hemianopia. One specific question is whether the presence of interhemispheric transfer of visual information depends on the location of the lesion causing hemianopia. Together with healthy control participants, we tested chronic hemianopic patients either with a lesion roughly restricted to V1 or with a more anterior lesion including visual extrastriate areas. The behavioural test used was the Poffenberger Paradigm that enables one to measure interhemispheric transfer time with a simple manual reaction time to lateralized visual stimuli. During behavioural performance we recorded visual Event-Related Potentials (ERPs) to compare latency and amplitude of the ERPs components evoked by stimulation of the direct or the indirect commissural (callosal) pathway. In controls both pathways yielded a normal response. In hemianopics we found that visual stimulation of the intact hemifield evoked a normal P1-N1 component in the intact contralateral hemisphere (direct pathway). However, when recording the indirect callosal response in the ipsilateral lesioned hemisphere we found a different result as a function of the site of the lesion. In patients with a lesion restricted to V1 there was an indirect P1-N1 response similar to that of controls while this was not the case in patients with a more anterior and extended lesion. A likely explanation of this dissociation is that in the former group the widespread callosal connections between the extrastriate areas in the two hemispheres are partly spared while they are largely damaged in the latter group. In conclusion, a substantial visual commissural input from an intact to a lesioned hemisphere is present only following lesion restricted to V1 and this might suggest a favourable prognosis for recovery of vision following specific rehabilitation training.

Adult ADHD: neurophysiological markers of disrupted attentional processing as an additional aid to a challenging clinical diagnosis?

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Attention Deficit/Hyperactivity Disorder (ADHD) is a prevalent childhood disorder, the assessment of ADHD in adults is often challenging and complex, particularly due to the absence of specific diagnostic criteria. Attentional processing deficits in children with ADHD have been investigated using event-related potentials with controversial results. We recently developed a triplet protocol and we applied it in a adult ADHD population to study both the Short-Term Habituation (STH) both the anticipatory attention (as reflected by the Stimulus Preceding Negativity, SPN). We recorded 26 adult ADHD patients (assessed with standardized psychiatric examination) and 26 age-matched control subjects. The triplet protocol provides for the delivery of trains (ISI 1 sec, inter train interval 8-12 sec) of 3 stimuli (triplets S1-S2-S3) where S1 and S2 always belongs to the same sensory modality (auditory or electric) whereas S3 can belong either to the same sensory modality (namely triplet "same") or to the alternative modality (namely triplet "different"). Subjects did not receive any information about the incoming stimuli. Amplitudes of N1-P2 evoked potentials in response to S1, S2 and S3 were measured and then compared to assess the STH entity. We also evaluated the presence of the SPN in the interval between S1-S2 and S2-S3. We found that the STH profile in the ADHD population was comparable to the healthy subjects group. Compared to controls, the ADHD group showed instead a significant N1-P2 amplitude reduction in response to S1 across different sensory modalities and also a significant attenuation of the SPN that precedes electric unpleasant stimuli. In our opinion, these neurophysiological findings could be related: we hypothesized that the dysfunction in the attentional bottom-up elementary process (as indicated by the attenuated N1) may prevent the generation of a SPN which, in turn, reflects the anticipatory attention directed to the expected upcoming salient stimuli. Our ADHD group was heterogeneous: further studies should be addressed to verify if the ADHD subgroups (e.g., inattentive versus hyperactive) present different neurophysiological patterns. We nevertheless think that our neurophysiological findings may reflect an atypical attentional processing in the ADHD group compared to the healthy subject group providing a level of analysis additional to the standard psychiatric clinical evaluation.

Stimulus preceding negativity in a non-motor triplet paradigm: role of the expectancy and the saliency

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Stimulus Preceding Negativity (SPN) is defined as a non-motor slow negative component potential elicited by temporally predictable stimuli without any coupled motor requirements. SPN is usually elicited using Contingent Negative Variation (CNV) protocols. However, the late part of the CNV includes two different psychophysiological events related to S2: the movement preparation (RP, the Readiness Potential) and the anticipatory attention for the upcoming imperative stimulus (SPN). Then, it is difficult to identify a pure SPN since a temporal overlap between RP and SPN. Our aim was to investigate anticipatory attention mechanisms in a healthy population using a non-motor paradigm without any stimulus-related task. Our protocol provides for the delivery of trains of three stimuli (triplets S1-S2-S3) where S1 and S2 always belongs to the same sensory modality (auditory or electric) whereas S3 can belong either to the same sensory modality (namely triplet "same") or to the alternative modality (namely triplet "different"). We recorded 30 healthy subjects who were not demanded to pay attention and they did not receive any information about the incoming stimuli. In each subject, we evaluated the presence of the SPN in the 500 msec preceding S1, S2 and S3. We did not find any negative shift preceding S1. In triplet "different", we could identify a slow negative shift (interpreted as SPN) preceding both acoustic and electric S3 and before electric S2. In triplet "same", we could observe a SPN preceding both S2 and S3 but only in the electric modality. Our triplet protocol seems to be able to elicit a slow negative component that electively anticipates the presentation of salient unpleasant stimuli. Since our protocol does not provide any instruction to be performed, we interpreted this negative shift as a SPN considering in each pair (S1-S2 or S2-S3) the 1st stimulus as the warning and the 2nd as the "imperative" stimulus. Our findings let us hypothesize that two factors mainly contribute to the SPN generation: firstly, the expectancy related to an automatic learning process (as indicated by the SPN preceding acoustic S3 in triplet different) and secondly, the stimulus saliency (as indicated by the presence of the SPN before electric unpleasant stimuli regardless the triplet protocol "same" or "different" used). Therefore only those stimuli learnt to be both predictable and salient are able to generate a significant SPN effect. Our protocol may offer the possibility to investigate both attention and elementary learning in healthy subjects and could be applied in peculiar pathological conditions where attentional processes are electively impaired.

Early correlates of agency perception in interaction scenes: preliminary evidences from Williams syndrome

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Our interaction and social skills are deeply rooted in the ability to quickly and properly detect other agents and grasp their intentions and emotions from their behaviour. According to direct access theories, those abilities are supported by innate "smart" perceptual processes, which extract relevant cues from complex scenes since the first stages of information-processing. Again, the atypical development of those abilities might be associated to clinical manifestations of Williams Syndrome (WS), a rare genetic disorder characterized by peculiar cognitive-affective profile and anomalous social behaviour. The present study aims at investigating early neural correlates of agency perception in interaction and electrophysiological specificities of WS during initial steps of social understanding. One participant with WS and 20 volunteers took part in the study. The genetic diagnosis of WS was established using Fluorescence in Situ Hybridization (FISH) probes for elastin gene. All participants were asked to carefully observe some dynamic visual stimuli (two static frames presented in close succession) showing realistic interactions, while EEG activity was continuously recorded. The interaction scenes included a human or artificial agent executing gestures. Event-Related Potentials (ERPs) were considered after the morphological analysis. Based on previous empirical evidences, we focused on two negative ERPs components – N2 and N3 – that proved to be sensitive to the manipulation of agent's nature. In order to properly compare controls' and patient's data, all signals have been re-referenced to individual averages. Moreover, the morphology and relative amplitude of selected components have been compared taking into account the statistical dispersion of group data for each data point (resolution = 1 ms). Differences in patient's responses were defined as significant only if they were outside a ±1 SD range from the control group mean. Direct comparisons of patient's and controls' ERPs responses highlighted similar early sensory components, but an enhanced N2 peak regardless of agent's nature – which has been associated to atypical processing of perceptual information for the detection of biological entities – and an increased N3 deflection – which has been associated to an increase in resource demand for pre-reflective detection of intentionality – for the WS participant. We suggest that our empirical evidences might mirror the peculiar uneven profile of WS social skills, with abnormally heightened sensitivity to social stimuli and remarkable difficulties in detecting and decoding others' mental states even in perceptual tasks, despite their spared social perception skills.

Neural networks for artifact reduction and vowel speech imagery classification in EEG data

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This work describes an EEG-based software system for brain-computer interfacing, having the long-term goal of creating an alternative speech tool for people with severe communication handicaps. The system is capable of recognizing with a high success rate, in the recorded EEG traces of the subjects, the imagined production of the Italian vowels /a/ and /i/. Twelve subjects were asked to perform one of two tasks: "imagine to produce the /a/ vowel", or "imagine to produce the /i/ vowel". Each task was triggered by an auditory stimulus (listening to recorded /a/ or /i/) presented 80 times to each subject (40 times for /a/, 40 for /i/, random order). The presentation tool was BCI2000. The brain activities of the subjects were recorded (at 250 Hz sampling rate) by an EEG system with 64 active scalp electrodes embedded in an electro cap (actiCAP, Brain Products). The recording software was Brain Vision Recorder. Data processing was performed by MATLAB, EEGLAB being used for preprocessing (down-sampling to 100 Hz; 2 to 30 Hz band-pass filtering; subdivision into labeled epochs). The software system can be divided into two parts: artifact reduction, and imagined speech classification. In the first part, in order to reduce the ocular and muscular artifacts, we performed Independent Component Analysis (ICA) on the EEG data. The spectra of the Independent Components (ICs) were examined: artifacts were visually identified in accordance with spectral power content, and labeled as such. A 2-layer, 3-hidden-neuron, feed-forward back-propagation ANN (Artificial Neural Network) was trained and tested for the recognition of the artifacts by LOO (Leave One Out) cross-validation, and the classification accuracy was assessed by the area under the ROC (Receiver Operating Characteristic) Curve (AUC). The six features used for artifact characterization were calculated from the power spectrum of the ICs, and the feature vectors for all the subjects were used together for classifier training/test. ICs identified as artifacts were rejected, and the corrected data were recalculated. In the second part, EEG epochs were processed by time-frequency analysis in the ambiguity plane. Values of the ambiguity function in the plane were chosen as features for vowel recognition. The 100 most discriminant points were identified by maximizing the Fisher contrast of the two classes, and formed the feature vector. A 3-hidden-neuron ANN was trained and tested for the recognition of the imagined speech, this time on single subjects. AUCs were

calculated both with and without artifact removal. Overall vowel classification accuracies as measured by the AUCs ranged from 0.89 to 0.98 (for the different subjects) without artifact reduction, while the insertion of the artifact remover had in many subjects a beneficial influence on accuracy. The obtained results point out a noteworthy potential for the use of vowel speech imagery as a speech synthesis controller.

D2 agonist administration restores impaired LTP-like cortical plasticity in AD patients

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In a recent study with theta burst stimulation (TBS) we showed that LTP (long-term-potentiation)-like cortical plasticity is impaired in AD patients. We recently showed that in AD patients the treatment with a subtype-2 receptor dopaminergic agonist (D2) leads to an enhancement of short latency afferent inhibition (SLAI), a neurophysiological measure under cholinergic control. We aimed at investigating whether administration of D2 agonist could modulate cortical plasticity induced with TBS over primary motor cortex (M1) in AD patients. We tested the impact of two weeks administration of D2 agonist (rotigotine) on LTP/LTD-like effects induced respectively by means of intermittent (i-) and continuous (c-)TBS delivered over M1 in eleven mild AD patients; eight of them have continued the rotigotine-based therapy for three further months. We also investigated SLAI circuits before and after rotigotine administration. All patients underwent a comprehensive neuropsychological (NPS) evaluation. After two weeks of D2 agonist administration we observed a marked change in the iTBS protocol effects, revealing that LTP-like plasticity was strikingly enhanced ($p > 0.05$), while the cTBS protocol did not show similar remarkable modifications. As expected, SLAI was also partially restored by D2 agonist therapy, confirming our recent findings. The NPS evaluation showed a significant improvement of the global measurement (MMSE) and of frontal functions (FAB). After three months of D2 agonist administration the effects on SLAI and NPS evaluation have been maintained, while we observed a slight modulation of LTP-like plasticity related to the two weeks administration, but however still highly significant ($p > 0.05$) in comparison to the baseline. These results increasingly highlight the role of dopamine in the pathophysiology of AD and suggest that a dysfunction of D2-like receptors is involved in abnormal cortical plasticity in AD. The NPS evaluation showed some surprising effects of dopaminergic modulation on cognitive domains, opening an important debate on a possible role of dopaminergic-based therapy in AD.

Feedback processing in Parkinson's disease: an ERPs study with the Iowa gambling task

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Behavioural and emotional problems have been clearly recognized in patients with Parkinson's Disease (PD). Recent evidences reported the presence of impaired decision making and learning processes, even in the earliest stages of PD. The aim of the present study was to investigate the neural correlates of feedback evaluation in medicated PD patients recording the Event-Related Potentials (ERPs) during the Iowa Gambling Task (IGT), a neuropsychological test commonly used to examine decision making capacity into a learning context. Fifteen medicated PD patients (11 M; mean age 61.4; sd: 9.6; MMSE score > 24) and 15 Healthy Controls (HC) (10 M; mean age 60.7; sd: 9.8; MMSE score > 24) were recruited for the study. Every participant underwent a computerized version of the IGT during Electroencephalography (EEG) registration. In the IGT participants were invited to gain the higher possible amount, choosing between advantageous (small wins and smaller losses, that conduct to a net gain) and disadvantageous decks (big wins with bigger losses, that conduct to a net loss). To evaluate ERPs components related to the presentation of positive (wins) and negative (losses) feedbacks, the epoch was set from 1000 ms before to 1000 ms after the feedback presentation. Group differences were explored analyzing both behavioural indices of learning and neural correlates of feedback evaluation. From the analysis of behavioural indices, results revealed a significant difference in the IGT performance between groups ($p < .05$): While HC performance improved progressively, showing a prevalent choice of advantageous decks and demonstrating the presence of feedback based learning, patients performance was almost the same among the task, choosing disadvantageous decks even in the last part of task and exhibiting impaired learning abilities. The analysis of ERPs data revealed significant differences between groups in the neural correlates of feedback evaluation. While HC showed significant differences ($p < .05$) in ERPs morphology (FRN, P3) between wins and losses, confirming that positive and negative feedbacks are differently evaluated and processed in healthy condition, PD showed the same ERPs morphology after both positive and negative feedbacks. The results of this study confirmed the presence of impaired decision making and learning processes in medicated PD. In addition, the ERPs patterns showed by these patients suggest that an incorrect feedback evaluation could be in part the reason of their cognitive and behavioural deficits.

Spatiotemporal mapping of response inhibition in the prefrontal cortex

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Current literature widely agrees that response inhibition for non-targets stimuli occurs after the stimulus discrimination and identifies the neural circuits underlying response inhibition in a complex network including frontal, parietal and subcortical regions. This network varies depending on the cognitive and behavioral demands of the task. In the present study we combined high resolution ERP and event-related fMRI to map in space and time the cortical activities during a typical go/no-go task with equal probability of targets and non-targets. Differently from previous studies, stimulus onset was not taken as time 0 of the brain processing; we included a wider time window initiating well before the stimulus onset. Results showed that brain activity starts with a slow rising negativity (BP-like activity) about 700 ms before the stimulus onset in bilateral Supplementary Motor Area (SMA), Anterior Cingulate Cortex (ACC), and the Prefrontal Cortex (PFC; pars triangularis in the Inferior Frontal gyrus, IFg). Between 60 and 100 ms after the stimulus onset, striate and extrastriate areas were active and immediately later (20-30 ms) activity was recorded in bilateral superior and inferior posterior parietal lobe. At the same time, a positive activity was also detected in left Insula (contralateral to the used hand). These activities were similar for both go and no-go stimuli, but at 130 ms they started to diverge. For go stimuli, activities in the left Superior Parietal Lobule (SPL, likely corresponding to the Anterior Intraparietal Area, AIP) and in the left Insula quickly increased reaching the peak 260 and 340 ms after stimulus, respectively, that is about 180 and 100 ms before the manual response. For no-go stimuli, at 200 ms after stimulus, the positive Insula activity ceased to increase and was substituted by a bilateral negative activity in PFC pushing the wave toward zero. Thus, this PFC negative activity seems associated with motor inhibition. Interestingly, this activity had similar polarity and source to that recorded before stimulus appearance, suggesting that both activities were associated with the same kind of processing. These results have important implications for the response inhibition theories, indicating that inhibition is deployed well before the stimulus onset by bilateral PFC and is then disengaged by the Insula. Concluding, the question about to go or not to go is so important for the rain that not only follows the stimulus discrimination, but anticipates stimulus appearance, setting the brain on a "no-go" mode while preparing the action and waiting for stimulus detection; finally the inhibition is quickly disengaged putting the brain in a go-mode.

Attentional reorienting in three-dimensional space

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Attentional reorienting between spatial locations within a two-dimensional front-parallel plane has been extensively studied and spatial-cueing effects have been well established. In agreement with the hypothesis of two-dimensionality of the attentional space, a considerable neural overlap between selective attention and saccadic programming system has been described. However, in real life the distance in depth of a potentially threatening/rewarding stimulus relative to the observer is crucial for its evaluation. Far stimuli may be less attention demanding with respect to those which appear close to us. This raises the question of how visuospatial attention is shifted in depth. Literature data do not prove definitely whether attention is "depth-blind" or "depth-aware". In the present work, we adapted a covert attention paradigm to a virtual three-dimensional world. The virtual environment consisted in a central fixation cross around which 4 placeholders were equally distributed but placed at a different depth plane. Without moving their gaze from the fixation cross, subjects had to discriminate the vertical or horizontal orientation of a visual target randomly appearing within one placeholder. Before the onset of the target, a visual cue was presented at the same spatial position of the target (valid trials, 70%) or at a different location (invalid trials). The visual cue was predictive of the target position. In two-third of the 30% invalid trials, the target was coplanar to the cue but occurred within a placeholder placed on the opposite side along either the horizontal (50%) or the vertical meridian (50%). In the remaining invalid trials the target was located within the cued placeholder, but at a different depth plane. All stimuli were presented in the Panum area and within the empirical horopter to ensure an ecologically valid perception of the virtual scene. Manual reaction times have been recorded and specific effects related to the direction of attention shifts were found. (1) RTs were faster when attention was reoriented towards a validly cued location with respect to when it was shifted to an unexpected position within the same depth plane; (2) covertly reorienting visuospatial attention towards an invalidly cued location in depth was accompanied by RT costs compared to when attention was reoriented towards a validly cued position; (3) RTs were faster when attention was reoriented towards unexpected targets in depth than when it shifted within the same depth plane. By dissociating depth planes of gaze and attention, our 3D paradigm provides evidence of gaze-independent spatial-cueing effects which follow the covert reorienting of attention (1) within and (2) between depth planes. The present study supports the proposal of three-dimensionality of the attentional space.

Autonomic adaptive changes in heart rate elicited by Valsalva maneuver are blunted in a group of female migraine patients

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Autonomic nervous system functioning is altered in migraine between attacks, as well as in other chronic pain syndromes, but the neurophysiological and behavioral meaning of the alterations is unclear. Valsalva maneuver is a simple test to assess the adaptive autonomic responses elicited by abrupt changes in the venous return. In 24 female migraine patients (M; 42.5 ± 2.3 yrs; m ± se) and 24 control women (C; 41.7 ± 1.5 yrs) we have tested the hypothesis that adaptive changes in Heart Rate (HR) elicited by the maneuver may be impaired in migraine. In absence of migraine attacks, they were asked to perform a Valsalva maneuver by exhaling for 20 s into a manometer, while lying in a semi-supine position with the upper part of the body tilted up at about 20°. An expiratory pressure was developed in the airways of 40 mmHg. During the maneuver polygraph recordings of thoracic respiratory movements and II lead ECG were acquired. According to the usual division of the effects of the maneuver into different phases, HR was calculated in the phases: zero (just before starting); III (the phase of maximal sympathetic tachycardia just before stopping the expiratory effort); V (the phase of maximal reflex vagal bradycardia, about 5 s after the end of expiratory effort). No significant difference was found in HR in the phase zero between M and C (70.3 ± 1.8 vs 71.4 ± 1.9 beats•min-1). In the phases III and V the changes in HR obtained in M with respect to the phase zero were: +19.5 ± 4.2 and +10.8 ± 5.3 beats•min-1. The changes obtained in C were +29.8 ± 4.8 and -2.8 ± 3.1 beats•min-1. The Valsalva Ratio was calculated as the ratio of HR in phase III to HR in phase V. Its values in M and C were 1.1 ± 0.1 and 1.5 ± 0.1 ($p = 0.002$). After analysis by 2-ways ANOVA the Valsalva maneuver was found to have not the same effect on HR changes in the presence or absence of migraine, with a significant interaction ($p = 0.008$). After Bonferroni post-ANOVA test the change in HR obtained in the phase V in M was found to be different than in C ($p < 0.05$). In the C subjects, the changes in HR in phase III and phase V were significantly different from each other ($p < 0.0001$). The same changes were not significantly different from each other in M patients. These results indicate that autonomic adaptive flexibility was blunted in the group of migraine patients. Results may be interpreted as an index of reduced adaptive resilience of the autonomic regulatory systems in the presence of stressful events. Resilience is a functional property which

prevents organisms from developing functional disorders. A reduced resilience may not specifically lead to the development of specific pathologies, but it may constitute a not specific basis upon which the occurrence of different kinds of somatoform disorders is facilitated, as migraine and other chronic pain syndromes.

Frequency-specific insight into memory for digits

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The digit span is one of the most widely used memory tests in clinical and experimental neuropsychology. In the forward version, sequences of digits of increasing length have to be reproduced in the order in which they are presented, whereas in the backward version items must be reproduced in the reversed order. The forward task is thought to reflect verbal working memory capacity, and the backward task primarily taxes executive functioning resources. Here, we assessed whether transcranial Alternating Current Stimulation (tACS) can increase healthy individuals' verbal memory span. Imperceptibly weak electrical currents in the alpha (10 Hz), beta (20 Hz), theta (5 Hz) and gamma (40 Hz) range, as well as a sham stimulation, were delivered over the left lateral posterior parietal cortex, an area which has been previously associated with digit span performance. In the forward digit span, stimulation in the beta range significantly increased the number of items recalled, confirming the critical role of beta rhythm in the maintenance and rehearsal of information in working memory. Only minor effects of tACS were observed in the backward task. These results provide one of the first evidence that tACS can have enhancing effects on memory, even on a relatively stable trait as memory span capacity. Our findings thus pave the way for clinical application of this technique in patients with memory disorders.

Dynamic sounds within peripersonal space modulate motor system: a TMS study

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The space immediately surrounding the body, the Peripersonal Space (i.e., PPS), mediates every physical interaction between ourselves and the external world. Within, but not outside, this limited sector of space the somatosensory information is integrated with external visual or acoustic inputs. This encoding of spatial position in an egocentric frame of reference supports efficient motor functions both in terms of reaching movements or defensive behavior. These motor proprieties of PPS have been showed in humans by means of Transcranial Magnetic Stimulation (TMS) study: a greater motor facilitation was evoked by static auditory stimuli presented near but not far from the body. Here, extending these previous results, we used dynamic sounds to assess the critical distance at which acoustic stimuli have an immediate effect on motor system along a spatial continuum between near and far space from participants' hand. To this aim, we recorded from First right Dorsal Interosseous (FDI) Motor-Evoked Potentials (MEPs) induced by single-pulse TMS while concurrent auditory stimuli approaching or receding from the body were presented. Precisely, TMS pulses were delivered when the sound source was perceived in six different positions from a location very close to subjects hand to 90 cm apart. Results showed that the MEPs amplitude was enhanced when sounds were delivered within and not beyond a limited distance (around 60 cm) from the hand, giving an estimation of the PPS spatial boundaries. Such findings support the view that PPS links together the multisensory representation of the space around the body with the motor representation of potential acts within that space.

Intelligent monitoring of subjects with severe disorder of consciousness

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Patients in vegetative or minimally conscious states need constant monitoring and a continuous stream of clinical/neurobiological information is required for appropriate healthcare by the medical and nursing staff in order to optimize neurorehabilitation. Patients are also administered sensory stimuli in order to improve responsiveness and reduce isolation; responses to stimuli depend in part on the autonomic system ortho/parasymphatetic functional balance. We describe an integrated system for continuous acquisition, storage, handling and analysis of clinical and functional data from subjects in the vegetative or minimally conscious states. The system is composed of two main sub-systems: an acquisition and integration system and a decision support system. The acquisition system collects from different devices and stores data in a centralized database directly accessible when the patient's clinical record and data are needed to support decision (diagnosis, prognosis, selection of rehabilitation protocols). Data are measurements of biological and environmental parameters as well measurements of heart rate and Heart Rate Variability (HRV). Purpose is to use these data and their relations to obtain objective diagnostic criteria, predict early and accurate prognosis of patients and define therapeutic pathways. The decision support system is composed of commercial and open source statistical packages and it is used to perform classical statistical analysis, such as the bayesian statistics, data mining, neural network and linear regression. We briefly describe the main objectives of our statistical analysis. Main goals are to investigate functional status, residual or recovered responsiveness, endogenous mechanisms of self-regulation such as circadian/ultradian cycles; to recognize processes to be relied on as prognostic indicators; to identify changes in the vital parameters related to contingent events and indicative of residual/recovered responsiveness or of use when customizing the rehabilitation treatments according to tolerability; to achieve an integrated model of analysis and prediction.

Alien hands and defensive peripersonal space

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The Defensive Peripersonal Space (DPPS) is a vital "safety margin" surrounding the body. The DPPS has a crucial role for survival: whenever a salient and potentially dangerous stimulus approaches or enters it, the individual engages in more efficient actions aimed at self-protection. We have recently identified a DPPS in humans, by recording the enhancement of the Hand-Blink Reflex (HBR) when the hand is close to the face. Such enhancement results from a tonic, top-down modulation of the excitability of the brainstem interneurons mediating the HBR when the hand is near the face. In two experiments we investigated whether the sense of body ownership modulates the HBR and its increase depending on the position of the hand within the DPPS. In Experiment 1 we tested whether the HBR elicited by the stimulation of the participant's hand could be modulated by the presence of an alien hand situated either outside ("far") or inside ("near") the participant's DPPS of the face. There were two conditions. In condition "own hand" the HBR was elicited by stimulating the participant's hand in the "far" and "near" positions. In condition "alien hand" the HBR was elicited by stimulating the participant's hand always in the "far" position, while an alien hand was located either outside ("far") or inside ("near") the participant's DPPS. The results showed a strong "ownership" × "hand position" interaction ($p = 0.0010$), indicating that the HBR is enhanced only when the own stimulated hand is near the face, regardless of the position of the alien hand. In Experiment 2, we tested whether the HBR could be modulated by the position of the participant's hand in respect to an alien face. There were two conditions. In condition "own face" the HBR was elicited by stimulating the participant's hand located either outside ("far") or inside ("near") the participant's DPPS. In condition "alien face" the HBR was elicited by stimulating the participant's hand located either outside ("far") or inside ("near") the alien DPPS. There was a trend for a main effect of "face ownership" ($p = 0.052$), "hand position" ($p = 0.0001$), and a "hand position" × "face ownership" interaction ($p = 0.026$) interaction, indicating a smaller effect of hand position when the hand was inside the alien peripersonal space. Importantly, there was a positive relationship ($p = 0.0095$, Pearson r) between the HBR increase when the hand was inside the alien DPPS and the Perspective Taking scale, which assesses the tendency to spontaneously adopt the psychological point of view of others. Experiment 1 suggests that the HBR enhancement occurs only when the position of the own stimulated hand is altered (there was no clear modulation when the alien hand underwent postural manipulation). Experiment 2 extend the interpretation of the HBR modulation to the domain of the empathy, showing that empathic individuals show an enhanced defensive response even when the aversive stimulus is delivered inside the alien peripersonal space.

Effective connectivity and cortical information flow under visual stimulation in migraine with aura

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The study aims to evaluate effective connectivity applying non linear Granger causality to EEG rhythms under repetitive visual stimulation in migraine with aura patients, and to compare these findings with Blood Oxygen Level Dependent (BOLD) signal changes. Functional and effective connectivity represent a significant added value to neuroscience, since they allow to pinpoint the temporal pattern of activation and information transfer between cortical areas. They may possible contribute to explain the mechanism of aura symptoms perception. Fifteen Migraine With Aura (MWA) and 15 Migraine Without Aura (MWoA) patients were evaluated interictally. Ten non migraine subjects served as controls. All subjects were submitted to high density (65 channels) EEG during visual stimulation by black and white checkerboard gratings with two spatial frequencies (0.5 and 2.0 cpd) at 5 and 10 Hz (10 and 20 reversal/s). The same visual stimulation was employed to evaluated BOLD signal changes in 6 MWA and 6 MWoA. MWA patients showed increased non linear Granger causality values in beta band under all types of visual stimulation, with increased information flow toward frontal regions, in respect to MWoA and controls. The FMRI confirmed a larger extension of cortical areas activated by visual stimulation, also outside the occipital cortex with involvement of parieto-temporal zones. Our results outline important pathophysiological difference between migraine phenotypes. An increased capacity in cortical connections and transfer information may subtend the perception of aura symptoms, probably favoring the progression of cortical spreading depression.

Temporal characteristics of episodic memory formation investigated through repetitive transcranial magnetic stimulation

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It is well known that episodic memory formation relies on the brain processes set in train immediately before and during the encoding of an event. However, recent evidence suggests that post-stimulus processing may also play a key role in determining whether an event will be remembered or forgotten. Here, we used repetitive Transcranial Magnetic Stimulation (r-TMS) to assess the influence of post-stimulus processing on episodic memory formation on a fine-grained scale. Participants were asked to encode words through shallow and deep operations, while 20-Hz r-TMS was applied on their left Dorsolateral Prefrontal Cortex (left DLPFC) for 500 ms. r-TMS was delivered at six intervals, randomized across different blocks: 500 ms before the offset of the word, at the offset of the word, and 100, 200, 300 and 400 ms after the offset of the word. As control conditions, we also applied rTMS on the vertex and a performed a no-TMS block. Memory was tested one day later through a yes-no recognition memory task. Results showed that recognition accuracy considerably decreased when r-TMS was applied from 100 to 300 ms after the offset of the word during encoding. The time-course of this drop in accuracy differed depending on the strength of the memory trace, with a slight delay for deeply-encoded words. r-TMS delivered during the actual processing of the word produced only minor effects on recognition accuracy. We hypothesize that post-stimulus r-TMS over the left DLPFC may disrupt involuntary, automatic rehearsal processes that are crucial for the formation of a long-lasting memory trace.

Dynamic causal modeling of cortical activity during execution or imagination of movements with a paralyzed limb

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Many studies have shown that cerebral regions recruited during motor imagery and during motor execution overlap substantially. However, techniques examining the effective connectivity networks have also shown, in normal subjects, a neurophysiological dissociation between the two tasks. Indeed, even though the Supplementary Motor Area (SMA) is active during both imagination and execution, the functional connectivity between SMA and the primary motor cortex (M1) shows a facilitatory effect during execution and an inhibitory effect during imagination. Here, we asked whether this neurophysiological dissociation between imagination and execution is also present in pathological conditions where, after brain damage, the possibility to move contralesional limbs is lost (i.e., hemiplegia), and neither execution nor imagination produces any visible movement. Using functional magnetic resonance imaging and changes in effective connectivity (dynamic causal modelling), we examined the activity associated with imagined and executed movements of the intact and the paralyzed hands of 6 right-brain-damaged hemiplegic patients. We also included a group of 5 aged-matched healthy controls, in which our results replicated the above described modulation of the functional connectivity, depending on imagination or execution of the movement. On the contrary, in hemiplegic patients, our results did not show any difference in connectivity between SMA and M1 during the two tasks. It might be expected that, when the movement execution is lost, patients can only imagine the movement, always showing the inhibitory effect subserving imagination. However, unexpectedly, hemiplegic patients always showed a facilitatory effect during both execution and imagination. We discussed this result referring to the motor awareness domain. All hemiplegic patients of the present study were fully aware of their motor deficits and they were tested in the chronic phase (more than three months after stroke), when their motor system have well "learned" the paralysis. One possibility is that, because the system "knows" that no movement can be performed, inhibitory mechanisms, necessary to block the overt movement execution, appear to be useless and therefore are not implemented. Different results can be expected when not only the movement is lost but also the awareness of movement

is impaired, and patients obstinately claim they can move their paralyzed limb (i.e., anosognosia for hemiplegia). Future studies can verify if, in this kind of patients, a difference between execution and imagination subsists, relying on the activation of distinct cerebral networks.

Detection, identification, and discrimination of /i/, /u/, and /ɛ/ in Italian cochlear-implant children: a behavioral and neurophysiological study

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This study investigates behaviorally and neurophysiologically whether the length of Cochlear-Implant (CI) use promotes auditory pathways' maturation for speech sound processing by Italian CI children. Compared to previous studies, our study (i) examines Italian CI children for the first time, (ii) focuses on vowels, (iii) combines behavioral and Event Related Potential (ERP) measures, and (iv) relies on natural speech. Eight CI children (mean age at testing = 109 months, mean age at surgery = 33 months, mean length of CI use = 76 months) and nine age-matched Normal-Hearing (NH) children were selected. The vowels /i, u, ɛ/, produced by a male Italian native speaker and normalized for duration, intensity, and F0 were used. Behavioral identification of isolated vowels (/i, u, ɛ/) and discrimination of vowel pairs (/i-i/, /u-u/, /ɛ-ɛ/, /u-i/, /ɛ-i/) were studied. Using the oddball paradigm, auditory evoked responses were passively recorded from 32 active channels while children were watching a silent movie during presentation of /u/std-/i/dev and /ɛ/std-/i/dev. Auditory P1 and N1 were identified on the waves evoked by each stimulus type. Auditory MMN was calculated as the difference wave (deviant minus standard). At the behavioral level, identification and discrimination scores were comparable in CI and NH children for /i/, /ɛ/, /i-i/, /u-u/, /u-i/, and /ɛ-i/, but not for /u/ and /ɛ-ɛ/. Longer CI use (range = 28-97 months) did not influence the behavioral performance of CI children. At the neurophysiological level, it was possible to identify P1, N1, and MMN in all CI children. As found in previous studies, the P1/N1 amplitude was reduced in CI compared to NH children, whereas their latency was comparable. Unlike previous studies, where MMN has been rarely found, the MMN latency, amplitude, and area were comparable in CI and NH children. For CI children, the area was wider when MMN was evoked by /u/std-/i/dev compared to /ɛ/std-/i/dev. ERP results revealed that CI children benefit from a longer CI use: children using their CI by at least 70 months presented a shorter P1/N1 latency. Despite no difference emerged at the behavioral level as well as with respect to the ERP latencies,

the reduced P1/N1 amplitude could nonetheless indicate a challenged processing in CI children. Neurophysiological vowel processing appeared faster in CI children benefiting from a CI use of at least 70 months (as indexed by P1/N1 latency). The contrast /u-i/ was easier to discriminate compared to /ɛ-i/ only neurophysiologically (as indicated by MMN area). This is probably due to the acoustic distance between vowels (847Mel for /u-i/ and 332Mel for /ɛ-i/) and to the CI stimulation parameters. Despite the initial auditory deprivation, CI use may promote auditory pathways› maturation for vowel processing in early-implanted children, suggesting that some maturation aspects of auditory processing (i.e., P1/N1 latency) relate to the duration of CI use.

Effects of transcranial alternating current stimulation on spontaneous motor tempo and sensorimotor synchronization: preliminary data

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Recent data suggest that beta oscillations reflect functional coordination between auditory and motor systems during processing of isochronous rhythms. Transcranial Alternating Current Stimulation (tACS) allows modulation of brain oscillations in a frequency-specific manner by interaction with ongoing brain activity. In the present study, we used on-line tACS to modulate brain oscillations during spontaneous motor tempo and sensorimotor synchronization tasks to evaluate the effect of specific frequencies on motor performance. Nine healthy subjects participated to the study. Subjects performed self-paced finger movements in which they were asked to tap regularly at their most comfortable rate and auditory-paced finger tapping (synchronization-continuation task) with isochronous rhythmic sequences of 500 and 1500 ms interstimulus intervals (ISI). During each task, tACS was delivered to the left M1 ("reference" electrode on Pz) at an intensity of 1 mA in 5 randomized conditions: 5, 10, 20, 40 Hz, and sham. Baseline recordings (without tACS) were performed before and after each experimental session. In synchronization task with sequences of ISI 500 ms, 20 Hz tACS modified anticipatory mechanisms as revealed by a reduction of the negative mean asynchrony between the onset of the auditory cue and the motor response. Namely, mean asynchrony expressed as percentage of baseline was significantly lower for 20 Hz tACS compared to other experimental conditions. Forty-Hz tACS produced a reduction of the negative mean asynchrony in synchronization task with sequences at longer ISI (1500 ms), however this effect did not reach statistical significance. No significant effect emerged in the spontaneous motor tempo task. We hypothesize that the reduction of the negative mean asynchrony may reflect a slowing of the motor output. These preliminary data are in line with previous studies reporting specific effects of tACS at beta frequency on motor functions and cortical excitability.

Assimilation of L2 vowels to L1 phonemes governs L2 learning in adulthood: a behavioral and ERP study

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According to the Perceptual Assimilation Model (PAM), acoustic similarity/dissimilarity between sounds of the second language (L2) and the native language (L1) governs L2 learnability in adulthood and predicts L2 sound perception by naïve listeners. The study addressed two questions: (1) whether the discrimination patterns predicted by the PAM for L2 naïve listeners are also reflected in the modulation of Mismatch Negativity (MMN) component of the Event-Related Response (ERP) and (2) whether L2 classroom learning is associated with the typology of L2 naïve listeners, as recently suggested by behavioral studies on cross-linguistic research. We measured the behavioral and ERP responses in two groups (10 subjects per group) of Salento Italian (SI) undergraduate students of British English (BE) attending the first the fifth year of the Foreign Languages and Literatures Faculty, compared with 10 inexperienced subjects of BE as L2 (only for the ERP experiment). An identification test examined the perceived phonetic distance between the L1 (/i, ɛ, a, ɔ, u/) and L2 (/iː, ɪ, ɛ, æ, ʌ, ɑː, ɒ, ɜː, ɔː, ʊ, uː/) vowel system. The contrasts /iː/-/uː/ and /æ/-/ʌ/ (for which the PAM's framework predicted an excellent and a good discrimination, respectively) were selected for an oddity discrimination test and the ERP experiment. In the ERP experiment, using an oddball paradigm, the contrasts /iː/-/uː/ and /æ/ -/ʌ/ were tested while subjects watched a silent movie. As a control condition we introduced the L1 within-category contrast /ɛ/-[e] for which poor discrimination is predicted for all subjects. Following the PAM predictions, the two groups of students did not differ in their behavioral discrimination performance: they exhibited excellent discrimination of /iː/-/uː/ and moderate to good discrimination of /æ/-/ʌ/. MMN amplitudes confirmed that the L2 contrasts were well discriminated. Crucially, no difference was found between the groups of students and the inexperienced group for the L2 contrasts /iː/-/uː/ and /æ/-/ʌ/, and,

as predicted, all the subjects showed poor discrimination for the L1 within-category contrast. MMN peak latencies were modulated by the contrast type: /i/-/u/ elicited a faster MMN than /æ/-/ʌ/ and /ɛ/-[e]; in turn, /æ/-/ʌ/ evoked a faster MMN than /ɛ/-[e], reflecting the acoustic distance between the stimuli. Furthermore, the MMN was right lateralized. In line with the PAM model, we extend the findings of previous behavioral studies showing that, at the psychophysiological level, classroom instruction in adulthood relies on assimilation of L2 vowels to L1 phoneme categories and does not trigger improvement in L2 phonetic discrimination.

Excitatory deep repetitive transcranial magnetic stimulation with H-coil improves motor planning in Parkinson's disease: evidence from mu event-related desynchronization

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In the present pilot study, we aimed at defining a new approach of repetitive Transcranial Magnetic Stimulation (rTMS) in patients suffering from Parkinson's Disease (PD). Indeed, contrasting results of rTMS applied at various intensities, frequencies and scalp locations have been reported in PD patients in the literature. Although many studies have shown encouraging results, there still remains the need to determine new stimulation paradigms that would induce efficient, stable, and reproducible symptom relieves in patients. Since it has been demonstrated that primary Motor cortex (M1) and Prefrontal Cortex (PFC) induce striatal dopamine release, we proposed a new stimulation approach combining PFC-M1 rTMS using a new coil: the Hesed coil (H-coil) which is designed to generate deeper and wider magnetic field without increasing the stimulation intensity. Our objectives were thus to investigate the clinical and neurophysiological effects of non-invasive, deep rTMS in PD, using the H coil. Twenty patients (3F; 63 ± 9 y.o.; PD duration: 6 ± 3 y) were included and underwent 12 deep rTMS sessions in 4 weeks. Excitatory 10 Hz rTMS was applied over M1 contralateral to the patient's worse side (WS) and over the bilateral prefrontal cortices. Motor control was assessed before and after deep rTMS, OFF medication, using clinical (UPDRSIII, lateralized scores, timed arm tapping, and Nine-Hole Peg Test) and neurophysiological measurements (Event-Related Desynchronization – ERD – of the mu and beta sensorimotor rhythms during self-paced WS wrist extensions). No drop-outs or adverse events were recorded. Our results showed that UPDRSIII (global and subscores) and timed tests significantly improved after treatment ($p < 0.001$). Mu and beta ERD latency onsets were also significantly increased after treatment (Mu: -1237 ± 177 ms before, and -2024 ± 215 ms after; beta: 1247 ± 151 ms before, and -2229 ± 179 ms after; $p < 0.01$). We could thus demonstrate that deep rTMS is a safe treatment for PD. It improved motor symptoms and significantly modulated the cerebral activity related to motor planning. The delayed mu and beta ERD shows that deep rTMS facilitated the activity of hypofunctioning cortico-striato-thalamo-cortical circuits,

probably through the release of dopamine. This study highlights the importance of the use of the H-coil for rTMS treatment of PD patients, as well as the importance of repeating the rTMS sessions for more than two weeks. Further placebo controlled, randomized studies are needed in order to assess the therapeutic efficacy deep rTMS and its consequences on cortical motor control.

Hormonal phases affect hemispheric asymmetry in spatial attention

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Fluctuating sex hormone levels during the menstrual cycle have been shown to affect Functional Cerebral Asymmetries (FCAs) in cognitive domains, contributing to sex-related differences in functional cerebral organization. Although some contradictions exist, it has been shown that FCAs fluctuate over the menstrual cycle, presumably due to cycle-related hormonal variations. Recent studies, also, investigated whether fine motor coordination, as reflected by manual and cerebral asymmetries, is also susceptible to natural sex hormonal variations during the menstrual cycle. This study aims to observe whether there is an effect between hormonal components and spatial attention. Twenty-three healthy volunteers (ten fertile women and thirteen women in menopause) was investigated during a line-bisection task (considering the position 1: central; 2 low distance on right; 3 high distance on right; 4 low distance on left; 5 high distance on left) and during three conditions: baseline (B), sham (S), tDCS (T). The group of fertile women was investigated during follicular phase, secretive phase and menstrual phase. During the line-bisection task was recorded and analyzed the ERP's component, particularly P300. In women in age of fertility ANOVA was significant for latency (L) in Left Lateralization ($p < 0.05$) and Central Amplitude (A) Lateralization ($p < 0.05$) in all conditions (follicular, secretive and menstrual phases). Post hoc analysis (Bonferroni Test) for Left L in Lateralization indicated a significant effect in follicular condition ($p < 0.05$), in secretive condition ($p < 0.05$) and in menstrual condition ($p < 0.05$). No significant effect in Post hoc analysis in Central A. About conditions (B, S, T) we found a significant effect only for Left L Lateralization ($p < 0.05$). Post hoc analysis indicated a significant effect only in T condition ($p < 0.05$). In line-bisection conditions there were significant effects in L for all the channels (left, right, central) and in A only in Central position ($p < 0.05$). Post hoc analyses showed significant effect ($p < 0.05$) in all significant conditions for 5 position (high distance left). In menopause group, analyses for Condition showed in all lateralization channel significant values in A and in L ($p < 0.05$). Post hoc analyses indicated a particular effect for T vs B ($p < 0.05$) in all derivations, in direction of lower latencies and higher amplitudes in T conditions. Analyses for Position showed in all lateralization channels significant values in amplitudes and in L ($p < 0.05$) except in L position. Post hoc analyses indicated a lower latency and higher amplitude in 5 position ($p < 0.05$). We can conclude that hormonal phase can influence spatial perception and it could be in direction of a predominant activation of Left Asymmetry. Furthermore these results are not affected by stimulation like tDCS.

Gender difference and hormonal phases can affect spatial attention

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Fluctuating sex hormone levels during the menstrual cycle have been shown to affect Functional Cerebral Asymmetries (FCAs) in cognitive domains, contributing to sex-related differences in functional cerebral organization. The line-bisection task is usually used to quantify disorders in spatial attention. Respect to spatial representation, it has been demonstrated that men outperform women in spatial analysis of complex auditory scenes. Although the line-bisection task is a rather indirect measure of callosal function, the importance of the corpus callosum in line-bisection, especially of posterior callosal areas, is demonstrated by several studies. This study aims to observe whether gender difference and hormonal effect can affect hemispheric asymmetry in spatial attention. Thirty-three healthy volunteers (ten women in age of fertility and thirteen women in menopause and ten man) was investigated during a line-bisection task (considering the position 1: central; 2 low distance right; 3 high distance right; 4 low distance left; 5 high distance left). During the line-bisection task the groups were recorded with a 64 EEG, acquiring the ERP's component, particularly P300 waves. A General Linear Model (GLM) was made considering the effect group and the effect of position in Lateralization for the component Amplitude (V) and Latencies (L). Level of significance was fixed at $p < 0.05$. GLM showed a significant effect (Wilk's Lambda < 0.05) for Group (G) and Target Position (TP) but not for interaction Group and Target Position. Particularly we found a significant effect in Left L and V ($p < 0.05$) and Central L for TP; for G GLM found significant effect in Left L and V ($p < 0.05$), in Right V ($p < 0.05$) and Central L and V ($p < 0.05$). Post hoc analysis showed a significant effect in 5 TP, in direction of a ampler and faster P300 in all groups, and a significant effect in all the groups in Left L and V ($p < 0.05$) and Right V ($p < 0.05$) in direction of slower latencies and higher amplitudes in groups of menopause women and faster latencies and less amplitudes in women in fertile age for Left Hemisphere. Gender difference and hormonal variations can influence spatial attention during a line-bisection task, especially in extremely left position from the center, and it could be in direction of a different activation of Left Hemisphere.

Does my hand feel emotions? Effects of the observation of hand movements with emotional valence on cortico-spinal excitability

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In humans, action observation activates a neural network, namely the Mirror Neuron System (MNS), that involves the premotor cortex, the supplementary motor area, the primary somatosensory cortex and the inferior parietal cortex. Also, studies with Transcranial Magnetic Stimulation (TMS) showed a facilitation of the Corticospinal System (CS) during action observation. Further, CS excitability seems to be influenced by emotional static images. We wanted to study the effects of the observation of a hand involved in a movement with emotional valence on CS excitability. 15 healthy and right-handed subjects (7 males, mean age 23.12 ± 5.77) underwent an experiment that involved TMS of the left primary motor cortex and EMG recording from the contralateral hand muscle (abductor pollicis brevis, APB). The intensity of magnetic pulse was set to evoke 1 mV MEPs at rest on APB. Subjects were asked to carefully watch 5 videos, each repeated 5 times, presented in a random order on a screen placed in front of them. In all videos a right hand moving was showed, but 3 videos had an emotional valence, whilst 2 videos were neutral. In particular, emotional videos elicited sadness (hand cherishing a coffin), disgust (hand touching a very dirty toilet) and pleasure (hand touching an appetizing cake). The neutral videos showed the hand grasping a glass (neutral condition with object) and the hand reaching the table (neutral condition meaningless). Each video lasted 5 seconds and the next video was displayed after 5 seconds of black screen. TMS was delivered randomly 200ms before or 200ms after the contact between the hand and the object. Data showed a significant increase of CS excitability when subjects observed the hand grasping the glass compared to the meaningless condition ($p < 0.005$). Regarding the emotional contest, videos evoking sadness and disgust reduced significantly the facilitation induced by the presence of the object (glass vs sadness $p < 0.05$; glass vs disgust $p = 0.05$). On the contrary, pleasant video maintained facilitation (glass vs pleasure: $p = 0.28$). First, our results confirmed data present in literature: observing a meaningful action towards an object enhances CS excitability. Further, we found that MNS was inhibited during observation of an action with a negative emotional valence. Mirror neurons may be important for understanding the actions of other people, and for learning new skills by imitation. It is well known that emotions can have enormous effects on learning, as the "on-off switch to learning". When

the switch is off, as in negative emotions, learning is reduced. The opposite is true for positive emotions. When we are joyful and hopeful we are more receptive and learning and memory are enhanced. In this framework, our results suggest that the emotional valence of the observed action modulates motor resonance likely influencing learning processes.

Visuomotor coupling and executive functions in elite soccer players: the Stroop test revisited

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Competitive agonistic athletic performance often requires fast and precise motor reactions to visual stimuli. The speed of reaction to moving stimuli requires rapid analysis of the situation and decision. The ability to achieve a motor response as quickly as possible to a visual stimulus, however, is not sufficient to ensure an excellent sport performance: of equal importance is the ability to prevent and control inappropriate motor reaction. However, response speed is often achieved at the expenses of precision. The success of an athlete greatly depends on optimization of these two features. The objective of the study was to evaluate visuomotor function and attentional control in professional soccer players using simple and complex reaction-times to the Stroop test. Two groups of male subjects were studied: 38 professional (first division) soccer players (age 25.82 ± 6.2 yrs) and 36 control subjects (age 25.29 ± 5.6). They underwent computerized simple (SRT) and choice Reaction Times (CRT). In the CRT, subjects were asked to provide as quickly as possible an alternative mouse button press in relation to a congruent (colour name written in the same named colour) or incongruent visual stimulus. To also test inhibitory control, a variant has been introduced asking not click any button in response to presentation of a congruent stimulus in red colour ("red" written in red colour). An independent samples t-test was used to compare variables between groups. Pearson's r coefficient of correlation was calculated for bivariate analysis statistic. Compared to controls, soccer players showed a faster SRT (186 + 22 ms vs 225 + 56 ms, $p = 0.006$). A greater Stroop effect, calculated as RT increase to incongruent vs congruent stimuli, was found in soccer players, at the limit of statistical significance (players: 62.9 + 57 ms; controls: 32.4 + 71 ms, $p = 0.053$). Only in soccer players, the number of choice errors was inversely correlated to RTs, both to congruent ($r = -0.44$, $p = 0.006$) and to incongruent ($r = -0.354$, $p = 0.029$) stimuli. High visuomotor speed in soccer players at the Stroop test supports the view that elite sports are associated with better psychomotor performances outside the specific field of practice. Other factors, such as a greater engagement and motivation may have played a role. With this respect, the significant inverse correlation between errors and reaction time only in soccer players may suggests that exposure to highly competitive situations may increase the trade-off between speed and accuracy, which is often the case at least in this type of sport.

Does action sequence violation elicit syntax-like ERP components?

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A linguistic utterance, a goal directed action and a musical phrase are all composed of small elements that are chained together according to specific rules to build-up a meaning over the temporal course. There are strong analogies between these domains in terms of hierarchical organization and recursion. Broca's area was originally identified as an area specific for language production but nowadays experimental evidences corroborate the assumption that this area is also recruited in many motor tasks, such as action execution, imitation, observation, motor imagery. The organization of the motor system shows some interesting parallel with that of language. Specifically, goal-directed actions can be sequenced in simpler units which are organized according to a hierarchical plan, resembling the organization of language. The present study addresses whether a syntax-hub exist also in the domain of action. Specifically, our questions were: What happens in the brain during the processing of complex actions? Do we get the same brain responses (effects) we usually have during complex sentences processing? We designed an ERPs study using an action-observation paradigm in which we presented video clips of complex familiar actions. This actions consists of many small "elements" which will get a meaning only if put together in a correct way (correct sequence). We manipulated the entire set of complex actions in two ways, either to introduce a "semantic violation" (the use of an implausible object to execute a given action), or a "syntactic violation" (the disruption of the common temporal sequence of the elements of a given action). We found a dissociation-pattern in the ERPs responses between "semantic" and "syntactic" conditions similar to the language- related ERPs components described in the literature.

May ERP and SPECT investigations represent early markers of Mild Cognitive Impairment (MCI)?

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The present study aimed at investigating both ERP and SPECT evaluations for testing possible early markers of cognitive decline in Mild Cognitive Impairment (MCI) patients and specifically in Subjective (SCI), amnestic (aMCI) and multidomain (mMCI) subtype of this clinical entity.Forty-three patients (age 66.4 ± 7.6; 31 women; MMSE 27.1 ± 2.3; education 10.7 ± 4.1) underwent ERP recordings (P300 and N400) by means of 30 electrodes and 99 mTc HMPAO brain SPECT. General cognitive status, short- and long-term verbal memory, episodic memory, non-verbal general intelligence, constructional praxia and verbal fluency were assessed by means of standardized neuropsychological tests. Comparisons between SCI vs aMCI and mMCI were analysed. Distribution of MCI subtypes was the following: 7, 18, 18 subjects with SCI, aMCI and mMCI respectively. Among MCI subtypes, altered P300 were recorded with significant increasing proportion in SCI (28.6%) and mMCI (70.6%) patients whereas aMCI patients had a lower percentage of abnormalities (16.7%). Regarding the N400 effect, the range of alterations reached 85.7% in SCI up to 100% in mMCI subjects with lower percentage of impaired effect in aMCI (72.7%). As a whole, all patients showed significant regional hypoperfusion compared to the database of healthy subjects with any significant differences between cerebral lobes and specific Brodmann Areas (BA). Instead, among groups, significant differences of reduced cerebral perfusion flood were found in left BA45, BA 19, BA21 and right BA5 between SCI and mMCI subtypes. Correlational analyses indicate a poor relationship between ERPs and SPECT findings between subtypes of MCI even when patients were considered as a whole. No significant correlations were observed between ERP, SPECT and neuropsychological findings with age, sex, depression and disease duration. Our findings indicate that SCI subjects, despite normal neuropsychological profile, show significant altered ERP and SPECT patterns compared to other subtype of MCI. These results suggested that the functional impairment may be ahead of detectable structural changes and cognitive defects Thus, ERPs and SPECT may provide to clinicians a valuable tool to screen and monitor longitudinally subjects who complains memory dysfunction with any pathological results on neuropsychological tests. The final goal may be to early objectivate the underlying cerebral pathology of MCI and possibly to predict conversion from MCI to dementia.

Cortical representation of Italian vowels within the auditory cortex: an ERP study

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Some anterior regions of the superior temporal cortex are engaged in phonetic features extraction of speech stimuli. Previous MEG findings proposed different mapping principles governing the neural representation of speech sounds by analyzing N1m modulation and yielded evidence of a phonemotopic organization of the human auditory cortices. However, the mechanism through which the human brain automatically decodes and represents speech signals is to be fully understood. In this study, cortical responses to the natural Italian vowels /a/ and /i/ were analyzed during the perception and production tasks by using the Event-Related Potential (ERP) technique. Aims of the study were: (1) to determine whether also the N1 ERP component could be used in searching for a cortical speech sound distinction based on acoustic and articulatory dissimilarities between vowels; and (2) to test whether, at different neuronal modulations due to different stimuli, separable vowel representations were correlated by fitting the N1 cortical generators. To do this, the auditory evoked potentials to the vowels were recorded with an ACTIcap 64Ch system in 12 Italian healthy subjects during several speech tasks. In three different EEG sessions, subjects, seated in front of a black screen, were asked to listen to the vowels, randomly presented (Perception task), and to realize an articulatory task when a white screen appeared: (i) Acoustic Production, (ii) Silent Production and (iii) Articulation Imagery of the vowel previously perceived. In the present report, only the results concerning the Perception task were considered. Since in each EEG session each vowel was presented 80 times (ISI 3400-4300 ms), perceptual data were computed on 240 trials. First, we found that also the N1 component is a useful parameter in understanding the functioning of the auditory cortex in phonetic feature extraction of Italian vowels: the spectro-acoustic features distinguishing the two vowels are reflected in early brain electric signals as revealed by the N1 response which has a larger amplitude and a more medial topographic distribution for the vowel /i/ relative to /a/. Second, by N1 source analyses both vowels resulted localized in superior temporal cortex, but the /a/ was more anterior than /i/ showing that the N1 cortical source was affected by vowel features. In conclusion, the data suggest the selective responsiveness of different neural populations within the auditory cortex which play a crucial role in categorization vowels. We can assume that the specific spectral

envelope of the considered vowels determines the principles of functional mapping of auditory cortex and moreover, that the cortical activity reflects the main spectro-acoustic dissimilarities. Indeed, the fact that in this study the vowel /i/ recorded a greater activity could be explained by referring to inhibitory formant principle for which vowels with close formant peaks result in a reduction of neural activity.

Sustained phasic alertness during priming effect: an event-related potentials and transcranial magnetic stimulation study

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Alertness improves behavioural responses and induces a priming effect on the target stimulus. In the present study, we investigated the functional characteristics of sustained phasic alertness associated with the priming effect and examined the role of a specific brain area, i.e. the right Dorso-Lateral Prefrontal Cortex (DLPFC), during attentional processing of the stimulus related to primitive priming learning. The evaluation of these processes was conducted on healthy subjects by means of Event-Related Potentials (ERPs) and repetitive Transcranial Magnetic Stimulation (rTMS). This study was composed of two experiments. In the Experiment I, ten subjects performed for three consecutive times a CNV motor tasks. In experiment II, the CNV was evaluated in basal, and after 30 min of real or sham 1-Hz rTMS stimulation of the right DLPFC in twelve subjects. Repetition of a Contingent Negative Variation (CNV) ERP motor task resulted in a reduction of the Reaction Times (RT) and was associated with the stability of the CNV phenomenon. Transient virtual inhibition of the right DLPFC induced by real 1-Hz rTMS stimulation was associated with a significant decrease in total CNV and W1-CNV areas if compared with the basal and post-sham rTMS conditions. RTs did not decrease after inhibitory rTMS, but they did improve after sham stimulation. These results suggest that the continuous recruitment of attentional resources without any attenuation phenomenon in the presence of repetitions of a behavioural task is critical for the learning of a motor task. Moreover, the right DLPFC appears to play a crucial role in the genesis and maintenance of the alerting state and the learning processes.

Arousing auditory stimulus improves performance in a discriminative reaction time task

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Arousal reflects a state of generalized physiological activation closely related to a variety of phenomena such as attention and motivation. Reaction Times (RT) represent an indirect measure of arousal, and in a condition of increased arousal it has been showed a reduction of RTs, denoting a performance improvement. Hence, the possibility to modulate arousal in order to obtain a better performance could have potential applications in rehabilitation contexts. The aim of the present study was to investigate the effect of an arousing auditory stimulus (brief bursts of white noise presented to a volume of 90 decibel, able to induce a startle reflex) during a discriminative RT task. Twenty healthy volunteers (15 females, mean age 27.3) participated in 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. In the first condition of the task, subjects had to press response buttons for target digits (8-9) which were presented after a warning digit (1). In the second condition, during the same task a burst of white noise was presented to the subject through headphones concurrently to the presentation of the warning digit. The order of the two conditions was balanced between subjects. Results showed a significative interaction between the condition and the order of presentation ($p = .006$), with a steep reduction of RTs in the subjects who heard the arousing stimuli in the second part of the task. Subjects who heard the arousing stimuli in the first part of the task didn't show any difference between the two conditions, with reduced RTs already from the beginning. In the light of these results it is possible to conclude that the arousing auditory stimulus improved the performance of the subjects during its presentation and in the following part of the task, due to an increased arousal maintained over time. It is also feasible that the arousing stimulus strengthened a possible learning effect between stimulus and response.

Orienting attention in time in context of temporal expectancy versus prediction: a HD-ERP study

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The implicit use of timing is a fundamental cognitive mechanism allowing the prediction of events' occurrence. Two distinct but interacting processes have been described as specifically contributing to it. On one hand, temporal "expectancy" can be established according to endogenous or exogenous cues, resulting in both motor Reaction Time (RT) reduction and perceptual processing enhancement when events happen at the exact moment when they are expected. On the other hand, temporal "prediction" relays upon exploiting the unidirectional temporal flow. In this case the elapsing of time itself intrinsically biases stimulus probability occurrence conforming a Cumulative Hazard function'. It is not yet clear, however, whether and how these two processes interact with each other within the same task and what are the neural mechanisms that characterize them. In the present study we recorded High-Density brain electrical activity (HD-ERP) in adults performing a simple-RT task within a cue-target paradigm. The cue informativeness (temporal vs neutral) and the ISI duration (short vs long) were manipulated within a block-randomized experimental design in order to compare behavioural and ERP data in a context of temporal expectancy versus temporal prediction. As a main result we found a significant interaction between cue informativeness and ISI, showing that only at short ISI participants responded faster for temporally expected versus unexpected targets. Whereas, this cue-related behavioural advantage disappeared at long ISIs. The differential advantage of temporal cues at short versus long intervals was due to the influence of the hazard function during neutral-cue trials. In line with behavioural findings, cue-locked ERP analyses showed that only for short ISIs temporal cues elicited larger and steeper Contingent Negative Variation (CNV) responses compared to neutral cues at central and posterior left scalp sites. Brain source analysis mainly located this effect on the Supplementary Motor Area (SMA) and on the left Inferior Parietal Cortex (l-IPC). By contrast, no cue-related differences were found in the CNV at long ISIs. A second finding was that target-locked ERP analysis revealed a larger posterior P300 for temporally expected versus unexpected targets. Furthermore, for neutrally-cued targets an ISI-related modulation of the P2 component at central and right-anterior sites was found. More specifically, P2 amplitude was larger as a function of the conditional probability of target occurrence in time, reflecting a cumulative hazard function. Brain source analysis located this effect on the SMA and on the right Prefrontal Cortex (r-PFC). In conclusion, both the cue-related temporal expectancy as well as the cumulative hazard function-related temporal prediction dynamically contribute to the orientation of attention in time. However, while the SMA seems to be a common neural correlate of these two mechanisms, they nevertheless involve additional distinct neural networks, including the l-IPC and the r-PFC respectively.

Executive function and default mode activity in ALS

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Amyotrophic Lateral Sclerosis (ALS) is a fatal and progressive neurodegenerative disorder affecting motor neurons. Cognitive symptoms are described and there is evidence that ALS and Fronto Temporal Lobar Degeneration (FTLD) overlap. Most patients have mild cognitive impairment with subtle executive deficits and 5% have a subtype of FTLD. Cognitive impairment can be found in typical ALS and symptoms have implications for management and treatment of these patients. The most consistently reported cognitive changes in ALS patients involve deficits of executive functions. An executive dysfunction might impact on patients everyday care and planned interventions. Advancements in neuroimaging can be of help in assessing ALS patients in rehabilitation and the use of measures of functional connectivity with resting state fMRI, a technique which has highlighted a default mode network in the brain showing complex interactions among distributed neural networks underlying brain functioning. With this study we plan to investigate whether the analysis of functional connectivity patterns and their relations to executive dysfunction in ALS patients can be of assistance in planning rehabilitation and in assessing the effectiveness of rehabilitation by highlighting the deficits in default mode activity patterns and in cognitive tests which influence disability and quality of life in ALS patients. Clinically defined or probable (El Escorial criteria) ALS patients have been admitted for rehabilitation, all assessed by ALSFRS-R and FIM. We studied twelve ALS patients in the early disease stage. 13 healthy individuals with no history of neurological or psychiatric disorders and a normal neurological examination, matched for age and education, served as control subjects Neuropsychological tests assessing language, attention, memory, visuo-spatial functions and executive functions. Language performance have been measured with the Boston Naming Test and the AAT (Aachener Aphasie Test), verbal and non-verbal memory have been assessed, executive functions have been assessed with the modified version of the Wisconsin Card Sort Test (NCST), a letter fluency task and the Tower of London task. Volumetric structural and echo planar imaging has been acquired with a 1.5T Philips Achieva MRI system. In seven of these patients structural MRI shows atrophy of frontal and temporal regions. In this study, there is a reduce activity in 6, 7, 39 and 40 Brodmann areas (CTRL more vs ALS covariant GM; cluster corrected threshold: $p < 0.01$, cluster size 100 contiguous voxels). In addition there is a correlation with the digit span forward/backward difference. Our preliminary findings seem suggest an early subclinical involvement of executive functions in ALS; in detail suggest a early impaired activity of the bilateral prefrontal areas and probably a disconnection of the network between prefrontal and temporal areas (impairment of working memory).

Differences between musicians and non-musicians in exogenous attentional orienting: a preliminary study

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Musical training induces structural and functional neuroplastic changes, which produce behavioral and cognitive differences between musicians and non-musicians. Several studies have focused on differences in hemispheric asymmetries, with musicians showing reduced asymmetries in inter-hemispheric transfer times, as well as reduced leftward biases in line bisection tasks. As for visuo-spatial attention, faster response times have been described in musicians. However, little is known about visual hemifield asymmetries in visuo-spatial attentional tasks. The present study aims at investigating visual hemifields biases in musicians and non-musicians in an exogenous attentional task, using a version of the Posner paradigm. Right-handed professional musicians (n = 17) with at least 10 years of study and non-musicians (n = 17), aged 23-50 years, were administered the Posnercueing task. Participants fixated a central cross flankered by three boxes on either side. A flashing cue preceded by either 100 or 600 ms the target stimulus marked by an "X" within one box. Participants responded to the target as fast as possible. The spatial relationship between cue and target defined three conditions: valid (target at the same location as the cue), invalid (target in a different location but in the same visual hemifield as the cue), and crossed (target in the opposite hemifield). Furthermore, in catch trials (20%) the cue appeared without a subsequent target. Results show a main effect of Condition for both musicians ($p = 0.002$) and non-musicians ($p < 0.001$). Furthermore, we found a marginally significant Group by Visual hemifield interaction ($p = 0.08$), with non-musicians exhibiting faster response times for right hemifield stimuli, and no apparent hemifield bias in musicians. Despite the preliminary nature of these results, they suggest that musicians have more bilateral neural connectivity than non-musicians and a reduced visual hemifield asymmetry in spatial attention. Musical training could be a powerful opportunity to develop a more balanced cerebral way to pay attention to the external world.

Mirror motor activation during music listening in professional pianists: a neurophysiological study

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Neuroimaging studies have reported mirroring motor activation to music listening in skilled musicians. Actual corticospinal modulation, together with hand specificity of such activation remains to be clarified. We tested the dynamic functional motor cortex modulation in professional pianists while listening to well-known, predictable melodic sequences, using Transcranial Magnetic Stimulation (TMS) and Electroencephalography (EEG). Two groups of subjects were studied: professional pianists (n = 10, 3 women; age 26 + 5.8 yrs) and control naïve subjects (n = 10, 3 women, age 25 + 4.5 yrs). Participants listened to a melodic tone sequence containing the alternating repetition of a pentatonic scale in two different octaves. Participants, unaware of the scope of the study, were asked to detect a random deviant tone in the sequence, remaining still and especially not moving their arms/hands during the whole experiment. Using a circular coil on the vertex, Motor Evoked Potentials (MEP) were recorded bilaterally (abductor pollicis brevis-APB; abductor digiti minimi-ADM) at different time points, with 32 channels EEG monitoring. MEP amplitudes were expressed as percentage of that obtained in a resting condition. EEG Event-Related Desynchronization (ERD) of the mu rhythm was assessed by comparing its spectral power during listening vs rest. A significant side x time x group interaction on MEPs amplitudes (repeated measures ANOVA, p = 0.009) was found. Pianists showed a significant (post-hoc paired t p = 0.001) MEP modulation of right hand muscles according to the timing of their actual activation when playing the piano sequence. This modulation was significantly higher (post-hoc unpaired t p = 0.01) vs controls, who did not show significant MEP changes. Moreover, a subgroup of pianists preferring the right hand to play in the low-octave scale had a trend for left hand inhibition. Left sensori-motor frontal mu ERD to the melodic sequence played with the right hand was present in 9 pianists vs 4 control (chi-square, p = 0.029). Pianists display a dynamic auditory induced motor resonance to piano listening. This phenomenon, suggesting the presence of an audio-motor mirror system activated by piano music in professional pianists, can be related to their ability to confer a gestural meaning to well-known melodies.

Sound-waves' effect on haematic cortisol level: a pilot study

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Noise is known to impact human brain at a pre-attentive level and to influence cognitive performances, but the physiological impact of noisy sound-waves was never investigated. In this study we assayed if different sound-waves trigger a different cortisol release in healthy volunteers by the way of their vibrational impact on the bodies. We exposed 55 testers to different frequencies of noisy sound-waves. Both analogical and digital sounds were used and a control session (silent reading) was performed. Testers were divided in two groups of 31 (A) and 24 (B) individuals. We involved the first group (A) in four sessions in different days, at 08.00 p.m, and with the following exposures: (1) analogical frequencies between 20 and 100 Hz; (2) analogical frequencies between 8400 and 16000 Hz; (3) analogical mixed radio-waves; (4) reading. The second group (B) was exposed to (1) digital frequencies between 8400 and 16000 Hz; (2) digital frequencies between 20 and100 Hz. Finally, a mixed group of testers from A and B was exposed to analogical high frequencies between 4250 and 14200 Hz. After each session, testers expressed their opinion on the experience. During every session we collected two blood samples for each tester: ex ante and ex post the exposure. Blood cortisol level was measured with the Access Cortisol Kit (Beckman). We analyzed ex ante data, assessing the basal cortisol level at night. Lacking of bibliographical parameters, we used a non parametric statistics analysis performing both the Kruskal-Wallis and the Mood Median Tests. We found the basal cortisol level at night does not significantly change over year's time. Nevertheless, the experimental conditions are effective to measure cortisol level and its fluctuations in a frame time of 40-60 minutes. The low-frequencies, both analogical and digital, the mixed-radio waves and the high digital sound-waves are sleep-inducing and they do not significantly affect cortisol nocturnal decrease. The high analogical frequencies, otherwise, raise cortisol values up, disrupting its expected physiological reduction. Appreciation of the low frequencies sessions by the testers corresponds to lowered cortisol levels, while strong dislike of analogical high frequencies fits with increased cortisol values. Digital high frequencies are not liked nor disliked. Interestingly, to the decreased cortisol levels after the mixed-radio waves exposure corresponds a general displeasure of the session. Therefore the physical properties of sound-waves might interfere with cortisol release over emotional status and acoustic experience.

Understanding the underlying mechanisms of "non conventional medicine" in the therapy of pain: a laser evoked potential study

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Pain represents a behavioral response to a noxious stimulus that alerts us to the presence of an actual or a potential tissue damage. A different concept of what pain is and how to treat it is present in the Eastern tradition where pain is thought to result from blockage or stagnation of the normal movement of energy (qi) in the area that hurts and acupuncture is thought to restore the normal flow of qi. In modern scientific study, acupuncture has been shown to have multiple effects on the central and peripheral nervous systems. These effects are presumed to change pain perception, although the exact mechanism is unknown. No studies have been conducted on the abdominal acupuncture, that is very effective in reducing acute pain and that permits a standardized treatment. The objective of our study is to evaluate if the abdominal acupuncture is able to modify pain perception. We studied 10 healthy volunteer by recording the Laser Evoked Potentials (LEPs) before, during and after a real and sham abdominal acupuncture protocol. Each session included 3 times: (1) Baseline, in which LEPs to stimulation of the skin of both right and left dorsal wrist were recorded before real of sham acupuncture; (2) acupuncture, in which LEPs were recorded to stimulation of the same sites as at the baseline during real or sham acupuncture; (3) rest, in which LEPs were recorded 15 minutes after the needle removal. After each sessions subjects rated the perceived pain by using a visual analog scale (VAS). We found a significative reduction of N2/P2 complex after the real abdominal acupuncture protocol and a reduction, non significant, in the placebo protocol. Concerning the VAS results we obtained a significant reduction during the abdominal acupuncture treatment, this reduction was not observed during sham treatment. The results of our study showed that abdominal acupuncture is able to reduce pain perception, both measured with objective tool (LEPs) that with psychophysics measures (VAS). The results we found proved that abdominal acupuncture is efficacy in reducing pain, now clinical studies conducted on patients are needed in order to prove its efficacy also in patients suffering from pain.

Acute effects of moderate dynamic exercise on brain plasticity

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Regular participation in physical activity has been demonstrated to be associated with improved cognitive functions across the lifespan and would help in preventing cognitive decline and dementia. The mechanisms underlying these phenomena are poorly understood. It has been suggested that modifications in cognitive processes may develop over time as the response to repeated individual bouts of exercise. During acute exercise concentrations of BDNF have been shown to augment. Brain plasticity could be enhanced and executive functions, learning and memory processes could result improved. Our aim was thus to evaluate the effect of a single bout of aerobic exercise on visual perceptual learning, that is considered to reflect brain plasticity. 32 healthy males (age: 23 ± 2 yrs, mean ± SD) volunteered for this study. The subjects were randomly assigned to an exercise-group (exe-group; n = 16) or a control group (ctrl-group; n = 16). All subjects exercised on a cycle-ergometer for 30 min: exe-group pedaled at an intensity eliciting 70% of individual maximal Heart Rate (HR), i.e. at 159 ± 45 Watts; ctrl-group pedaled at 20 W, that represented an almost unloaded task. The subjects were administered an Orientation Discrimination Task (ODT), in which they had to decide whether the presented stimulus was tilted clockwise or counter- clockwise relative to the previously presented stimulus. ODT lasted about 5 min and was performed before (block-pre) and six times after the exercise (block 1, 2, …, 6). The orientation sensitivity was calculated as d' value for each subject and for each block. HR was continuously recorded throughout the experiment. In exe-group, at the end of cycle task HR was 152 ± 12 b/min, corresponding to a mean increase of 70 b/min above resting value. In the initial 2 min of recovery HR dropped by about 50 b/min and then further slowly decreased. In ctrl-group, a slight increase in HR (8-12 b/min) was observed during pedaling. An improved performance in ODT was found at block1 compared to block-pre in both groups (d' +130% in both exe- and ctrl-group; $p > 0.05$). In exe-group, the orientation sensitivity showed a continuous increase in the successive blocks, being d' value at block 6 more than doubled compared to block 1. In contrast, in ctrl-group no modification in d'value occurred from block1 to block 6. Performance in all blocks was significantly different in the two groups. The results of this study indicate that a single bout of aerobic exercise does enhance visual perceptual learning. Thus, suggestion can be made that acute exercise, at least of moderate intensity, can have an influence on brain plasticity.

Anticipating expected emotions: the role of prefrontal and occipital areas

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The emotional perception has been extensively studied in literature. However, only few studies have investigated the brain activity preceding exposure to emotional stimuli, and little is known about the neurophysiological mechanisms underlying emotional anticipation, especially when emotional stimuli exposure is not externally triggered. To investigate the brain activity related to self-generated emotional experiences, we recorded high-density EEG during a self-paced paradigm in 15 healthy subjects. The participants were asked to alternatively press two keys with the index and middle right fingers every 4-5 s. Every key press displayed an emotional picture on the screen, and the subjects always knew the affective valence associated with it. A total of 320 pictures were selected as emotional stimuli and equally divided into four categories: pleasant, unpleasant, neutral (based on their valence and arousing ratings on International Affective Picture System, IAPS) and scramble (unaltered perceptual features without affective content). To investigate the effect of emotional anticipation on cortical activity, the Motor Related Cortical Potentials (MRCP) were obtained averaging the EEG in relation to the key-press that triggered the onset of the visual stimulus. Results reveal a significant valence effect from -500 ms until movement onset over prefrontal and occipital areas showing larger prefrontal positivity in pleasant and unpleasant categories compared to scramble, and larger occipital positivity during anticipation of unpleasant pictures compared to neutral and scramble. In addition, analysis over occipital area show a significant valence effect even in the earlier interval from -1000 to -500 ms revealing a larger positivity in unpleasant anticipation compared to neutral and scramble. The main results of the present study show a bilateral positive activity in prefrontal areas during the anticipation of more arousing pictures (pleasant and unpleasant), and an early and sustained positivity only during unpleasant anticipation over occipital areas. Based on this and other evidences, we hypothesize that prefrontal cortex could play a key role not only in the evaluation, but also in the anticipation of affective events. Considering also the role of this cortical structure in the interaction between thoughts and action planning, is possible that the ability to anticipate future events represent an adaptive behavior whose aim is the fight/flight response to more arousing experiences. On the other hand, occipital area appear to be more sensitive to the valence effect. As well as revealed by fMRI studies, the activation of visual areas is greater when people view aversive stimuli and, based on our results, is possible to suggest an enhanced pre-processing in the to be stimulated area. In conclusion, is possible that the activations elicited by emotion's expectancy allow us to better coping with affective experiences in comparison to unpredictable events.

Combined effect of cerebellar cathodic tDCS and music listening

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According to the state dependency theory, the effects of any external stimulus are not only determined by the properties of that stimulus but also by the activation state of the brain. Previous studies reported that music listening can modulate brain activity and spatial performance and an involvement of the left cerebellar hemisphere in both music perception and visuospatial tasks. The aim of the present study was to investigate the effect of cerebellar activation state on the impact of music listening on a Line Bisection Task (LBT).Ten healthy subjects performed the LBT following cathodic or sham transcranial cerebellar Direct Current Stimulation (tcDCS) on the left hemisphere while listening a Mozart Sonata or white noise listening. These mean accuracy scores on the LBT task were analyzed by a within subjects ANOVA. There was a significant difference between the combined condition (cathodic stimulation / music listening / LBT) in respect to the baseline condition (sham stimulation / white noise / LBT). No differences were found among the other experimental conditions (sham stimulation / music listening / LBT; cathodic stimulation / white noise / LBT). This combined effect showed a shift of attention from left to right, reversing the natural trend toward left space in healthy subjects, known as pseudoneglect. The effect of music on spatial attention could specifically emerge when the excitability of the left cerebellar hemisphere is down-regulated and the tcDCS neurophysiological effects could better modulate spatial attention when followed by music listening.

Reverberant cortico-cortical interactions in early phases of movement inhibition

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Living in dynamic environment continuously requires the rapid generation of motor responses when necessary but also the promptly inhibition of actions when they would be unsuitable. In the last years many studies have investigated the role of various cortical and subcortical brain regions in inhibitory control and converging evidence suggest a crucial role of the right Inferior Frontal Gyrus (rIFG) and of the pre-Supplementary Motor Area (pre-SMA). However the precise role and the exact timing of the contribution of these areas remain unclear. The aim of the present study was to investigate the role of rIFG and pre-SMA in motor inhibition by establishing the specific time course and the causal interactions of these regions in relation to the left primary motor area (LM1). In a sample of 10 healthy subjects paired Transcranial Magnetic Stimulation (TMS) was delivered over the rIFG-LM1 and over pre-SMA-LM1 before and 50, 75, 100, 125, 150, 175 and 200 ms after the presentation of visual stimuli in a simple GO/NOGO task. For each interval, Motor Evoked Potentials (MEPs) and Reaction Times (RTs) were collected. To further gain information about rIFG/pre-SMA control over M1 an EEG/TMS study was also performed. When the conditioning stimulus was applied over the rIFG, MEPs were markedly and selectively increased for the NOGO trials at 50 ($p = 0.003$), 100 ($p = 0.002$) and 150 ms ($p = 0.001$) after the stimulus onset. No differences were found at 75, 125, 175 and 200 ms after cue presentation for the NOGO trials and at any delay for the GO trials. A similar temporal profile of cortico-cortical activation was found for the pre-SMA-LM1 connectivity for the NOGO trials peaking at 50, 100 and 150 ms after the cue onset. RTs were slowed down at 100 ($p = 0.004$) and 150 ($p = 0.013$) ms after the stimulus presentation in all experimental conditions. EEG/TMS session revealed that magnetic pulse over the rIFG and, to a lesser extent over SMA, evoked an increase in the beta activity over M1 ($p = 0.03$). The temporal profile of MEPs modulation, peaking every 50 ms and the beta increase over M1 indicated by the EEG/TMS session, strongly suggest a common monitoring action of rIFG and pre-SMA in stop processing mediated by reverberant oscillation in the beta rhythms.

Occurrence of sensori-motor interaction and long-term potentiation in human primary facial motor cortex investigated through non-invasive brain stimulation techniques

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Non-Invasive Brain Stimulation (NIBS) techniques, namely Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS), are frequently used to test and modulate brain activity in neurological and psychiatric disorders. Despite the importance of facial muscles in social life, their massive engagement during emotional and behavioral responses as well as their frequent and disabling involvement in stroke or movement disorders, conclusive data concerning sensory-motor integration and modulation of plasticity of synaptic connections in the facial primary motor cortex (face M1), are not available yet. This work proposed to investigate, in face M1 innervating lower facial muscles, firstly sensori-motor interaction and then Long-Term Potentiation (LTP)-like plasticity. To the first aim, Short- and Long-Afferent Inhibition (SAI and LAI, respectively) were studied by pairing Electrical Stimulation (ES) of the facial nerve (intensity 3 times the perceptual threshold) with TMS of face M1 (110% of motor threshold) at ISIs of 15, 20, 25, 30 ms for SAI and of 150 and 200 ms for LAI. Ten unconditioned Motor Evoked Potentials (MEP) and 10 MEPs for each ISI were collected from the relaxed depressor anguli oris muscle of 15 healthy subjects. LTP-like plasticity of face M1 was investigated in the same subjects with paired associative stimulation (PAS: 200 pairs of ES and TMS: 0.25 Hz, 20 ms ISIs) and in 4 subjects using anodal tDCS (13 minutes at 1 mA intensity, anode over face M1). Twenty MEPs were acquired before and after 20 minutes from PAS and tDCS delivery. Student's paired t-test and ANOVA were performed with significance set at $p < 0.05$. Results showed that facial nerve stimulation in the SAI paradigm did not affect MEP amplitude, whereas a significant MEP inhibition ($p = 0.035$) was observed at 200 ms ISI in the LAI paradigm. PAS and tDCS protocols induced a significant MEP facilitation ($p = 0.018$ and $p = 0.045$, respectively) after 20 minutes from the intervention. In conclusion, in face M1 sensory-motor interaction, namely the afferent inhibition, occurs only at long-latency but not at short-latency intervals and, moreover, its excitability is prone to plastic changes after both PAS and anodal tDCS. The latter phenomenon

provides first evidence for a LTP-like effect, being long-lasting (up to 20 minutes) and requiring short times of administration (less than 15 minutes). Evaluation of sensori-motor interaction and plasticity in facial motor cortex may provide further physiological insight into neurological or psychiatric pathologies involving the facial motor system.

Facilitation effects of cathodal stimulation in a perceptual learning task: behind a simplistic approach of tES

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Transcranial Direct Current Stimulation (tDCS) is a non-invasive technique that allows the modulation of cortical excitability in a polarity-specific manner (i.e., anodal – a-tDCS – induces an increase in excitability of the cortex while the cathodal – c-tDCS – decrease it). However no clear correlation emerges between tDCS polarity (anodal vs cathodal), increased or diminished cortical excitability and behavioural improvement or impairment. Contradictory results are present mainly for the cathodal stimulation both at physiological and behavioural levels. Moreover it is important to consider that the effects of tDCS depend on several parameters related to the use of this technique. To clarify the importance of some parameters of c-tDCS (i.e., time of application and presence of pauses) on the behavioural effects, we performed two experiments. In Experiment 1 the purpose was to investigate when c-tDCS can modulate plasticity in the healthy adult brain in relation to timing of application (before vs during a task performance). In Experiment 2 the aim was to understand if the presence of pauses during the stimulation may alter significantly the effect of c-tDCS. The stimulation was delivered by a battery-driven stimulator through a pair of saline-soaked sponge electrodes, one applied on visual primary cortex (4 × 4 cm) and the other on the right arm (10 × 6 cm). We used an Orientation Discrimination Task (ODT). Participants had to decide whether the presented stimulus was tilted clockwise or counterclockwise relative to the previously presented stimulus. In Exp. 1 we applied 1.5 mA c-tDCS with intervals (paused stimulation) both before and during the execution of ODT. In Exp. 2 we applied 22 minutes c-tDCS without intervals (continuous stimulation). All the procedures were identical of the Exp. 1. We measured the percentage of accuracy (d' values) for each subject in each condition. The results showed an improvement of the performance when c-tDCS was applied before the task whereas online c-tDCS was similar to sham (Exp. 1). In addition, we demonstrated that the presence of pauses during cathodal stimulation doesn't influence facilitatory effect (Exp. 2). The central point of our study is that the same protocol of induction of neuroplasticity can provoke different effects depending on the excitability level of the stimulated neurons at the moment of stimulation. Moreover we speculate that mechanisms of metaplasticity and the homeostatic priming effects of tDCS are likely involved. Therefore, cathodal stimulation not necessarily induce a detriment in behaviour, but the effects are state dependent and should be considered in relation to the timing of application and to the executed task.

VEP habituation distribution in the families of migraine children

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In spite of the bulk of studies showing reduced Visual Evoked Potential (VEP) habituation in adult migraineurs, this abnormality has never demonstrated in children with migraine. VEP habituation can be assumed as a marker of the visual cortex excitability, whose abnormality in migraineurs is related to the genetic background of this disease. In pediatric age, it is debated whether the presence of migraine in the families of young migraineurs is due to a hypothesized genetic background or is a consequence of the "psychological environment". The aim of our study was to investigate whether neurophysiologic or psychological elements are segregated in families of migraine children. We studied 11 children (2 siblings) with migraine without aura and their parents. VEPs were recorded in six successive blocks to test the change in amplitude of N75-P100 from the first to the sixth block (habituation). The psychological profile was made according to the CBCL/6-18 for children, YSR 11/18 for 11-18 years old patients and ASR for parents. VEP habituation was significantly lower in both patients and migraineur parents than in non-migraineur parents (two-way ANOVA: $F = 14.7$, $p < 0.001$). As for the psychological tests, no significant "between groups" difference was found when we compared the internalizing ($p = 0.5$), externalizing ($p = 0.3$) and total scales scores ($p = 0.1$). This is the first study showing a reduced VEP habituation in migraine children. Our results suggest that the familial distribution of the disease is due to a genetic background, while the "psychological environment" does not have a significant influence.

Interaction between functional variation of the dopamine D2 receptor gene and sound background on brain activity during implicit emotional processing

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Dopamine signalling is strongly involved in emotion processing and control of emotional behavior. Consistently, recent studies demonstrated that a functional polymorphism of the dopamine D2 receptor gene (DRD2 rs1076560, G > T) is associated with amygdala activity during implicit processing of facial expressions. Music is capable of reliably affecting the emotional state of individuals, possibly by regulating dopamine levels in the brain, as testified by evidence of dopamine release in the striatal system during intense pleasure to music. Furthermore, music is capable of inducing a change in an affective state in the laboratory, which in turn might cross-modally alter the behavioral and neural responses to facial emotions. However, this power of music to induce emotions and even to regulate the subjective emotional state is highly variable across individuals. To date, nothing is known on the genetic origins of these individual variations in the power of music to affect the emotional, and particularly dopaminergic system. The aim of this study was to explore with functional Magnetic Resonance Imaging (fMRI) the potential interaction between DRD2 rs1076560 genotype, sound background, and brain activity during implicit processing of facial emotions. Thirty-eight healthy volunteers, genotyped for DRD2 rs1076560 (G/G = 26; G/T = 12), underwent fMRI at 3 T performing an implicit emotion-processing task. In this task, subjects were asked to identify the gender of angry, happy, and neutral facial expressions while listening to a relaxing music sequence (Music Session) or while listening to amplitude-modulated noise (Noise Session). Multi-factorial ANOVA revealed a significant interaction DRD2 genotype x Facial emotion in the left amygdala, a significant interaction DRD2 genotype x Sound background in the bilateral amygdala and a significant interaction DRD2 genotype x Facial emotion x Sound background in the right Inferior Frontal Gyrus, IFG (all $p < 0.001$; FWE corrected). Our results suggest that the DRD2

rs1076560 polymorphism modulates music and noise processing in the bilateral amygdala, and that implicit processing of facial emotions is affected by sound background and by the DRD2 polymorphism particularly in the right IFG. We hence identified a putative source of variation in the emotional impact of music and sound in general to an individual's affective state and responses.

Processing literary metaphor with and without original context: ERP evidence

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The fundamental role of metaphor in cognition and communication has been confirmed in several experimental investigations on everyday metaphors. On the contrary, creative metaphors, such as those drawn from literary works, have been almost completely disregarded in experimental studies and no ERP evidence is available about their processing. Within this framework, the present study has two main aims. First, exploring possible distinctive ERP signatures for literary metaphor, and second understanding to what extent context can affect the process. To this purpose, we designed two ERP experiments. In Experiment 1, twenty-seven participants read a set of Italian literary metaphors (e.g., "grass of velvet"), literal phrases ("throne of velvet") and anomalies ("marble of velvet") presented out-of-context. Target words ("velvet" in previous examples) were constant across conditions, while the other words were balanced for length and frequency of use. In Experiment 2, a different group of twenty-two participants read the same set of literary metaphors and literal phrases embedded in their original context (prose and poetry). In both experiments, participants-unaware of the ultimate goal of the study-performed a word matching-task at the end of each trial. EEG was recorded with a 64-channel EasyCap system and ERPs were time-locked to the onset of the target word. Results showed that when presented out-of-context (Exp. 1), literary metaphors were more costly than literal phrases in both early and late time-windows (P200 and LPC effects). Unexpectedly, no N400 effect was observed. Literary metaphors did not elicit greater amplitudes than literal phrases whereas anomalies did. When presented in their original context (Exp. 2), literary metaphors elicited an early and sustained negative effect (N400), which proved significantly different from literal controls. These results suggest two main discussion points. First, when presented without their context, literary metaphors asked for greater effort in the stage of lexical access (indexed by P200) and in the pragmatic enrichment process (indexed by LPC) compared to the literal counterparts but no extra effort in the stage of linking material with previous context (N400). Second, when the context was added, literary metaphors showed extra-cognitive efforts in the process of integrating semantic and pragmatic information in context since the very early stages of processing (as shown by the sustained N400). Collectively, our results suggest that the specificity of literary metaphor might emerge in relation to the pragmatic aspects of the comprehension process and that context might not facilitate but rather increase the comprehension

effort. The observed extra effort is likely to correspond to greater aesthetic benefits, as probably happens in the real experience of literary works. In this light, the present study constitutes a first step towards a successful combination of literary studies and neuropragmatics.

Perception of pain in the disorders of consciousness: a heart rate variability pilot study

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The involvement of higher-order associative brain structures beyond primary somatosensory cortex in response to noxious somatosensory stimuli in the Vegetative State (VS) is questioned. Aim of the study was to assess the sympathovagal changes during noxious stimulation. Heart Rate Variability measures (5-min baseline; 2-min nociceptive stimulus; 5-min post-stimulus) were obtained by EKG from 12 controls and 10 VS/UWSand 10 Minimally Conscious (MCS) subjects. Noxious stimuli were applied on the finger nail bed by algometer at intensity above threshold. The EKG was processes in the time and frequency, linear and non-linear domains. Data Mining techniques and s Support Vector Machine classifier were used for data analysis and groups classification. Result in the training test for the groups classification were validate by 10 fold cross validation test. Approximate Entropy (ApEn), peak of High Frequency (pkHF) and normalized value of Low Frequency (nuLF) proved the most significant attributes at the Chi Square Attribute Evaluator. In baseline, controls and DOC patients were classified with 100% accuracy in both training and validation tests; MCSvs VS/UWS were classified with 100% and 81.8% accuracy at the training and validation tests, respectively. Nociception was differenciated from baseline with accuracy higher than 90% in all subjects' groups at the training test and with 89%, 90% and 64% accuracy at the validation test in the controls, MCS and VS/UWS groups, respectively. No differences were found between baseline and post-stimulus phase in all groups. The study confirms the applicability of Heart Rate Variability techniques in the functional classification of the VS and MCS subjects' neurovegetative responsiveness to noxious stimuli.

Awareness of symptoms amelioration after low-frequency repetitive transcranial magnetic stimulation in a patient with tourette syndrome and comorbid obsessive-compulsive disorder

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The Tourette Syndrome (TS) is a neurological disorder involving motor and vocal tics with onset during childhood. TS patients often display comorbid symptoms of Obsessive-Compulsive Disorder (OCD). Few recent studies suggest that the application of low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) over the Supplementary Motor Area (SMA) may be effective in treating TS disorders. In the present study we aimed to apply this rTMS treatment in a 49-year-old man with severe TS (motor and vocal tics, strident screams accompanied by violent self-injurious behaviors) and comorbid OCD. The patient was evaluated before and after rTMS applications using the following functional and neuropsychiatric scales: Yale-Global Tic Severity Scale (YGTSS); Motor tic, Obsessions and compulsions, Vocal tic Evaluation Survey (MOVES); Beck Depression Inventory (BDI); Beck Anxiety Inventory (BAI); Quality of Life in AD (QOL-AD). In addition, the number of weekly self-injurious behaviors, the intensity of the crisis and their interference with everyday activities were quantified using an ad-hoc questionnaire. Two 1 Hz Rtms sessions were administered at an intensity of 80% of the resting Motor Threshold over the SMA. The first day the patient received three trains of 5 minutes, with an inter-train interval of 2 minutes (900 stimuli/d).The second day he received six trains of 3 minutes, and 1 train of 2 minutes, with an inter-train interval of 2 minutes (1200 stimuli/d). After the second session the patient dropped out, refusing to continue the rTMS intervention, although he showed initial symptoms improvement on the MOVES and the YGTSS, and reduction in the number, intensity and interference with daily life activities of the crises. Although symptoms improvement on these scales was based on the patient's description of specific events and items, he was nonetheless not aware of the improvement, as he overtly reported no benefits from the treatment. These results confirm that rTMS might represent a useful tool for the treatment of TS. However, they also indicate the dissociation between implicit and explicit awareness of symptoms amelioration in patients with TS and comorbid OCD. Indeed the comorbidity with OCD may reduce the awareness of improvements and affect the patient's compliance with the treatment. Future double-blind placebo-controlled studies on large groups of patients are needed to further explore the effectiveness of rTMS on TS symptoms and the impact that comorbid OCD may exerts on the patient's compliance.

Baseline performance predicts gamma-tACS enhancement of fluid intelligence

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Our abstract reasoning abilities allow us to solve problems in novel situations and are commonly referred to as fluid intelligence (Gf). Recent evidence supports the idea that 40Hz transcranial Alternating Current Stimulation (tACS) applied to the left middle frontal gyrus might selectively reduce the time taken to solve visuo-spatial abstract reasoning problems classically utilized to measure Gf. Anyway, wheter gamma-tACS might induce enhancement of logical reasoning via modulation of Working Memory (WM) processes, or via increased cortical excitability, or as a function of individual differences in Gf are still debated questions. Here we addressed these issues by conducting two experiments, both implementing a Gf task, composed by randomly presented "Relational" and "Logical" visuo-spatial matrices, and a WM task (change localization), randomly presented in order to avoid carry-over effects. During Experiment 1, 24 participants underwent Gf and WM tasks while receiving gamma (40 Hz), theta (5 Hz) and sham tACS in a fully randomized manner (bipolar montage with active electrode on left middle frontal gyrus [MFG] and Cz reference; 1 mA stimulation intensity). In Experiment 2, another 24 participants underwent the same tasks by receiving a high-frequency transcranial Random Noise Stimulation (tRNS) (101-640 Hz) instead of theta-tACS, using the same electrodes montage. As a control task for experimental tiredness, additional Reaction Times (RTs) were measured throughout the sessions, by using a low-cognitive load odd/even pc-based task. The relationship between performance (Accuracy [ACC] and Response Time [RT]) and the predictors of interest, i.e. tACS (sham/5/40 Hz) or tRNS, and kind of test (LOGIC, RELATIONS and WM) was investigated through repeated measurements ANCOVA models including gender, age, Gf-WM tasks order and tACS/tRNS conditions order as covariates. Moreover, potential individual differences in the response to tACS have been explored through a partial correlation analysis computed between the individual Gf improvements and baseline performance of the entire sample (n = 48). Finally, separate ANCOVA models taking into account only wrong responses have been computed in order to control for possible speed-accuracy trade-off (SATO) effect. As expected, gamma-tACS reduced the time taken to correctly solve LOGIC matrices with no effect neither for RELATIONS trails RT nor for ACC levels in general. No SATO has been detected in both experiments. Additionally, no modulation of the performance at WM task was observed in both experiments, and the pattern of Gf modulation was consistent with gamma-

tACS but not tRNS enhancing Gf. Finally, subjects with relatively lower Gf abilities at baseline showed a significantly greater improvement with gamma-tACS. These findings support the functional relevance of gamma-band activity within the left MFG in high-loading Gf tasks. Moreover, that gamma-tACS induced improvements correlated with sham performance could suggest those individuals with slower RTs on sham benefit more from exogenously induced gamma oscillations (possibly due to suboptimal endogenous gamma oscillations), making the obtained finding an intriguing achievement for neuro-rehabilitation purposes.

A case of ocular myasthenia: the role of single fiber electromyography

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The Ocular Myasthenia (OM) is a clinical picture often difficult to identify especially if seronegative. For a correct diagnosis, the use of neurophysiological investigations and in particular of the Single Fiber Electromyography (SFEMG) is very important, as confirmation. We report the case of a 66 years old patient admitted to the Emergency Department of the AOUP, for dyplopia in lateral gaze to the right, initially interpreted as vascular, but in which the electrophysiological investigations allowed a correct diagnosis. We report a case of a 66 years old man who went to the Emergency Department of the AOUP for dyplopia in lateral gaze to the right lasting about 10 days associated with fronto-orbital headache on ipsilateral temporal right region. The neurological examination showed only dyplopia in lateral gaze without obvious deficits of oculomotor muscles. For this reason was made a CT scan (negative for acute hemorrhagic-ischemic lesions) and a Doppler ACV and TD (normal findingd). He was hospitalized at the Emergency Medicine Department, performed also MRI brain (encephalopathy ischemic vascular disease) and, therefore, discharged with a diagnosis of "diplopia in lateral gaze to the right due to vascular encephalopaty" therapy with ASA and statins. A subsequent neurological evaluation for the persistence of symptomatology prescribed a Desmedt test, run on facial nerve recording from right nasal muscle (normal) and SFEMG, which showed abnormal jitter values with the presence of conduction blocks, and execution of anti-AChR receptors (positive) and anti Musk (negative). The symptomatology regressed rapidly with the introducing of Pyridostigmine therapy. This case emphasizes the importance of neurophysiological investigations targeted for the diagnosis of neuromuscular disorders, associated with clinical examinations, neuroimaging and seronegative tests, especially in cases of persistent and of uncertain cause dyplopia.

Nocebo effect dissociates the laser-pain rating from the N2/P2 laser evoked potential amplitude

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The aim of this study is to investigate whether Laser Evoked Potential (LEP) amplitude and subjective perception of laser-pain could be affected by a nocebo effect. Ten subjects underwent either a Conditioning Nocebo Session (CNS) or a Learning Nocebo Session (LNS). At time 0 (baseline), LEPs were acquired from both right and left hand stimulation. At time 1, Vaseline was applied on the right hand and subjects were informed that they were receiving an hyperalgesic cream. In CNS, LEPs were recorded from both right and left hand using the same stimulus intensity as in the baseline. In LNS, right hand LEPs were recorded initially by a stimulus intensity secretly increased, so as to make the healthy volunteers believe that the hyperalgesic treatment really worked. Then, Vaseline was applied again and right and left hand LEPs were recorded at the same stimulus intensity as in the baseline. After each LEP recording, subjects were asked to rate laser-pain, by using a 101-points numerical scale. In CNS, laser-pain rating to right hand stimulation was increased after nocebo treatment, as compared to baseline. On the contrary, in both CNS and LNS the N2/P2 amplitude change induced by nocebo treatment, as compared to the baseline, was not different for both right (experimental) and left (control) hand stimulation. Our results showed that, differently from the study conducted in the placebo experimental, in the nocebo setting LEPs do not change in both experimental setting (CNS and LNS) when compared to control, while the laser-pain rating in CNS increase after nocebo session. Our results support the hypothesis that LEP amplitude cannot be considered as an objective measure of laser-pain perception.

Heart rate variability profile and personality variables before and after animal assisted activities on early adolescent's risk-taking behaviors: a pilot project

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Such innovative research project is aimed to conjugate psychophysiological and personality measures in the framework of Animal Assisted Activities (AAA) on a sample of early adolescents' risk-taking behaviors. Adolescence period have instrumental role in the development of competencies that can affect wellbeing and resilience. Adolescents with a strong sense of efficacy are more resilient and better able to resist the adverse life influences, have better performance in academics and sports and future job satisfaction. Self Efficacy can also influence better health in general and physiological reactions, for example how an individual makes a judgment of personal ineffectiveness, interpreting own rapid heart rate or sweating palms. On the other hand adolescence is also a vulnerable time in which emotions and risk-taking tendencies are amplified. Without positive outlets, levels of self-efficacy tend to decrease and youth are potentially left to destructive alternatives, such as conduct problems, antisocial behavior, low academic performances. Research suggests that engaging youth in constructive activities during out-of-school hours can enhance psychosocial protective factors. AAA can help adolescents in this direction. Studies say that the first mechanism is related to animals as agents of socialization, the second mechanism is due to beneficial effect of AAA on physiological indicators of stress/distress, and the third mechanism is related to animals as facilitators to improve self-efficacy. In this study we will try to comprehend all three mechanisms. During 6 months, 3 time in week, on 12 early adolescent's risk-taking behavior, indicated by the City Council, we will apply 2 hours AAA sessions, with horses, led by a expert equestrian technic. We will measure Heart Rate Variability (HRV), before and after AAA sessions one time at month. ECG will be recorded in supine position while breathing at spontaneous rate (S: 0.25-0.35 Hz) and at 0.2 Hz paced rate (P). FFT spectra of HRV will be obtained from RR intervals time series in S and P conditions. Power will be assessed in the bands VLF (0.02-0.04 Hz), LF (0.04-0.15), HF (0.15-0.4). The "Heart and Emotion" software (Elemaya Inc.) will be used to process the ECG data. Personality variables such as measure of self-efficacy/resilience, psychopathologic levels and stress events will be also assessed at the start and at the end of AAA protocol through self reported standardized test respectively as "EQ-i:YV Emotional Quotient Inventory", "SAFA" and "CLES". The hypothesis is that the levels of HF activity and self-efficacy/resilience likely will rise with significant effect in conjunction with AAA, improving the overall well-being of those involved. This research plan is supported by "Regione Puglia" grant named "Principi Attivi 2012" (Atto Dirig. n. 94/2012) through the winner project of "C.E.R.R.U.A. Ricerca-Intervento" association.

The effect of divided attention on the nociceptive system

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Imaging studies have characterized the effect of selective and divided attention on the elaboration of different features of visual stimuli, showing that these two attentional mechanisms tap on different brain regions outside visual networks. Such a characterization is still missing in other sensory modalities, and in particular, to the best of our knowledge, no study has compared the effect of selective and divided attention to different features of nociceptive stimuli. Our aim was to characterize behavioral and electrocortical responses to nociceptive stimuli in a condition of selective or divided attention. Twenty healthy volunteers underwent an EEG experiment (64 channels), in which they were administered couples of nociceptive stimuli (inter-stimulus interval: 1000 ms) applied, for each attention setting, in four different experimental conditions: (1) SLSI: stimuli presented at the same location with the same intensity; (2) SLDI: stimuli presented at the same location with different intensities; (3) DLSI: stimuli presented at different locations with the same intensity; (4) DLDI: stimuli presented at different locations with different intensities. In selective attention conditions, participants had to detect changes in a specific feature (e.g., either location or intensity), while in divided attention condition, participants had to respond to any change occurred. We observed a hierarchy in reaction time with faster responses in the location selective attention condition, then in the divided attention condition and in the intensity selective attention condition. Reaction accuracy was greater in the location selective attention condition, while no significant difference emerged in the divided vs intensity selective attention comparison. In contrast with behavioral results, a point-by-point one-way ANOVA analysis on the Event Related Responses (ERPs) evoked by nociceptive stimuli did not reveal any significant difference. Although a recent fMRI study has highlighted that selective attention to differences in location or intensity of nociceptive stimuli recruited both shared and distinct networks, our results seem to suggest that such differences are not reflected in the ERPs. As all our experimental conditions entailed recruitment of attention, our findings support the view that nociceptive ERPs mostly reflect attentional engagement or re-orienting towards nociceptive stimuli, rather than mere nociceptive elaboration. We conclude that selective attention towards the location of a stimulus enhances motor responses to it. This suggests, in line with recent models, that we prioritize the elaboration of where a potentially dangerous stimulus happens rather than its intensity.

Desynchronisation of cortical alpha rhythms during resting-state condition is reduced in healthy obese subjects without eating disorders

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It is well-known that obese subjects without eating disorders are characterised by abnormal Electroencephalographic (EEG) alpha rhythms during resting-state eye-closed condition. Here we tested the hypothesis that also the desynchronisation of alpha rhythms during resting-state eyes opening is abnormal. EEG data were recorded in 15 underweight, 20 normal-weight, and 18 overweight/obese subjects during resting-state eyes-closed condition and eyes-open condition. EEG sources were estimated by LORETA for alpha frequency band (divided into alpha 1, 8-10.5 Hz, and alpha 2, 10.5-13 Hz). The alpha desynchronisation was calculated as the difference eyes-open condition minus eyes-closed condition. The occipital alpha 1 desynchronisation was lower in overweight/obese and underweight subjects compared with normal-weight subjects ($p < 0.000005$). The same was true for parietal, occipital and temporal alpha 2 (10.5-13 Hz) desynchronisation ($p < 0.000002$). The parietal and temporal alpha 1 desynchronisation was lower in overweight/obese than in normal-weight subjects ($p < 0.00001$). These effects spatially matched those observed in the resting-state eyes-closed condition. In conclusion, subjects with abnormal weight and normal eating behaviour are characterised by poor alpha desynchronisation during resting-state eyes opening.

Neural underpinnings of superior action-prediction abilities in soccer players

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The ability to form anticipatory representations of on-going actions is crucial for effective interactions in dynamic environments and mounting research evidence has shown that action perception is strictly linked to motor representations. In this view, subjective experience has been considered to serve a crucial role in the recognition and simulation of ongoing actions. In sports, elite athletes exhibit greater ability than novices in predicting other players' actions, mainly based on reading their body kinematics. This superior perceptual ability has been associated with a modulation of visual and motor areas by visual and motor expertise. Here, we investigated the causative role of visual and motor action representations in experts' ability to predict the outcome of soccer actions. We asked expert soccer players (kickers and goalkeepers) and novices to predict the direction of the ball after perceiving the initial phases of soccer penalty kicks that contained or not incongruent body kinematics. The kicks could be directed to the left or to the right side of the goalpost, but in half of the trials the videos were manipulated so that an incongruent foot-ball contact followed the initial body running phase. During observation of the video-clips, we applied active or sham repetitive Transcranial Magnetic Stimulation (rTMS) over two critical nodes of the action observation network, namely the left dorsal premotor cortex (PMd) and left Superior Temporal Sulcus (STS). Results showed that STS-rTMS disrupted performance in predicting the fate of incongruent, but not congruent actions for both experts and novices, especially for those with greater visual expertise (i.e., goalkeepers). Conversely, PMd-rTMS impaired performance only for expert players (i.e., kickers and goalkeepers) who exhibit strong motor expertise into facing domain-specific actions in soccer games. These results show that the functional role of the motor system in action perception is dependent on direct motor experience with the observed actions. Thus, while both experts and novices can access to visual action representations in STS, only experts are equipped and use internal motor representations to predicts others' behavior. In conclusion, the results provide causative evidence of the complimentary functional role of visual and motor action representations in experts' action prediction.

Psychomotor and judgment performances in basketball referees

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Attention and reaction time to visual stimuli play a fundamental role in sports referees, who need to perceive, integrate and react to as many situations as possible in order to improve their decision-making performances. Motor reaction time, however, is not sufficient to ensure an excellent performance: the ability to prevent and control inappropriate responses is indeed of equal importance. In order to test the efficiency of visuomotor reactions to visual stimuli and the judgment capability in referees, we compared intermediate level basketball referees with control males (mean age = 21.97y ± 4.14). Subjects performed a simple (SRT) and a choice (Stroop task) reaction time computerised tasks. The Stroop task was characterised by 72 Stroop-like stimuli, separated by interstimuli intervals of 1.7 s. Subjects had to press as quickly as possible an alternative mouse-button in relation to a congruent (colour word written in its corresponding colour ink) or incongruent (colour name in a different colour ink) visual stimulus. In order to test also participants' inhibitory control, a variant has been introduced, asking them not to click any button in response to the presentation of a red congruent stimulus (word "red" written in red ink). Only participants with an accuracy rate ≥60% in the Stroop task were included in the analyses (17 subjects for each group). Our results showed no differences in SRTs between referees and controls ($p = 0.306$). In the Stroop task, even if the accuracy (percentage of correct answers) was not different between groups ($p = 0.720$), the detailed analysis of errors demonstrated that referees made fewer mistakes of congruence judgement ($p = 0.009$), to the detriment of inhibition errors ($p = 0.002$). Moreover, basketball referees were faster in choice reaction time of both congruent and incongruent conditions ($p = 0.013$). Finally, a positive correlation emerged between choice reaction time and percentage of accuracy in the referees group ($r = 0.656$; $p = 0.004$), i.e. increasing reaction times led to accuracy improvements. The present findings demonstrate a better psychomotor performance of referees compared to controls, not only confined in their own professional field. This was evidenced by an increased visuomotor speed in the choice condition, even if a positive correlation resulted between response time and accuracy. Thus, as required by their judging role, basketball referees showed faster and more efficient visuomotor reactivity in choice reaction time for every environmental conditions (congruent/incongruent), associated with an excellent judgment capability; indeed, the mild difficulty in inhibitory control did not affect their accuracy rate. These preliminary data could support the development of a research field in cognitive training, in order to improve performance related to visuomotor reactivity and accuracy in basketball referees or as an educational program for young referees at early stages of career.

Body representation of death awareness: a somatosensory-specific effect of mortality salience

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Although there is general agreement on the fact that thoughts of death significantly affect cognition and human behavior, few were the attempts to study its impact on the brain activity. No study to date investigated if and how death awareness accessibility may affect the somatosensory system. No study investigated its effects on pain perception and on cortical responses triggered by nociceptive stimuli. The functional investigation of nociceptive processing may disclose important information on perception, as cortical responses to nociceptive stimuli are largely influenced by state of arousal, vigilance, emotions and orientation of attention. The working hypothesis of this study entailed the experimental situation in which a person that remembered his/her mortal condition would have produced specific (and greater) effects compared to a mind-set in which he/she would be required to imagine/recall a negative valence situation (e.g., fail an important examination). Here we tested (1) the modulatory effects of mortality salience on Electroencephalography (EEG) and ratings of intensity and threat of nociceptive and auditory stimuli in a repetition suppression paradigm, and (2) the role of personality traits and demographics in mediating such effects. A specific increase of ratings of intensity and threat was found for both nociceptive and auditory stimuli following mortality salience induction. Conversely, EEG data differentiated between the two modalities. An aspecific effect of mind-set induction on nociceptive and auditory event-related potentials was paralleled by a specific impairment of nociceptive repetition suppression indexed by event-related theta oscillatory activity. In other words, mortality salience exerted a top-down modulation on EEG oscillatory amplitude which was specific to brain activity triggered by nociceptive stimuli and not by auditory stimuli. Interestingly, the higher the perceived threat of stimuli, the higher the modulatory effect found in participants. Our findings support the hypothesis that reminders of mortality have a specific effect on perception and neural responses associated to the somatosensory cortical system (compared to the auditory system). Such effect becomes stronger the more the somatosensory nociceptive inputs are judged as being threatening.

Peripheral and central nervous contribution to gastrointestinal symptoms in diabetic patients with autonomic neuropathy

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To explore the role of Diabetic Autonomic Neuropathy (DAN) in patients with long-standing Diabetes Mellitus (DM), we investigated psychophysical responses and neuronal activity recorded as evoked brain potentials and dipolar source modelling. Fifteen healthy volunteers and 14 type-1 DM patients with DAN were assessed with a symptom score index characterizing upper GI abnormalities. Multichannel electroencephalography was recorded during painful electrical stimulation of the lower oesophagus. Brain activity to painful stimulations was modelled using Brain Electrical Source Analysis. Diabetic patients had higher stimulus intensities to evoke painful sensation ($p \leq 0.001$), longer latencies of N2 and P2 components (both $p \leq 0.001$), and lower amplitudes of P1-N2 and N2-P2 complexes ($p \leq 0.001$; $p = 0.02$). Inverse modelling of brain sources showed deeper bilateral insular dipolar source localization ($p = 0.002$). Symptom score index was negatively correlated with the depth of insular activity ($p = 0.004$) and positively correlated with insular dipole strength ($p = 0.03$). DM patients show peripheral and central neuroplastic changes. Moreover, the role of abnormal insular processing may explain the appearance and persistence of GI symptoms related to DAN.

Inter-individual variability and the effect of catastrophizing on the perception of thermal grill illusion

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The Thermal Grill Illusion (TGI) has been suggested as a promising experimental model for studying paradoxical thermal painful sensation as present in e.g. neuropathic pain. The TGI can be evoked by simultaneous application of innocuous cold and warm temperatures. However, a large inter-individual variability has been reported for the provocation of painful TGI. So far, it is not known which factors contribute to this variability. The purpose of this study was to investigate the role of catastrophizing in the perception of thermal grill illusion. 37 healthy subjects were recruited (17 females and 20 males) and assessed using the pain catastrophizing scale. Subjects were asked to place the palm of their non-dominant hand on six bars interlaced with cold and warm temperatures of 20° and 40°, respectively. Subjects were also tested in a control condition where both uniformly warm (40 °C) and cold (20 °C) bars were presented. After each test, subjects were asked to report both the intensity and the unpleasantness of the stimulus using a Visual Analog Scale (VAS). The scale ranged from 0 (no sensation) to 10 (unbearable pain) and where 4 indicated the pain threshold. Furthermore, the quality of the TGI was assessed. The VAS intensity scale was divided into two categories: Responders and Non Responders according to the perceived intensity of the TGI. Subjects who reported intensities ≥ 4 where classified as Responders and subjects who reported intensities < 4 where classified as Non-Responders. Ten subjects were found to be Responders (felt a painful TGI), while 27 were Non-Responders (felt a non-painful TGI). T-test analyses showed that Catastrophizing levels ($p < .05$) were significantly higher in the Responders as compared with the Non-Responders. Furthermore, positive correlations were found in subjects with high-levels of catastrophizing scores and VAS intensity ($p < .0001$) and VAS Unpleasantness ($p < .01$). Furthermore, both warm intensity ($p < .005$) and unpleasantness ($p < .001$) ratings were significantly higher (but not painful) in Responders as compared with Non-Responders. A large inter-individual variability was also observed in the quality of the responses. Only, 10% of the participants experienced a burning pain perception while 7.5% heat pain while a greater 60% experienced an alternation or warm/cold. The remaining 22.5% reported a mix of (tingling, freezing pain, heat no-pain, and warm). In conclusion, an inter-individual variability exists in perception of a TGI. Catastrophizing is a factor which may modulate some of the perceptual processes and underlie part of the inter-individual variability.

Salience of painful stimulus in migraine patients: evidence from laser evoked potentials habituation studies

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The main neurophysiological feature in migraine is a dysexcitability in the interictal period expressed by a lack of habituation of evoked responses to repeated multimodal stimuli. The lack of response decrease after painful stimulation as well was confirmed by previous studies. Aim of the study is to test habituation and salience of painful CO2 laser vs visual flash stimuli in migraine. We evaluate long e short term habituation after laser and flash stimuli in 20 migraine without aura patients compared to 10 controls. We also evaluate pain relevance and dishabituation by introducing the stimulus of the different modality in stimulation series. Stimulation paradigms included a series of 10 tripletls of laser stimuli at 1 sec ISI and a series of 10 triplets of flash stimuli; then we delivered series of 10 triplets in which the third stimulus was of a different modality (LLF or FFL). Connectivity analysis by means of Granger analysis has been run out, in order to state the modality of cortical connections under salient stimuli in migraine patients and controls. We found a lack of long term habituation after both laser and flash stimulation in migraine patients, with a reduction of N2-P2 complex amplitude in the last stimuli in controls and a different modality of causal connections in migraine patients. Novelty reaction by visual stimuli seems similar between controls and migraine, but the percent change 3°f/2°l seems reduced in migraine. Novelty reaction by laser stimulus is significant in patients and controls, but the percent change 3°l/2°f is significantly increased in migraine. Reduced habituation to multimodal stimuli is a well known pattern in migraine, but in regard to stimulus "salience", pain seems to be the most important stimulus for migraine patients

ERP components elicited by a syntactically minimal music cadence

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In the last decade, a number of interesting components have been recognized and quantitatively described in the ERP responses to musical cadences (i.e., chord successions). We applied an experimental protocol based on a criterion of simplicity regarding both stimulation and signal analysis. The cadences were presented according to an oddball protocol. The standard stimulus was a minimal-length (three chords) unambiguous cadence according to the rules of the Western tonal system. In the deviant stimulus, the three chords sequence was closed by a third dissonant chord. Nineteen EEG traces were recorded from twelve subjects. EEG traces were band-pass filtered between 0.8 and 8 Hz and re-referenced to infinity reference. ERP responses related to each EEG trace were extracted for each subject and each condition averaging between trials. Non-parametric statistical analyses were carried out on the difference between subjects average responses to the more frequent stimulus and those to the deviant stimulus. A topographic representation of ERP components was obtained by means of 2D scalp surface mapping; cortical sources of the identified ERP components were studied using sLORETA. The most evident components we observed were a P2/N2 complex (principal anterior N2, posterior P2) peaking about at 300 msec; a temporo-parietal negative component with a latency of 400 msec; a later positive complex that we identified with a P3 both for latency (500-700 msec) and topography (centro-parietal localization). It is well known that semantic-based compatibility tasks or tasks that require greater amounts of attentional resources produce a delayed latency compared to classical acoustic oddball. Indeed, we recognized a later positive posterior component that can be identified with a LPC. The present findings suggest that the principles of rhythm, melody, and harmony underlying Western tonal music coupled with measures of brain activity, may aid the understanding of the brain dynamics involved in the formation and use of highly specialized cognitive constructs such as those that underlie music cognitive processing. Thus in our opinion, the proposed experimental protocol could be easily applied by clinicians to the study of cognitive disorders, possibly contributing to the psychophysiological evaluation of disorders of consciousness.

Level of dopamine modulates learning style and error-related negativity in Parkinson's disease

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Aim of this study was to investigate the effect of dopaminergic medication on behavioural performance and neural response in Parkinson's Disease (PD) patients during a reinforcement learning task. Ten PD patients and 10 controls were enrolled. PD patients performed the experiment both with High Level (HLD) and Low Level (LLD) of dopamine medication in two separate sessions. We employed a reinforcement learning paradigm previously shown to be sensitive to dopaminergic manipulation. Participants have to learn to choose one of two stimuli presented, on the basis of a probabilistic positive or negative feedback (Learning phase). To evaluate whether participants learned more from positive or negative feedback they were tested with a novel combination of training stimuli (Testing phase). Electroencephalogram (EEG) was recorded when the participants performed the task. The Error-Related Negativity (ERN), a negative deflection in the EEG elicited when human participants commit errors, was examined. Testing phase results are reported. Behavioural data analysis showed a main effect of learning style (positive vs negative feedback) ($p = .000$). Pairwise comparison (Bonferroni adjusted) highlighted that both PD patients with LLD ($p = .000$) and HLD ($p = .011$) learned more from positive than negative feedback, whereas controls learned similarly from positive and negative feedback. The comparison between high conflict and low conflict items pointed out that participants were more accurate with LC than HC items ($p = .003$). Pairwise comparison showed that patients with HLD learned more from positive than negative feedback in LC items ($p = 002$). Response-locked ERN analysis showed main effect of learning style ($p = .010$) indicating a larger amplitude in items associated to positive than negative feedback. Pairwise comparison demonstrated that ERN amplitude of PD with LLD was significantly lower than PD with HLD ($p = .029$) and controls ($p = 002$). More in detail, PD with HLD had significantly larger ERN amplitude than PD with LLD with items associated to a positive feedback. No effect of conflict level was found. In summary, PD patients with LLD were less accurate than those with HLD and healthy controls. In the same way, PD patients with LLD had a lower ERN than those with HLD and controls. Moreover, patients with HLD tended to learn more from positive rather than negative feedback and showed a larger ERN after errors with items associated to positive than negative feedback. In conclusion, the level of dopamine seems to modulate learning style suggesting that HLD leads to learn more from positive than negative reinforcement, confirming the data previously reported in the literature. Interestingly, this trend is supported also by psychophysiological data highlighting that HLD makes ERN more sensitive to errors in items associated to positive reinforcement.