The role of premotor and parietal cortex during monitoring of involuntary movement: a combined TMS and tDCS study.

XXIII National Congress of the Italian Society of Psychophysiology

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Abstracts

XXIII National Congress
of the Italian Society of Psychophysiology

MAIN LECTURES

The space of action

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There is a plenty of evidence that observing someone else acting recruits the same motor processes and representations as if one were actually acting. Over the last years several studies have shown that the richer is one's motor expertise the greater is her sensitivity to others' actions. Less research, however, has been dedicated to exploring how deeply motor processes and representations might impact on how we make sense of the actions of others. And even less research has been devoted to investigating whether and to what extent these processes and representations might ground the possibility of acting together with them. The talk aims to tackle both these issues. I shall present and discuss some experimental studies showing that others' actions are better captured when people share their own motor expertise and are in position to exploit it. But sharing motor processes and representations turns out to be critical also when people act together, or so I shall argue. All of this has consequences for better understanding both the individual and joint actions.

The responsible mind

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Our brain is an immense neuronal network, which, only in the cerebral cortex, is made by 176.000 km of myelinated fibres, it contains 10^{15} excitatory or inhibitory synapses, and it is fully plastic throughout our lifespan. Our mind is continuously shaped by this *dynamic functional architecture*. For centuries, vitalism attempted to discover the presence of vital forces in biology with no success. Therefore, we have to assume that our mind operates under the physical laws of the universe and that it is an emergent property of this functional architecture. During the biological evolution the neural network acquired specific competences due to genetic and environmental factors with the involvement of stochastic processes leading to a large variety of

specific modules. The state of consciousness emerges when in the cerebral cortex there is a high viability of signalling and the content of consciousness varies depending on the modules involved. The set of these structures correspond to the global workspace, which represents a store of knowledge ready to use in our daily lives and it may be considered the main site of our unconscious life. There is now evidence that what we consider a "free" conscious decision, free will, is in fact an illusion. This topic has been widely investigated with the most modern technologies and in various experimental conditions and it is difficult to deny that the brain decides to perform a movement and later the individual becomes aware of what happened. This means that our conscious mind has no independent decision power, as it happens with our unconscious mind. Therefore, one might suggest that there is only a responsible mind. What could be then the role of consciousness? Such a role is likely important to continuously shape the functional architecture through the processes of consolidation and reconsolidation of memory. In conclusion, consciousness appears to be an emergent property to train our brain to control our behaviour. This model brings to mind the gravity forces, which attract two bodies which in turn are able to generate the forces. These gravity forces have no freedom to move the two bodies at their will. In other words, they have no free will. Similarly our mind emerging from the functional architecture of the brain has no free will and it should be considered a cosmic entity not yet identified in its nature. The alternative explanation would require calling into play the vitalism.

SYMPOSIA ABSTRACTS

The processing of others' touch early in human development

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Among the other senses touch is the first to develop and it represents the primary means through which infants learn about their surrounding world from very early in life. Evidence in human adults indicates that touch is crucial not only for own corporeal sensations, but also for understanding others' tactile sensations likely through mirroring mechanisms. In recent years, there has been a growing interest on how infants process tactile stimulations on their own body but, to date, no study has explored how they process others' touching gestures. In this talk, I will first present results from experiments exploring how newborns visually process others' gestures that involve a tactile event. To explore this ability, we measured looking times and orienting responses in a visual preference task in which 2-day-old newborns were simultaneously presented with two videos depicting a gesture not involving a touch (no-touching gesture) and a gesture involving a contact (touching gesture) between human body parts (face, hand) and/or an object (spoon). Results have shown that only in the case of a human body-to-body contact, newborns could differentiate between a touching and a no-touching gesture. Crucially, newborns' early sensitivity to touch vanished when they were presented with gestures that involved an object as the agent of the touch. Another interesting issue refers to the development of mirroring mechanisms for touch. Recent lines of evidence in human adults have shown that viewing touch may vicariously activate a putative tactile mirror system, comprising the somatosensory cortices (SI and SII). I will present evidence of the origins of such "tactile mirror system", showing the vicarious activation of the somatosensory cortex during touch observation, as indexed by Somatosensory Evoked Potentials (SEPs), in 8-month-old infants.

Dynamic reorganization of functional connectivity during naturalist viewing

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One of the most intriguing principles in system neuroscience in the last ten years is that spontaneous brain activity at rest, in the absence of stimuli or tasks, is organized in large-scale ensembles of brain regions that show correlated ongoing activity (Resting State Networks or RSN). The topography of RSN closely resembles that of functional systems identified during task performance. A fundamental issue is then to understand how the organization of the resting brain into a finite number of topographically distinct networks is modified both spatially and temporally during task performance to support the high dimensionality and flexibility of behavior. To explore changes in RSN dynamics we employed Magneto-encephalography (MEG), while to study RSN topography we compared MEG- *vis-à-vis* fMRI-RSN, during naturalistic viewing as compared to visual fixation. Natural scenes stimulation is a relatively unconstrained paradigm, which has been extensively adopted to investigate the organization of the visual system in both human and non-human primates. Results showed that movie watching induces a decrement of MEG inter-regional temporal correlation of Band Limited Power (BLP) (i.e. the slowly varying envelope of neuronal oscillations) within a given frequency range, specifically in alpha-band, both within- and across-networks. However the overall RSN topography was maintained (both in MEG and fMRI). Moreover, in visual cortex, transient decrements of power correlation were associated with slowly changing features of the movie. Finally, watching the movie induced the formation of novel networks characterized by an enhancement of BLP correlation, specifically in θ and β bands. These findings suggest that RNS reflect "idling" cortical circuits, whose functional connections must be decremented or reorganized for task-specific activity patterns to emerge. Relevant to our discussion, is the observation that the relative decrease of within-network correlation and the enhancement of between-networks interaction, respectively in the visual cortex and between the visual and dorsal attention network, has been recently demonstrated also during a visuospatial attention task with respect to visual fixation. In particular, using fMRI we showed that such modulations of functional connectivity are behaviourally relevant. However, the connectivity within the dorsal attention network was relatively unaffected during attention, indicating that patterns of correlation in this network play a possible role as *priors* for incoming information, by anticipating an attentional stance. Overall, these results suggest that resting-state and task networks are clearly different in the frequency domain, despite maintenance of underlying network topography, and there exist key differences between networks in the relationship between rest and task patterns. These findings open new avenues of research aimed at investigating how naturalistic viewing influences the dynamic properties of integration and segregation among RSN in the human brain.

Home environment perception and virtual reality: cognitive and emotional reactions to domotic induced changes of colours and sounds

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The cognitive decline problem, which increases with age, needs a constant monitoring especially in old patients. Overall, the symptoms can be associated for example, to forgetfulness and to a progressive loss of problem solving skills. Cognitive decline does not affect all individuals equally, but it depends on lifestyle, cognitive training, nutritional style and genetic inheritance. The requalification of domestic and healthcare environments is an important methodology to allow a fast and economic solution to improve the habitability of the environment according to personal needs. However, before structural changes are made, it is necessary to analyze the user cognitive status, in base of some environmental parameters that can affect user status, e.g. lights color and intensity. As found in some studies, with electroencephalography (EEG) it is possible to evaluate and estimate cognitive state in relationship to the brainwaves. Moreover, a P300 and Event-Related Potentials (ERP) protocol can be used to evaluate the cognitive status of users. During the presentation of a stimulus, there is a significant increase in synaptic activity in a synchronized way. The potentials are called Evoked Potential (EP) or ERP that consist of a series of positive and negative waves that can be named numerically or according to their latency. The third positive wave of the ERP is named P3 or P300. The aim of this work is to reach new methodologies for realizing living environments dedicated to users with residual capabilities in the initial stage of autonomy loss. The virtual prototyping of life environments is greatly simplified through Virtual Reality (VR) that is relatively easy to change and modify without structural changes and costs. With a domotic system, installed in the environment, it is possible to change the lights color and their intensity, and it is also possible play music or ambient sounds simply modifying these parameters on a computer interface. According to the *Oddball Paradigm*, it was realized a VR system constituted by three different scenes in which are presented a target stimulus (bathroom door) enlightened by different colors, and some frequent stimuli (other rooms' doors). During the administration of the experiment, the EEG signal was acquired and, at the end, it was processed in order to evaluate the P300 parameters. In this way, the best environment parameters can be selected to improve the users' cognitive state in the real living environment. For this study 48 persons, tested after giving their consensus, were recruited: 18 subjects aged between 20 and 39 years, and 30 subjects older than 50 years. After the signals processing, it was found that P300 latency was related to stimulation colour and correlates with person's age. In addition, it was discovered that green colour elicit P300 peak faster than white or red colours.

From metaplasticity to interhemispheric connectivity: electrophysiological interrogation of human visual cortical circuits in health and disease

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The visual system is an excellent model for the study of short and long-range connectivity changes both in animal and human brain. Nonetheless, only recently it has been received a growing attention, mainly because of differences in ontogenesis, histological texture and neurotransmitters distribution compared with motor pathways; moreover, the location of primary visual area (V1) in the depth of interhemispheric fissure could theoretically represent an additional factor explaining the weak response to conditioning by Non-Invasive Brain Stimulation (NIBS) techniques. Electrophysiological methods, such as Visual Evoked Potentials (VEPs), can objectively evaluate excitability changes within primary and associative visual areas, as they reflect the activation of parallel rather than sequential anatomical pathways; while the first evoked response, formally named N1, arises from the activation of foveal retina and reflects processing of visual information along the parvocellular stream, thus reaching the ventral pathways ("what pathway"), the second one (P1) originates from partially segregated streams conveying to dorsal pathways within the occipito-parietal cortex ("where pathway"). In the past few years, we used transcranial Direct Current Stimulation (tDCS) and repetitive Transcranial Magnetic Stimulation (rTMS) to explore intracortical and cortico-cortical connectivity in the human visual system. We have recently proved the presence of a mechanism of "metaplasticity"; as occurs in the primary motor cortex, metaplasticity stabilizes intracortical networks through a dynamic adaptation of the modification threshold for Long-Term Potentiation (LTP) and Long-Term Depression (LTD), depending on the preexisting excitability state, in the face of developmental or learning-induced changes in drive. As concerns cortico-cortical connectivity, we have shown that transcallosal pathways interconnecting human visual cortices in the two hemispheres have an overall inhibitory function; they also appear to dampen neural responses to high-contrast stimuli, thus modulating the slope of the stimulus-response relationship in human striate cortex. Both transcallosal and metaplasticity-like dynamics seem to be active in primary, as well as in higher-order visual areas. Recognition and better description of such mechanisms are of critical importance in human pathology, as these phenomena are likely defective in some neurological conditions, including photosensitive epilepsy, amblyopia and neglect.

TMS-EEG coregistration in the exploration of human cortical connectivity

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Defining the human brain connectome has become one of the major goals of neuroscience, as confirmed by the large-scale economical investments on this topic (e.g., NIH-funded Human Connectome Project and the Brain Initiative; The European CONNECT Project and the Human Brain Project; the Asian Brainnetome Project). This field has been dominated by structural and functional MRI methods, enriched by new strategies of interpretation. However, the methods for interrogating the human connectome are not perfect and therefore cross validation with novel complementary methods is a wise way to proceed. I will highlight an emerging distinctive approach based on the direct activation of an area by non-invasive brain stimulation (TMS) and the simultaneous evaluation of the distribution of this activity in cortical networks by electrophysiological recordings (EEG). By reviewing TMS-EEG studies on network dynamics at rest and during cognition, and comparing them with fMRI-based functional connectomics, I will show how TMS-EEG data support the general principles of brain architecture inferred from graph theory models and provide further insights into the properties of effective connectivity.

An integrated approach to investigate the human neuroplasticity

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Neuroplasticity can be defined as the intrinsic ability of the brain to change itself in response to experience through the functional and/or structural reorganization of its neuronal connections. Neuroplasticity occurs during brain and behavior development, brain damage and motor learning. Indeed, motor learning induces plasticity under physiological conditions and results in Long-Term Potentiation (LTP)-like plasticity processes, namely potentiation of the primary motor cortex (M1). Further, many studies have shown that brain stimulation and motor learning can interact through homeostatic plasticity, thought to stabilize neural activity around a set point within a physiologically reasonable dynamic range. Recently, it has been described that a simple motor learning task could act as a "primer" for subsequent protocols inducing neuroplasticity at level of M1, and this interaction causes a temporary

occlusion of additional LTP-like plasticity. Action Observation (AO) is known to affect the primary motor cortex (M1) excitability. Recently we proposed a stimulation paradigm where the observation of repetitive thumb-index tapping movements performed with the right hand was coupled with the right median nerve electrical stimulation at the level of the wrist (AO-PNS). AO-PNS induced an increase of the left M1 excitability in the target muscle that was maintained up to 45 minutes after, suggesting that the conditioning protocol was able to evoke neuroplastic changes at cortical level. We also investigated whether and how the cortical modifications evoked by a motor training, known to plastically increase M1 excitability, interfere with the effects of AO-PNS. Participants practiced a motor training and after that they were exposed to AO-PNS. The results showed that motor training occluded the plastic increase of M1 excitability induced by AO-PNS, suggesting that AO-PNS and motor learning act, at least in part, on the same neuronal networks and evoke LTP-like plasticity.

The impact of sound environments on the brain circuits for mood, emotion, and pain

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Sound environments such as music and noise can reliably affect our moods and emotions, possibly by regulating the dopaminergic mesocorticolimbic system, which is strongly involved in emotional behavior and mood regulation. In our recent studies we presented 38 healthy adults with relaxing background music or control noise (matched with music in main acoustic features) while they performed an implicit emotion-processing task in which they had to classify the gender of happy, fearful or neutral faces. In one study the subjects' transient mood and anxiety traits were assessed with questionnaires and their task performance with button presses. In a second study their brain activity during music listening and task performance was measured by means of functional Magnetic Resonance Imaging (fMRI). Results showed that music successfully increased mood and speeded up the behavioral responses to happy faces, particularly in anxious individuals. In the brain these effects were reflected in down-regulation of the right amygdala by music listening. Sound environments can also interact with the descending pain matrix, inducing analgesia. Familiar, relaxing and pleasant music has the power to reduce pain induced in the laboratory and even to dampen the intensity of the chronic pain experienced by fibromyalgia patients, improving their functional mobility. In a recent study we measured 20 fibromyalgia female patients with functional Magnetic Resonance Imaging (fMRI) at resting condition before and after they listened to 10 minutes of preferred, relaxing music or control pink noise. The more analgesia the patients experienced after listening to

music, the higher was the low-frequency activity of the angular gyrus and its connectivity with frontal brain regions, presumably involved in decreasing pain perception. Overall, our studies encourage the use of individually tailored sound environments as non-pharmacological regulators of mood and emotions, with possible clinical applications in pain-suffering patients.

The motor cortex as integrator in sensorimotor behavior

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Primate behaviour is characterized by continuous sensorimotor interactions. One model classifies sensorimotor mappings into two general categories: stimulus-based mappings and rule-based mappings. Stimulus-based processes map sensory stimuli onto related actions with little flexibility: the stimulus' features activate a fixed motor program. For example, looking at someone grasping an object activates an obligatory motor program matching the observed object-directed action. Rule-based sensorimotor processes map sensory information onto one of any possible action in the motor repertoire that has been temporarily associated to the stimulus by means of a rule. For example, in a given behavioural context, seeing a hand grasping an object can require a motor response different from the observed one (e.g. releasing a handle). We have studied the interactions between the two mapping systems at the distal-most cortical level in the neural processes that produce behaviour, i.e. the motor cortex. We did so by testing the fluctuations of motor representations over time by means of Transcranial Magnetic Stimulation (TMS). We found systematic evidence in favour of the "stimulus-based vs. rule-based" model of behaviour. Stimulus-based and rule-based mappings represent different, dissociable, mechanisms. Specifically we found that, in our experimental conditions, conflict between stimulus-based and rule-based motor responses is not resolved until the motor cortex. Therefore, our evidence suggests that in the sensorimotor flow of information, the integration/competition between the two motor mappings occurs distally in the motor system, as distal as the motor cortex, which may act as integrator between alternative actions.

How (lack of) vision shapes the morphological architecture of the human brain: congenital blindness affects diencephalic but not mesencephalic structures

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Human behavior is greatly influenced by the strong reliance on vision and its relevance is well exemplified by the number of subcortical structures and the large proportion of neocortical surface devoted to the processing of visual stimuli. Several animal studies have described the adaptive changes following loss of sight that seem to affect both the architecture of the "visual" brain, as well as structures not directly involved in visual perception. In sharp contrast to the abundance of animal literature, a comprehensive characterization of the "human blind brain" is still lacking: in vivo studies generally suffer low sample size issues, pieces of evidence regarding the atrophy of visual cortices are inconsistent and very little is known about the reorganization of subcortical nuclei. Therefore, in order to explore the morphological characteristics of diencephalic and mesencephalic structures of congenitally blind humans, we recently conducted a multicenter study using MRI to measure volume of the superior and inferior colliculi, as well as of the thalamic nuclei relaying sensory and motor information to the neocortex. Our results suggest that loss of sight since birth leads to volumetric modifications within diencephalic, but not mesencephalic, nuclei: as compared to sighted subjects, blind participants demonstrate an overall volume reduction in the lateral geniculate nucleus and associative diencephalic structures that project to temporal, prefrontal, occipital, and premotor cortices. On the contrary, volumes of the thalamic nuclei directly involved in auditory, motor, and somatosensory processing, as well as the superior and inferior colliculi are not affected by visual deprivation. Two mechanisms may be responsible for this reorganization: (a) changes in reciprocal cortico-thalamic connections or (b) modifications in the intrinsic connectivity between relay and association nuclei of the thalamus. On the other hand, sparing of the superior colliculi is in line with their composite, multisensory projections, and with their not exclusive visual nature. In the last years, structural, together with functional, brain studies of visually-deprived subjects are offering a valuable tool to examine the role of visual experience in forming a representation of the world, as well as to understand to what extent vision is a mandatory prerequisite for the human brain to mature.

Objects within the sensorimotor system

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Objects, such as tools, enable us to achieve goals otherwise hard to reach. But just how deeply is object representation entrenched within the action production system? According to the embodied cognition theory, when we observe an object we re-enact its proper use, and such re-enactment would allow us to comprehend them. In this talk I will provide empirical evidence suggesting that our knowledge of the environment, and particularly of objects, is built via available information implicitly grabbed through potential motor behaviour, and is not necessarily reflected in conscious representations. Indeed, in the view I endorse, actual object knowledge encompasses the actions you can effectively perform with it, depending on the current context. Moreover, I will argue that this hypothesis might have interesting implications for theories of cognition, as it helps us to better qualify the notion of objects and of body/embodiment.

Relationship between perception and emotional responses to static natural scenes

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Pictures of emotional natural scenes may elicit affective reactions which are observable as modulations, compared to neutral scenes, in the activity of the central and autonomic nervous system. It is debated whether these affective reactions may be elicited in the absence of stimulus identification, or alternatively if identification is a necessary condition for the elicitation of emotional responses. In a series of studies, we investigated this issue by manipulating the visibility of natural scenes through different types of degradation (size reduction; blurring; spatial frequency filtering; phase scrambling), and tested the accuracy in perceptual tasks requiring stimulus identification. At the same time we manipulated the affective content of natural scenes, presenting both neutral and emotional stimuli, and measured the affective modulation of two hallmark indexes of emotional response, namely Skin Conductance (SC) and the Late Positive Potential (LPP) component of Event-Related Potentials (ERPs). In a first series of studies, we manipulated scene degradation by decreasing the size (visual angle ranging from 21 × 16° to 3 × 2°) of the pictures. As stimuli were more degraded, the affective modulation of skin conductance was reduced or

eliminated; dampening of emotional SC modulation was observed despite degradation parameters allowed for categorization accuracy above 80%. On the other hand, the affective modulation of the LPP did not vary with picture size, suggesting that this component of the emotional response is less sensitive to perceptual degradation; if this is the case, what happens when the stimulus is further degraded, to the point that its identification is limited or absent? In a further series of studies, we investigated whether the affective modulation of the LPP is maintained when stimulus degradation drops below identifiability; in these studies, scene degradation was obtained through spatial frequency filtering and phase scrambling. The results indicated that, when the content of the scenes was not identifiable, no modulation of the LPP was observed. Moreover, when pictures were phase-scrambled, the affective modulation of the LPP was dampened and delayed compared to the intact condition, even when categorization accuracy was high (above 80%). The above evidence is consistent with the claim that natural emotional scenes, because of their symbolic meaning, can activate representations of the real stimuli; eventually, these representations can trigger patterns of modulation of physiological responses, such as the affective modulation of SC and of the LPP. More generally, the results of the present studies support the notion that the identification of emotionally charged scenes depends on the same perceptual processing stages as neutral stimuli, and that identification is a necessary (but not sufficient) condition for emotional modulation of autonomic (SC) and electrocortical (LPP) components of the emotional response.

Influence of pain expectation and hypnotizability on auditory startle responses during placebo analgesia in waking and hypnosis: a brain potential study

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A study was conducted to determine whether individual differences in expected pain and hypnotizability are associated with altered modulation of Auditory Startle Response (ASR) and N100 and P200 waves of the Event-Related Potentials (ERPs). Expectation, for placebo analgesia, was produced by manipulation where by the intensity of a painful cold tin plastic cup was surreptitiously reduced after the administration of a sham analgesic cream ("Anedicaine"). Participants were thirty-eight healthy women volunteers. During waking and hypnosis conditions, participants were tested under three treatments: (1) resting (Baseline); (2) tonic pain, produced by holding in the right hand a painful cold glass (-10°C) for 3.4 min; (3) tonic pain as in (2), after verbal suggestions that the administration of the "Anedicaine" drug could produce pain relief. After each pain treatment, participants rated their experienced pain and distress levels. For each treatment, we measured the peak amplitude

and latency of eye blink ASRs and of the N100 and P200 ERP waves as elicited by an auditory Pulse-Alone startle (PA) probe and by pulses occurring 120 ms after a prepulse, to provide a Prepulse Inhibition (PPI) measure of the startle response. During placebo analgesia, High Pain Expectation (HPE) and High Hypnotizability (HH) participants had higher pain reduction and shorter ASR latency of the eye blink than Low Pain Expectation (LPE) and Low Hypnotizability (LH) participants. HPE was associated with a higher pain experienced during waking compared to hypnosis. ERP and eLORETA analyses to PA responses showed that HPE was associated with higher midline N100 amplitude and source activity in the cingulate gyrus (BA24) of the right hemisphere. In terms of N100 wave, HH, compared to LH participants, had higher activity in the cingulate and anterior cingulate gyrus (BA24 and BA33). During placebo analgesia, the higher activation of HH participants was more pronounced for the BA24 in the right hemisphere. The P200 wave to PA also showed higher activity for the HH participants in the BA24 and dorsal cingulate gyrus (BA32). The posterior cingulate (BA23) was found more activated in HPE-LH versus LPE-LH participants, while the BA32, BA10 (medial frontal gyrus), BA24, and BA23 were more activated in LPE-HH versus LPE-LH participants.

Feeling sensations on the other's body after brain damages

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Recently, a novel monothematic delusion of body ownership resulting from brain damage has been discovered. Patients suffering of this disorder misidentify other people's limbs as their own, displaying a pathological embodiment of alien body parts. This phenomenon reflects an embodiment mechanism able to alter patients' conscious behaviors in both motor and somatosensory domains. In this talk, I will focus on the somatosensory system, by reporting experimental evidence on the fact that top-down processes (i.e., the delusional belief that an alien hand is a part of the own body) can modulate physiological mechanisms; e.g., Skin Conductance Response (SCR) and Hand Blink Reflex (HBR). In a first experiment, right brain-damaged patients, with (E+) and without (E-) pathological embodiment, as well as age-matched healthy controls, were administered a nociceptive stimulation protocol during SCR recording. Noxious stimuli were overtly applied by using a nociceptive stimulator on both the own and alien hands, either on the right (intact) or on the left (affected) body side. The patients had to rate the perceived sensation on a 0-5 Likert scale. E- patients and healthy controls, as well as E+ patients in their intact side, reported to feel pain only when the stimuli were delivered to the own hand, also showing a related SCR enhancement. Crucially, in the affected side, E+ patients reported to feel pain on the alien (embodied) hand and, coherently, they showed a SCR enhancement comparable to that found when the own hand was

stimulated. In a second experiment, we investigated whether, in E+ patients, the delusional belief about the body modulates a subcortical defensive response, such as the HBR. The blink, elicited by the electrical stimulation of the wrist and recorded from the orbicularis-oculi, dramatically increases when the threated hand is inside the defensive peripersonal space of the face. In a between-subjects design, including patients and controls, the threat was brought near the face either by the own hand or by another person's hand. In controls, as well as in the patients' intact side, the response enhancement occurred only when the threat was brought near the face by the own hand. Crucially, in the patients' affected side, patients were convinced that the alien hand, undertaking the postural manipulation – up to or down from the face – was their own hand. Coherently, when the alien (embodied) hand was close to the face, they showed a HBR enhancement comparable to that found for the own hand. According to the classical neuropsychological inference, these findings suggest the existence, in the normal functioning of the human brain, of a specific neural process that binds self-awareness to one's own body, as opposed to other bodies.

Vicarious somatosensation – In touch and beyond

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In this presentation, I will show evidence that our somatosensory cortices are vicariously activated while we witness the somatosensory states of others. First, I will show how viewing other people touched on their skin vicariously activated sectors of the secondary somatosensory cortex involved in sensing touch on own body. Second, I will review data showing that we vicariously activate the posterior sectors of the primary somatosensory cortices (Brodmann Area 1 and 2) while witnessing the goal directed hand actions of others. I will then show how perturbing this latter region impairs our ability to perceive the actions of others and how vicarious somatosensory encoding in this region is connected with the motor mirror neuron system, thereby provide a somatosensory – motor simulation of the actions of others. Finally, I will show how regions of the somatosensory system specialized in nociception are vicariously activated while we witness the pain of others. Jointly, this suggests that the somatosensory system can vicariously encode all three major somatosensory qualities: touch in SII, kinesthesia in SI and nociception in the insula and cingulate cortex.

From specificity in timing and spatial computations to goal and action generality in prefrontal cortex

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A rich body of studies has shown that the prefrontal cortex has a fundamental role in the generation of goal directed behavior. We investigated the role of the dorsolateral prefrontal cortex in the generation of goals using a duration task. We used in addition both a distance task and a matching-to-sample task to study the same neurons recorded in the duration task to further understand the decision process. In the duration task two stimuli, a red square and a blue circle, were presented sequentially and the monkeys' task was to report which stimulus lasted longer, while in the distance task they were required to report which stimulus was farther from screen center. By studying the neurons in all the three tasks we could identify the neural prefrontal mechanisms that starting from the duration coding led to the target choice. I will present a schematic model of decision making in the duration discrimination task formulated by combining neural and behavioral analyses. The model describes how the comparison between durations depended on an intermediate neural computation mechanism based on the order of presentation of the stimuli and how this computation could generate across-task interference effects on the performance in other tasks. This order-based computation (first stimulus longer/shorter) was then followed by a domain dependent feature-based relative duration coding (red stimulus longer/shorter) and by a domain independent goal coding (red or blue goal) in which neurons coded the same goal in all domains. The identification of the object goal was then converted in the motor plan for target acquisition after the go signal. In summary our results show through a single cell analysis the complexity underlying a relatively simple decision.

Transforming the thermal grill effect by crossing the fingers

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An alternating pattern of innocuous cold and warm stimuli determines a paradoxical, potentially painful sensation termed Thermal Grill Illusion (TGI). According to the model suggested by Craig and Bushnell (1994), the spatial summation of

warm stimuli inhibited the cold pathway at a spinal level. Since the cold pathway normally inhibits nociceptive afferents at a thalamocortical level, inhibiting the cold pathway leads to unmasking the hot burning quality of nociceptive sensation, in skin regions that are cooled. The TGI has been widely used as an experimental model for studying factors affecting pain. However, the role of spatial representation of multiple thermal stimuli in experimental pain remains unclear. Here we applied the TGI on crossed and uncrossed fingers to investigate whether pain perception depends on the somatotopic or spatiotopic configuration of thermal inputs. Sixteen healthy participants (6 male, 14 right handed, mean age ± standard deviation: 25.3 ± 3.7 years) took part in the experiment. The right index, middle and ring fingers were cooled or warmed, while the middle finger either was or was not crossed over the index. We performed four conditions, defined by the factorial combination of target finger (index or middle) and the position (uncrossed or crossed). The target finger was cooled (14 °C) while the other two fingers were warmed (43 °C). Participants adjusted a temperature delivered to the homologous finger of the left hand until it matched the temperature perceived on the cold target finger. Participants overestimated the temperature when the target finger was central within the spatial configuration (warm-cold-warm, as for crossed index and uncrossed middle), but not when it was peripheral (cold-warm-warm, as for uncrossed index and crossed middle). In the thermal grill illusion, spatiotopic distribution of non-nociceptive thermal inputs can unmask acute pain. By applying the TGI on crossed and uncrossed fingers, we show that warm stimuli are remapped into spatiotopic coordinates, prior to interaction with nociception. The brain processes a broad spatial configuration of multiple thermotactile stimuli, rather than a single location, to produce the "space of pain".

Neural coding mechanisms of artificial and naturalistic sensory stimuli

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Starting from the pioneering studies of Hubel and Wiesel, the knowledge of how the nervous system processes sensory stimuli has steadily increased studying responses to simple artificial stimuli. However, in recent years an increasing number of investigations focused on the study of responses to complex naturalistic stimuli although these are inherently more difficult to analyze and discuss. The first reason is that this is the only way to fully understand the processing of sensory information, since our nervous system was shaped by evolution such in a way to respond optimally to naturalistic stimuli with precise spatiotemporal structures and not to abstract geometries. The second reason is that one of the current frontiers of neuroengineering is to develop biomimetic sensory neuroprostheses and we want these prostheses to properly respond to daily life situations. Two computational studies of neural responses

to naturalistic stimuli will be presented. In the first I will describe how the network activity in the primate primary visual cortex (V1) is modulated over different frequency bands by naturalistic movie clips presentations. With information-theoretic analysis of the Local Field Potential recorded from V1 of anaesthetized macaques presented with naturalistic movie clips we showed that non-redundant visual information is conveyed by Delta (1-5 Hz) and Gamma (30-100 Hz) frequency bands. We built then a spiking network recurrent model of a local cortical circuit and we injected it with stimuli ranging from constant inputs to Multi Unit Activity recorded in the Lateral Geniculate Nucleus of the macaques. In this way we were able not only to reproduce experimental data but also to understand which naturalistic stimuli features were modulating the two frequency bands. In the second I will describe how a hardware neuromorphic model of tactile peripheral nervous system was designed and tested with naturalistic stimuli, in the frame of the development of upper limb neuroprostheses. In state-of-the art neuroengineering, most robotic arms are able to correctly decode the patient motor intentions from the neural activity. However how to inject tactile feedback into the nervous system, a crucial goal both for proper motor control and prostheses embodiement, is far from understood. Our lab mimicked the activity of fingertip motoreceptors with an adaptive spiking neuron model embedded in a biomimetic finger. The finger was first tested with simple stimuli, but prior to the implantation in the neurorobotic arm we also tested it with daily life textures. We found that the fine temporal structure of the biomimetic spike patterns was conveying sufficient information to allow the decoding of the textures, even under varying sensing conditions. These studies show the methods to analyze, understand, and reproduce neural coding of naturalistic stimuli for both computational and neuroengineering purposes.

Multimodality in the clinical assessment and research of severe disorders of consciousness in pediatrics

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Patients emerging from coma shift to Unresponsive Wakefulness Syndrome (UWS), starting to show sleep-wake cycles, while (still) presenting a number of clinical signs of unresponsiveness. Then, possibly they gradually regain some level of awareness and interaction with the environment, moving to a Severe Disorder of Consciousness (SDoC). Because arousal levels fluctuate and patients suffer from perceptual, attentional and motor deficits, the detection of signs of awareness is extremely challenging in the SDoC, and particularly in UWS. Diagnosis of UWS nowadays relies on clinical examination and neuropsychological assessment. Both tools bear serious limitations, as they result in a very high rate of misdiagnoses and/or insufficient

prognostic indications. This fact becomes even more important in the case of pediatric patients, in which the acquired brain injury disrupts the normal development process and negatively interacts with the learning curves, in all the cognitive and motor domains. As a consequence, the quest for suitable instrumental methods, capable of cutting the edge of the behavioral assessment, has been gaining increasing relevance in both the clinical and research settings. SDoC are essentially disconnection syndromes, manifested through a combination of damage to brainstem and to long-range thalamo-cortical and cortico-cortical pathways. Disruption of white matter integrity most often results in associated alteration of diffusion characteristics at the Diffusion Tensor Imaging (DTI); these include decrease of axial anisotropy, and increased mean diffusivity along the three dimensions. These changes on their turn result in the reconstruction of incomplete, insubstantial and/or spatially-limited fiber tracts during the employment of fiber-tracking techniques. Functionally, pediatric patients with SDoC show reduced connectivity of the brain networks with respect to healthy peers. In adults, increased level of consciousness has been found to correlate with increasing connectivity of the resting-state networks activity, after functional Magnetic Resonance Imaging (fMRI); the default mode, frontoparietal, salience, auditory, sensorimotor and visual networks were all found to have high discriminative capacity for separating adult patients in a minimally conscious state from those in UWS. Functional neuroimaging of pediatric cohorts in a UWS has also been attempted by applying Near Infrared Spectroscopy (NIRS). NIRS is an affordable, portable and ecologic optical technology which allows the independent measurement of the concentrations of oxygenated and deoxygenated hemoglobin in the brain. Despite the measurement repeatability candidates NIRS as an elective tool for the functional assessment of patients in a UWS, results are controversial, due to the limited capability to penetrate tissues. Among the neurophysiology methods, polysomnography (PSG) is successfully employed in the assessment of patients with SDoC. PSG has proved to correlate more adequately than evoked potentials with the clinical evaluation and the level of consciousness. In adults with SDoC, the main contribution to higher clinical scores is determined by the concomitant presence of Rapid Eye Movement (REM) sleep and sleep spindles. Analogously, in pediatric patients in UWS the presence of both REM sleep and sleep spindles correlates with good outcome; yet, REM activity was observed to reappear earlier with respect to NREM, differently from findings in adult cohorts. As a conclusion, the employment of different techniques in the study of pediatric SDoC allows the characterization of the neurovascular response in the brain with different temporal and spatial resolutions, and with respect to different epiphenomena. The combined interpretation of results requires cross-disciplinary skills, but it guarantees a holistic approach to the patient, and it promotes a comprehensive approach to the clinical assessment.

Acupuncture analgesia: clinical and experimental evidence

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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. There are several conclusions that is possible to infer by these studies; the first is that the afferent nociceptive pathways are essential for acupuncture to induce analgesia. Second, acupuncture analgesia is mediated by release of various endogenous neurotransmitters. Third, there is a significant overlapping between the pain and the acupuncture pathways. Imaging studies also showed that hypothalamus-limbic system plays an important role in acupuncture analgesia. Similar results were obtained by Positron Emission Technology (PET), used to visualize the effect of *de qi* (the sign of acupuncture activation). The comparison of electroacupuncture and sham acupuncture showed that only real acupuncture is able to activate the hypothalamus, thus concluding that the *de qi* sensation seems to be the conscious perception of nociceptive input due to the acupuncture stimulation. Concerning the clinical trial what is evident is the poor quality of the most part of Randomized Controlled Trial (RCT) published on this topic. A review about the use of acupuncture as a treatment for pain found that a small analgesic effect of acupuncture was found but its clinical significance remains unclear also because of the presence of several biases. A more recent paper reports the results of two large, well-designed clinical acupuncture trials on knee osteoarthritis that showed the efficacy of acupuncture in treating this pathology; the trial were reliable and thus their results. Concerning a common pathology such as low back pain Authors of two different RCT conducted in USA and Europe found a benefit for patients treating with acupuncture respect to usual pain but both studies confirmed that this improvement was found also for patients undergone sham acupuncture. Several other studies have been conducted on different kind of pain with positive results. In conclusion, although the research in acupuncture field is growing in the last years, the debate on how and where it acts is still matter of discussion, moreover the most part of clinical studies still lack of a rigorous setting and sometimes it depends on the characteristics of acupuncture itself.

Network remodelling within an epileptic focus in mouse visual cortex

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Epilepsy affects over 0.5% of the world population, with a high socio-economic impact. A percentage of patients (30%) remain resistant to drug treatments, in particular those with focal epilepsy. Electrophysiological studies of refractory epilepsy are currently in progress to get insights into the mechanisms of circuit remodelling. However, how plastic rearrangements within the epileptic focus trigger cortical dysfunction and hyperexcitability is still incompletely understood. In the latter decade, the visual cortex of mice has represented one of the areas most exploited for physiological studies. This is due first of all to the easy manipulation of sensory inputs. The visual cortex is well accessible for in vivo electrophysiology and imaging experiments. These features, together with the availability of mouse strains genetically marked, have made the visual cortex the election model for plasticity studies. We used the mouse visual cortex to assess plasticity in pathological conditions. We focused on plastic rearrangements induced by epileptic seizures. We employed a model of neocortical, non-lesional epilepsy based on local delivery of the clostridial enzyme Tetanus Neurotoxin (TeNT) in mouse visual cortex. TeNT is a metalloprotease that enters synaptic terminals and cleaves the synaptic vesicle protein VAMP/synaptobrevin, resulting in preferential blockade of inhibitory neurotransmission. Delivery of TeNT to the adult cortex results in refractory epilepsy with electrographic seizures persisting for several months, even after the toxin has been cleared from the system. Delivery of the toxin into the visual cortex leads to a model of focal neocortical epilepsy, resembling occipital epilepsy in humans. We used anesthetized TeNT mice to investigate how epileptic rearrangements impact on sensory processing. We recorded local field potentials and spiking activity both during baseline conditions and after presentation of visual stimuli, in control and TeNT-injected mice, at the completion of TeNT effects (i.e., 45 days following injection). In TeNT-treated cortices we found that spontaneous neuronal discharge was increased and visual responses were less reliable, with a higher proportion of failure trials, associated to higher spiking activity before stimulus presentation. Remarkably, visual acuity was lower than normal, both at electrophysiological and behavioral level. We also investigated how contrast-driven modulations in spiking activity and local field potential spectra were affected by TeNT injection. To further understand layer-specific rearrangements within the epileptic focus, we recorded control and TeNT mice using multichannel linear probes (16 channels), spanning the whole cortical thickness, allowing a layer-specific analysis. We also found a significant remodeling of the dendritic arbors of pyramidal neurons, with increased dendritic length and branching, and overall reduction in spine density but significant preservation of mushroom, mature spines. These data demonstrate robust, long-term remodeling of visual cortical circuitry associated with specific disturbances of network function in focal neocortical epilepsy.

Constructing models of perception, cognition and action: novel decoding and encoding approaches to brain functional data

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In the field of in vivo brain functional exploration methodologies, such as functional Magnetic Resonance Imaging (fMRI), there is an increasing interest in using the tools of machine learning to identify distinctive features that can allow "brain-reading", prediction of mental states or behavior, or recognition of mental disorders directly from brain functional data. Indeed, brain functional imaging has long been used to test specific hypotheses about brain-behavior relationships. Previous studies have relied on univariate analytical approaches that typically found an area to be recruited for a particular mental process and inferred that this process must be engaged whenever that region is found to be active. However, recent developments in the application of statistical multivariate pattern classifiers to brain functional data are providing the means to directly test how accurately mental processes or cognitive states can be classified. Different multivariate approaches to fMRI analysis using powerful pattern-classification algorithms directly decode or encode the neural content of information that is represented in that pattern of activity. In particular, in our lab, machine learning approaches have been applied to multi-voxel patterns of functional activity to assess supramodal processing of perceptual information, to decode semantic representation in sighted and congenitally blind individuals, and to encode/decode motor movements. These novel approaches are not only providing original information to understand brain functioning, but also enhancing the advantages of brain functional imaging for clinical neuroscience, neurorehabilitation and bioengineering.

Smart and resilient: on the connection between intelligence, brain connectivity and robustness towards perturbations

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The human brain is a complex system of interconnected regions spontaneously organized in distinct networks, with such organization being highly correlated with

individual differences in manifest behaviour, including complex phenotypes like intelligence. Latest advances in brain modeling based on graph-theory allow to describe brain complexity in terms of local and distributed networks properties (e.g. modularity, power-law distribution of nodal importance, small-worldness), showing how specific topological organizations might correspond to increased resilience against system failure (i.e. random error) or deliberated lesioning procedures (targeted attacks). Several complex biological systems spontaneously show the same organization principle, which often leads to higher survival rates and longevity, reinforcing the assumption that such intrinsic properties of network organization might hold an evolutionary advantage. Interestingly, recent functional connectivity fMRI evidences suggest a link between individual intelligence level and variability in resilience to perturbation in humans, a finding which might contribute explaining the neurobiological underpinnings of the Cognitive Reserve theory. Whether a higher intelligence level is the result of an optimized developmental process which in turn corresponds to increased resilience or just a disjointed phenomenon is not clear yet. The nature of such relationship and possibilities for brain stimulation interventions aimed at counteracting brain deterioration over time will be discussed.

Multimodal approaches for human brain mapping

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The clinical functional neuroimaging techniques, able to noninvasively monitor brain functions and disease, provide a cornucopia of anatomical and physiological data which help to guide diagnosis and therapy in clinical practice. These techniques fall within two major categories: (1) techniques able to directly measure neuronal activity, like electroencephalography (EEG) and magnetoencephalography (MEG); (2) techniques that measure the hemodynamic response in cortical tissue mediated by the so called neuro-vascular coupling mechanism, like functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET). While EEG can be performed with low cost and portable instrumentation, MEG, fMRI and PET rely on expensive and bulky (about the size of a room) set-up. Moreover, EEG sets basically no constraints to the type of tests that a subject can undergo (e.g. measurements during movement execution are feasible), conversely the other methods basically require the subject to stand still (either sitting or laying) limiting the applicability only to protocols not involving movements of the body. Further, in the case of PET the use of radioactive tracer is mandatory. EEG and MEG suffer from a limited spatial resolution in the order of a few cm, while fMRI can improve down to few mm, allowing also superposition of anatomical and functional information. PET is in between with cm spatial resolution. The co-registration of EEG and fMRI is typically performed at research level to combine the advantages of both techniques. Besides these well established techniques, another methodology is gaining

interest at research and clinical level: functional Near Infrared Spectroscopy (fNIRS). Like fMRI, fNIRS measures the hemodynamic response function following neuronal activation. Differently from fMRI that exploits the magnetic properties of deoxy-hemoglobin, fNIRS uses the different absorption spectra of oxygenated and deoxygenated hemoglobin to infer the concentration changes in the brain for these components. fNIRS employs optical radiation in the red and Near Infrared spectral Region (NIR). Thanks to the low absorption of tissue constituents (i.e. water, blood, lipids) in the NIR, light can penetrate the scalp and the skull, reach the brain cortex and be remitted at the surface, carrying the information on hemodynamic changes occurring on brain cortex. Due to the diffusive properties of biological tissue, NIR light is not only absorbed but also scattered. Light scattering on one hand reduces the achievable spatial resolution to the order of a cm, and on the other hand it introduces additional attenuation therefore preventing imaging of deep (i.e. sub cortical) brain structures. Despite these limitations fNIRS has been extensively validated against fMRI and it proved to provide comparable results when imaging cortical brain functions.

Hierarchical action coding within the human brain

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In everyday life, we continuously interact with objects within our environment. These interactions require the specification of specific muscular patterns for smoothly executing an appropriate action. At the same time, the same action needs to be represented also in terms of its more general aim irrespective of how it will be achieved, suggesting that it is also represented at a more abstract level. Adopting a combination of univariate, multivariate and connectivity analyses of neuroimaging data, we investigated how actions are represented within the brain during motor planning and execution. Results from a series of studies support the idea that executed actions might be represented at different levels of abstraction ranging from the representation of specific motor features (e.g. the adopted effector or the type of executed movement) to "abstract" action representations (i.e. generalizing across the very same motor features). Our data widen previous investigations on motor control by demonstrating that actions are represented at different levels of abstraction, possibly following a hierarchical organization, and that this organization might be at the basis of the extreme flexibility of our daily behavior.

ORAL AND POSTER PRESENTATIONS ABSTRACTS

Spatiotemporal fractal indexes in wakefulness and sleep: intermittency and connectivity

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Although brain activity consists of a large degree of parallel computing, consciousness needs an integration process and production of "streams", i.e. serial information. Models of consciousness denote this streaming process with the term "global workspace". The hypothesis that brain behaves like a system at criticality may explain this phenomenon and other features of consciousness. In physics, complex systems, either critical or dissipative, naturally result in stream-like information grow, through the dynamics of the so called "order parameters". These are integrative, macroscopic variables, normally coupled to external environment (i.e. responding to stimuli), which display, at criticality, scale-free fluctuations in time and space. The dynamical counterpart is the presence of metastable states, with quasi-abrupt transitions, where the system components, both micro- or meso-scopic, undergo "avalanches", namely scale-free domino-like cascades. Avalanches, in other words, are distributed as inverse power laws in terms of mass (number of components involved) and of duration times. We studied the aforementioned phenomena in brain activity by extracting events, i.e. Rapid Transition Processes (RTPs) between stationary states, from high-density EEG recordings. We extracted network events from 29 night EEG recordings that included pre-sleep wakefulness and all phases of sleep, where different levels of mentation and consciousness are present. We show that while critical avalanching kept unchanged, at least qualitatively, temporal complexity and event-related functional connectivity, present during conscious phases (wakefulness and REM sleep), broke down during both shallow and deep non-REM sleep. We provide a heuristic theory that explains how temporal complexity is hindered by a fragmentation of brain activity, without any need for the brain to depart from criticality. This breakdown suggests that the main difference between conscious and

unconscious states resides in the backwards causation, namely on the constraints that the emerging properties at large scale induce to the lower scales. In particular, while in conscious states this backwards causation induces a critical slowing down, preserving spatiotemporal correlations, in dreamless sleep we have a self-organized maintenance of moduli working in parallel. Critical avalanches are still present, and establish transient auto-organization, whose enhanced fluctuations are able to trigger mechanisms that protect sleep and sleep-related unconsciousness, by reinstating parallel activity in different brain moduli. This happens through a complex interplay between cortico-thalamic entrainment and the elicitation of neural bistability, whose EEG correlates are, respectively, sleep spindles and sleep slow (< 1 Hz) oscillations. The plausible role of critical avalanches in dreamless sleep is to provide a rapid recovery of consciousness, if stimuli are highly arousing.

Electrophysiological evidence for the domain-general nature of proactive monitoring

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Monitoring – evaluating the current (actual) state *vis-à-vis* the goal-related (desired) end state – is a critical executive function to optimize our daily behavior. This executive process can act either by reactively checking for the occurrence of behaviorally relevant events or by proactively checking the probability of occurrence of these critical events based on prognostic environmental changes, with the goal of optimizing responses to those events. This study aimed to investigate the electrophysiological correlates of proactive monitoring, with the specific aim to test the hypothesis of a functional specialization for this executive process regardless of the cognitive domain used in the experimental task. To this aim, a verbal and a spatial tracking tasks were designed, in which participants had to constantly monitor sequences of visual stimuli and check for the occurrence of a target that was presented after a variable number of stimuli. Crucially, two types of sequences were used with different degrees of regularity/predictability: in the regular, predictable (REG) sequence, the stimuli followed one another so to be informative about the occurrence of targets, thus involving proactive monitoring; in the random, unpredictable (RND) sequence, the occurrence of targets could not be predicted and thus only reactive monitoring could be exerted to perform the task. We analyzed participants' (N = 24) behavioral performance and Event-Related Potentials (ERPs) while they performed this novel behavioral paradigm in which monitoring processes (reactive vs. proactive) and cognitive domain (verbal vs. spatial) were manipulated within-subjects. ANOVAs carried out on behavioral data revealed better performance for REG than RND sequences regardless of the cognitive domain, thus validating our experimental manipulation.

ERP analysis carried out through a channel – and time – uninformed mass univariate approach revealed that, as compared to reactive monitoring, proactive monitoring processes at the stimulus immediately preceding the target (T - 1) were related to sustain (400-1000 ms) ERPs distributed over both frontal and parieto-occipital scalp regions. To control for possible confounding effects of stimuli-target similarity, we also contrasted the REG-RND monitoring effect at stimulus T - 1 with that at stimulus T + 1 (i.e., that immediately following the target). This analysis showed a cluster of significant differences in a late time window (≈ 600-720 ms) over right frontal and centro-parietal channels. Crucially, these effects were not modulated by the cognitive domain. These results confirm and extend previous findings showing the key role played by monitoring processes in optimizing responses to behaviorally relevant events in temporal and spatial domains. Overall, our findings provide support to the idea that proactive monitoring is a domain-general executive process that allows anticipating the occurrence of critical events for the optimization of behavior.

Tracking the time-course of top-down contextual effects on action comprehension: a TMS study

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From a predictive coding framework, recognizing an observed action is accomplished by minimizing an error signal at different levels of a cortical hierarchy, namely: the muscle, the kinematics, the goal and the intention levels. Previous neuroimaging studies on action observation suggest that context plays a key role in coding high-level components of motor behaviour, including the goal and the intention of an action. However, little is known about the possible role of context in shaping lower-levels of action processing such as reading action kinematics and simulating muscular activity. Furthermore, there is no evidence regarding the timing of this modulation. Here, we combined single-pulse TMS and Motor Evoked Potentials (MEPs) recording to: (1) explore whether top-down contextual information is capable of modulating low-level motor representations and, (2) track changes in MEP amplitude over time. We recorded MEPs from forearm and hand muscles while participants watched videos about everyday actions embedded in congruent, incongruent or ambiguous contexts. In addition, we delivered TMS pulses at different delays: 80 ms, 240 ms and 400 ms after action onset. Videos were interrupted before action ending, and participants were requested to predict the course of the observed actions. At a behavioral level, we found that congruent or incongruent contexts improved or decreased, respectively, accuracy in action prediction as compared to ambiguous contexts. Interestingly, both

effects were mirrored in a muscle-specific fashion during action observation but with different timings. More specifically, at 240 ms after video onset, we observed a selective facilitation of motor resonance (higher normalized MEP amplitudes) for actions embedded in congruent contexts, as compared to those occurring in incongruent and ambiguous ones. Later on, at 400 ms, we found a selective inhibition of motor resonance (lower normalized MEP amplitudes) for actions embedded in incongruent contexts, as compared to those taking place in congruent and ambiguous ones. At 80 ms, not muscle-specific contextual effect was observed, suggesting a general modulation of motor activity rather than mirror-like motor responses. These findings indicate that motor resonance is not an entirely automatic process, but it can be modulated by prior context-based expectations with different timings depending on the (in)congruency of the information among hierarchical levels. The different time-course of these effects suggests that they stem from partially independent mechanisms. The early facilitatory effect may directly involve M1, while the later inhibitory one is likely to be mediated by high-level structures that modulate motor representation.

Functional mapping of language before neurosurgery with magnetoencephalography: a preliminary study

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Functional mapping of the brain is a critical issue in neurosurgery. Presurgical mapping of eloquent cortical areas is helpful in guiding the surgical approach (for example in the case of a tumor resection) and can be critical in determining the outcome of an operation. One of the most common evaluations required before neurosurgical intervention is on the hemispheric dominance for language. Although the gold standard to study language lateralization is the intracarotid amobarbital tests, recent studies suggest that non-invasive techniques can be valid alternatives. A promising technique to evaluate language dominance and to identify language-related areas is magnetoencephalography (MEG). Compared with fMRI (the other non invasive technique recently proposed for presurgical mapping of language areas) MEG has some advantages. First, the MEG environment is almost noiseless. Second, a MEG examination is a more direct measurement of the electrical activity of the brain rather than that detected with an fMRI study. Third, an overt response is not problematic with MEG, since head position is continuously monitored throughout the recording and the impact of mouth movement on MEG recording is negligible. In the present study we present preliminary evidence of the feasibility of a simple naming task in MEG with the aim of mapping language related areas. We tested a

small sample of patients with brain tumor (N = 3) before they underwent neurosurgical intervention. Two of the patients were right-handed, and one patient was left-handed. In the naming task, patients were asked to name aloud 150 pictures selected from a wide database of picture and controlled for several variables (Concreteness, Naming Agreement, Frequency, etc.). MEG data were analyzed to localize lateralization for language. After pre-processing (filtering, epoching, artifact rejection, etc.), we performed source reconstruction of MEG activation on the whole brain volume using the Minimum Norm solution. To maximize spatial precision, source reconstruction was performed on the individual structural MRI of the patients. Preliminary analyses showed a meaningful time-course of Event-Related Fields (ERF) after the stimulus presentation, with an activation of occipital areas followed by an activation of fronto-parietal areas. The lateralization of language was consistent with the expectations associated with each participant's handedness. All patients, regardless of their cognitive status, understood very easily how to perform the picture naming task. These preliminary results support the feasibility of MEG as an alternative technique that could aid presurgical mapping of eloquent brain areas. These preliminary results will be validated against external criteria (i.e., fMRI activations, intraoperative mapping) to further support the usefulness of MEG in functional mapping of language before neurosurgery.

Multiple object processing in Alzheimer's disease: behavioural and electrophysiological evidence

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The ability to process concurrently multiple visual objects is fundamental for a coherent perception of the world. Enumerating multiple items requires two distinct mechanisms: an early individuation mechanism, which enables the simultaneous identification of a small amount of items; and a later mechanism, relying on Visual Working Memory (VWM), which enables to maintain active the representation of the identified objects. Previous studies showed an age-related decline in multiple objects processing and indicated that both individuation and VWM mechanisms are involved in the decline of enumeration abilities associated with healthy aging. The present study aimed at investigating how the two distinct mechanisms involved in enumeration are affected by pathological aging, specifically in Alzheimer's Disease (AD). Seventeen AD patients (mean age: 76.47 years; MMSE score: 22.16) and

twenty healthy elderly (mean age: 69.15 years; MMSE score: 27.83) were enrolled. We recorded EEG activity while participants were counting a varying number of targets (from 1 to 6 green dots) presented among distractors (red dots). We focused on two posterior ERP components, namely N2pc and Contralateral Delay Activity (CDA), which have been associated with individuation and VWM processes, respectively. Behavioural results indicated that, compared to healthy elderly individuals, AD patients were overall less accurate in enumerating all target numerosities and were able to process simultaneously a smaller number of items. Considering electrophysiological data, both N2pc and CDA componentswere modulated by target numerosity. Both healthy elderly and AD patients showed an increase in N2pc and CDA amplitude with increasing number of targets presented. Furthermore, CDA amplitude was overall reduced in AD patients compared to healthy elderly individuals. Concluding, our results showed that in pathological aging (specifically in AD) there is an overall deterioration of enumeration performance together with a reduction of objects that can be processed simultaneously as compared to healthy aging. The suppression of CDA amplitude in the group of AD patients suggests that the VWM processes, reflected by CDA component, are less efficient in pathological aging and may be the underlying neural correlates of the overall impaired behavioural performance in enumeration abilities.

Sleep reverts changes in human grey and white matter caused by wake-dependent training: a structural and diffusion weighted magnetic resonance imaging study

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Recent studies revealed that experience-dependent learning is associated with rapid microstructural changes in Grey (GM) and White (WM) Matter. Do such modi-

fications continue to accumulate if subjects stay awake and continue to practice a task at night, when they would normally be asleep? And if so, does sleep have a role in counteracting these changes? To address these questions we used structural (T1) and Diffusion Weighted (DWI) Magnetic Resonance Imaging (3T MRI) in 16 healthy volunteers studied during 2 experiments, each including 5 MRI sessions: (1) after a wake day spent outside the lab (~7pm); (2) after a night of sleep (~8am); (3) after 12h of extensive training in the lab (~8pm); (4) after 24h of continuous wake with training (~8am); (5) After ~8h of recovery sleep (~8pm). During the 24h of wake participants completed six 2h-training sessions of either a Driving Simulation game (DS experiment), or a battery of tasks based on Executive Functions (EF experiment). Moreover, task-sessions alternated with ~1h blocks of behavioral tests, including a 5 min Psychomotor Vigilance Test (PVT), used to track variations in individual alertness. Repeated measures ANOVAs were used to investigate volumetric and Mean Diffusivity (MD) changes in cortical GM, subcortical GM, WM and ventricles throughout the 2 experiments. Moreover, a support vector regression approach was applied to evaluate the potential relationship between structural and behavioral modifications. Compared to baseline wake, 12h of training led to a decline in cortical MD ($p < 0.05$, Bonferroni-Holm correction). The decrease became even more significant after 24h of task practice combined with sleep deprivation. Prolonged practice also resulted in increased GM and WM subcortical volumes and decreased ventricular volume. All changes reverted after recovery sleep. Moreover, structural parameters allowed a successful prediction of the individual vigilance level ($R^2 \geq 0.46$, $p < 0.001$). Present findings indicate that extensive task practice may lead to the accumulation of microstructural brain modifications and that sleep's ability to counteract performance deficits may be linked to its effects on these changes. Observed effects of sleep may depend on its role in promoting the production of cerebrospinal fluid and the decrease in synapse size/strength, as well as on its recently described ability to enhance the clearance of brain metabolites.

The peripersonal space in expert tennis players

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The aim of this study was to test whether the peripersonal space, defined as the portion of the space immediately surrounding the body, is modulated by the long-term motor experience with a specific tool. To this end we enrolled a group of expert tennis players, regularly using a tennis racket to train themselves, with an audio-tactile integration paradigm. Participants were requested to verbally respond to a tactile stimulus administered at the right wrist while hearing a task-irrelevant sound emitted by speakers positioned either near (NEAR) or far from the hand (FAR). The task was performed in a preliminary phase with the back of the hand laying

on the table, than it was repeated while subjects handled a generic tennis racket or their own racket. The time to react to the tactile stimulus was assessed in FAR and NEAR conditions for the two rackets. Preliminary results showed that the reaction times in the FAR condition were significantly higher than in the NEAR condition in presence of the generic racket, but this difference disappeared when subjects held their own racket. This result suggested that the peripersonal space varied when participants held the tool used to train themselves but not a generic tool, even though closely linked to sport activity. Therefore, one might propose that in expert tennis players a daily practice provides a stable embodiment of the specific tool they used during training.

Impaired interhemispheric processing in early Huntington's disease: putative role in cognitive dysfunction

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Changes in interhemispheric connectivity in Huntington's Disease (HD) have recently received growing attention, although little is known about their significance and temporal relation with clinical features or gray matter atrophy. Callosal disruption could contribute both to cognitive dysfunction and impairment of associative functions and likely occurs many years before clinical onset, especially within occipital and parietal areas, along a posterior-to-anterior direction. Moreover, little is known about the impairment of interhemispheric processing as assessed by electrophysiological methods. Among these techniques, Transcranial Magnetic Stimulation (TMS) provides a unique opportunity to evaluate functional relationships between neural targets and clinical phenotype. In HD and healthy volunteers we assessed ipsilateral Silent Period variables (onset latency, iSPOL, and duration, iSPD) and Transcallosal Conduction Time (TCT). Recordings were made from the Abductor Pollicis Brevis (APB) muscle. In patients, we correlated TMS data with cognitive (UHDRS-II), motor (UHDRS-I) and genetic (CAG-length, Disease Burden Index) scores using the non-parametric Spearmann's correlation coefficient. Compared with healthy subjects, HD patients showed a marked decrease of iSPD, paralleled by a significant lengthening of iSPOL and TCT ($p < 0.001$ for all comparisons). TMS changes significantly correlated with cognitive and motor performances, as

well as with the mutational load ($p < 0.01$ for all the comparisons). Interestingly, when recordings were made from the non-dominant hand, then by stimulating the ipsilateral dominant motor cortex, electrophysiological changes were less marked compared with those obtained from the dominant hand (right M1: iSPOL $p = 0.0007$, iSPD $p < 0.0001$, TCT $p = 0.0041$; left M1: $p = 0.012$, iSPD $p = 0.004$, TCT $p = 0.029$). Our data suggest that interhemispheric processing is impaired in early HD and significantly correlates both with cognitive and motor scores, as well as with mutational load. To our knowledge, this is the first study using a TMS protocol to unveil and quantify the functional disconnection between hemispheres in HD patients. Our results may also have implications for the impaired sensorimotor integration and motor control, as revealed in HD; finally, differences between dominant and non-dominant motor cortex also suggest that preceding cognitive involvement could contribute to motor dysfunction in early HD.

Cerebellum modulates defensive responses within the peripersonal space

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The cerebellum is involved in a wide number of integrative functions, ranging from working memory and associative learning to motor control; it also plays a role in the sensory-motor integration aimed at antinociceptive behaviour, as well as in salience-related affective and behavioral responses to nociceptive stimulation. Here, in healthy subjects we evaluated the role of cerebellum in defensive responses, as assessed with the so-called Hand Blink Reflex (HBR), by modulating cerebellar activity with transcranial Direct Current Stimulation (tDCS). HBR is mediated at brainstem level, undergoing tonic top-down modulation from higher order cortical areas responsible for encoding the location of somatosensory stimuli in external space coordinates. tDCS was applied using a pair of electrodes in two saline-soaked synthetic sponges with a surface area of 25 cm^2. For cathodal stimulation the cathode was centered on the median line 2 cm below the inion, with its lateral borders about 1 cm medially to the mastoid apophysis, and the anode over the right shoulder. For

anodal stimulation, the current flow was reversed. Direct current was applied for 20 minutes with an intensity of 1.5 mA. For the recording of HBR, electrical stimuli were delivered using a surface bipolar electrode placed on the median nerve at the wrist and EMG activity was recorded from the orbicularis oculi muscle, bilaterally, using pairs of surface electrodes with the active electrode over the mid-lower eyelid and the reference electrode a few centimeters laterally to the outer canthus. Depending on the hand position respective to the face, we explored four different conditions: "hand far", "hand near" (eyes open), "hand side", "hand near" (eyes closed). EMG signals from each participant were high-pass filtered (55 Hz), full-wave rectified, and averaged separately for the four conditions at the ipsilateral and contralateral recording sides. While anodal stimulation had no significant effect, cathodal one dramatically dampened the magnitude of the HBR, as measured by the Area Under the Curve (AUC), when the stimulated hand was inside the peripersonal space surrounding the face at eyes closed ($p < 0.0001$) or when it was placed laterally ($p = 0.004$). Concurrently, HBR latency increased in both conditions "hand near" (eyes closed) and "hand side" ($p = 0.002$ and 0.023, respectively). These results support a critical role of the cerebellum in the defensive responses within the peripersonal space, thus selectively modulating defensive behavior when the visual feedback is lacking.

Diffusion tensor imaging study of orbitofrontal cortex in post-traumatic anosmia

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The olfactory loss due to Traumatic Brain Injury (TBI) is a common clinical condition. The understanding of the cortical areas involved in ability to detect, discriminate and identify the odors is still limited. However, it has been shown that the Orbitofrontal Cortex (OFC) is involved in olfactory information processing such as discrimination and identification and in particular the right OFC has a dominant role in the central elaboration of odors. This study describes the case of a 40 year-old female patient who, after a car accident, reported a TBI with decreased of sense of smell. The olfactory function was evaluated by Magnetic Resonance Imaging (MRI) and psychometric test called Sniffin' Sticks Test (SST) at T0 (baseline) and T1 (after one year). The SST consists in separate sub-tests for olfactory threshold, discrimination and identification. The sum of these three sub-tests, called TDI score, allows a classification of olfactory function as normosmia (TDI = 48 - 31), hyposmia (TDI = 30 - 16), or anosmia (TDI ≤ 15). Diffusion Tensor Imaging (DTI), with fiber track-

ing, was used for 3-dimensional visualization of the central nervous system. DTI was performed in the axial plane with a single-shot, diffusion-weighted EPI sequence and T1-weighted to provide the anatomical reference. MRI examination confirmed the presence of a post-traumatic scarring localized in the right OFC. The TDI score was increased from T0 (TDI = 10) and T1 (TDI = 25). This occurs mainly for improvement the score in threshold sub-test, whereas the scores in discrimination and identification sub-tests remain below normative values. Moreover SST findings are confirmed by DTI. In fact, we observed, in the right OFC, an increase of tract numbers (T0: N = 57; T1: N = 121) and a mean decrease of fractional anisotropy (T0: 0.84 ± 0.17; T1: 0.42 ± 0.14). The obtained results confirmed our hypothesis that the patient's anosmia is due to a selective deficit in the odors recognition, rather than in the perception of them, giving an important pathogenetic role to the scarring in right orbitofrontal area. In the olfaction assessment, the combined approach including the psychophysical test SST and MRI examination with fiber tracked has a prominent role to clarify the degree, nature and the possible recovery of olfactory abilities. Moreover, DTI examination demonstrated that a fiber regeneration and cortical/subcortical reorganization could occur after 1 year the diagnosis of post-traumatic anosmia.

Short latency afferent inhibition during recognition memory task

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Short Latency Afferent Inhibition (SLAI) is a paired-pulse Transcranial Magnetic Stimulation (TMS) protocol that consists in the inhibition of the Motor Evoked Potentials (MEPs) by afferent sensory impulses. It was measured by applying an electric Conditioning Stimulus (CS) on the median nerve at wrist that precedes the Transcranial Magnetic Stimulation Test Stimulus (TS) applied over the contralateral primary motor cortex (M1) by 20-25 ms. SLAI is abolished by scopolamine, a potent muscarinic antagonist and it has therefore been suggested that the inhibitory effect of peripheral stimulation is mediated by cholinergic projections over M1. For this reason, SLAI is considered a putative marker of cholinergic activity. Central cholinergic system is critically involved in all known memory processes. Pharmacological data clearly indicate that both muscarinic and nicotinic acetylcholine receptors have a role in the memory processes, modulating performance of subjects in memory task. The present study investigated the effect of the ongoing memory processes (encoding, consolidation, retrieval) on the Interstimulus Interval (ISI) known for inhibition (20 ms) during the execution of two computerized recognition memory taskinvolving words or faces. SLAI protocol was recorded in 10 healthy

subjects during: pre-task; encoding; consolidation; retrieval and post-task phases. The TS was applied over left M1 400 ms following the word or face onset and it was preceded by CS applied over the contralateral median nerve at wrist. In the encoding phase, 30 stimuli were presented and subjects were instructed to judge whether the stimulus presented was "pleasant" or "unpleasant". In the recognition phase, subjects were asked to recognize the previously presented stimuli by a three alternative forced choice task, after 10 m from the end of the encoding phase. During pre-task, consolidation and post-task phases, SLAI was performed for 30 consecutive trials and with same timing of encoding and retrieval phases. Subjects responded vocally and the experimenter registered their response. We found an increase of SLAI for retrieval compared to pre-task phase, specificfor face task. This result suggests an involvement of central cholinergic system for memory processes according to pharmacological and neurophysiological data.

Brainstem reflexes can help to differentiate idiopathic from psychogenic cervical dystonia

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Cervical Idiopathic Dystonia (CID) is the most common kind of primary dystonia, but its pathogenesis remains still unclear. As in other movement disorders, the major challenge is to recognize the organic from the psychogenic phenotype. Our objective was to evaluate reliability of Blink Reflex Test (BRT) in detecting powerful differences in patients with diagnosis of CID or (clinically presumed) Psychogenic Dystonia (PD). Twelve subjects were enrolled (6 CID, 6 PD) and BRT was assessed in term of R1 and R2 latencies and habituation phenomenon (trains of 10 stimulus, 1 Hz of frequency, 200 ms of duration). Electrodes were placed over the orbicular inferior muscle (recording electrode) and lateral canthus (reference). CID patients showed both an enhanced latency of polysynaptic R2 responses and a lack of habituation compared with subjects diagnosed as PD (t-test, $p < 0.001$). Our results support the hypothesis of a dysfunction of brainstem reflex circuits on the basis of CID. As in Parkinson Disease, one could speculate that this phenomenon relies on changes in the inhibitory drive from basal ganglia output structures, via tecto-reticular projections, to the superior colliculus.

Role of acupuncture in pain control in Parkinson's disease: clinical and instrumental evidences in a single case

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Pain is a major aspect of non-motor symptoms of Parkinson's Disease (PD) and could evolve independently of the motor symptoms. Pain is also typically non-responsive to levo-dopa therapy and could hide both peripheral, musculoskeletal and neuropathic causes. It could depend on abnormal processing of nociceptive input in the Central Nervous System (CNS), as a consequence of a dysfunction of both dopaminergic and monoaminergic systems. Acupuncture exerts its analgesic effect in a not yet completely understood way, but many evidences exist about its effectiveness in PD patients. In this study, we describe the case of a woman with a 27-years history of PD, which was implanted with a pulse generator for Deep Brain Stimulation (DBS) 1 year ago, with beneficial effects on motor symptoms, but not on painful sensations. The aim of this study is to evaluate the effects of acupuncture as an add-on treatment to pharmacological approach. The patient received acupuncture therapy twice a week for 6 weeks in the following acupoints: 58BL, 40ST, 39GB, 4CV, 36ST, 6SP, 3LV, 4LI, 14GV, 3KI, 63BL, 5TB, 11LI. Before and after acupuncture treatment, we recorded CO2 Laser Evoked Potentials (LEPs) in order to show any changes in the neurophysiological responses to painful stimuli. A Nd:YAG laser was used (wavelength 1.04 m, pulse duration 2-20 ms, maximum energy 7J); signals were then amplified, band pass filtered (0.1-200 Hz, time analysis 1000 ms), storaged and analysed. The dorsum of the left hand and foot were stimulated by laser pulses (individual variability: 3.89-15.75 J/cm^2) with short duration (5 ms) and small diameter spots (5 mm); the inter-stimulus interval was varied randomly (10-15 s). The outcome parameters included Unified Parkinson's Disease Rating Scale (UPDRS), Visual Analogue Scale (VAS), Short Form Health Survey (SF-36), Neuropathic Pain Scale (SDN), Hospital Anxiety Depression Scale (HADS), Epworth Sleepiness Scale (ESS). Our results show both a subjective improvement of general wellness and a substantial enhancement in clinic scales scores. Analgesic effect is confirmed also by neurophysiological parameters, with increased latency and reduced amplitude of the LEPs, in both arms and feet. We speculated that acupuncture is effective in modulating nociceptive responses in PD. Particularly, acupuncture affects both psychophysiological and electrophysiological parameters since has an effect on both sensory and affective pain's components. These results confirm that acupuncture could be a useful therapeutic approach in the treatment of pain in PD. Future studies with a larger sample should be conducted in PD patients with a painful syndrome to confirm the analgesic effect of acupuncture in this kind of patients.

The role of premotor and parietal cortex during monitoring of involuntary movement: a combined TMS and tDCS study

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Recent studies, involving both brain-damaged patients affected by anosognosia for hemiplegia and non-invasive brain stimulation in normal subjects, show that the right Premotor Cortex (PMC) is involved in the motor monitoring of voluntary movements. In the present study, we asked whether the PMC is involved in the motor monitoring of involuntary movements, externally triggered. We take advantage from the transcranial Direct Current Stimulation (tDCS), in order to investigate if cortical excitability shifts in this area interferes with the motor monitoring of an involuntary hand twitch induced by a single pulse of Transcranial Magnetic Stimulation (sTMS) over the hand area of the primary motor cortex (M1). Two alternative hypotheses can be formulated: (1) Because of the absence of the voluntary component of the movement, the PMC is not involved in the motor monitoring processing; in this case, no difference should emerge in the performance of the subjects after the stimulation over PMC. (2) The PMC is involved in the motor monitoring processing also when motor intention is not implemented; in this case, a modulation of the subjects' motor monitoring capacities after tDCSover PMC should emerge. Ten neurologically healthy subjects participated in the study; they were all right-handed. The experimental design comprised three conditions: (a) cathodal tDCS over the right PMC; (b) cathodal tDCS over the right posterior parietal cortex (PPC); (c) sham tDCS over PMC or PPC. tDCS intensity was of 1.5 mA and was applied for 10 minutes. Intensity of sTMS has been determined according to the individual resting Motor Threshold (rMT). At the end of the tDCS, participants performed the motor monitoring task: while being blind folded, they had to detect and verbally report hand twitches induced by sTMS. The results showed that stimulation of the right PMC does not affect the monitoring of involuntary movements. Rather, it was the cathodal tDCS of the right PPC to affect motor monitoring abilities. In particular, after PPC stimulation, we found a significant increase of the false alarms rate (the subjects reported a muscle twitch, although no movement was triggered by the sTMS of M1), as compared to both PMC or sham tDCS. This finding is supports by previous evidence that intracranial stimulation of the parietal cortex during awake brain surgery generates a non-veridical feeling of movement.

The sensory attenuation effect comparing kind and intensity of stimulation

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The phenomenon known as sensory attenuation, namely the fact that self-generated stimuli are subjectively attenuated compared to the same stimuli generated by others, is described as an universal effect that arise with any kind of stimulation and independently from their intensity. If we consider sensory attenuation as a defensive mechanism that select stimuli generated by ourselves, decreasing their perceived force, by contrast stimuli coming from another agent are perceived as stronger, to be eventually ready for a reaction. In this methodological study, we proposed three kind of stimulations (sensory electrical, nociceptive electrical and vibrotactile stimulation), with three different levels of stimuli intensity. Our aim was to check which is the ones that generates more sensory attenuation comparing a condition of self-generated and self-directed action vs. other-generated motor acts. The setting was composed by an electrical stimulator with two types of electrodes, a classical type and a nociceptive one that stimulates only alpha peripheral fibers, and a vibrotactile stimulator. Electrodes and the vibrator were attached on subjects' right index finger: in some cases, subject had to push the button on the device to produce by himself the stimulation (condition self) and in other cases the experimenter generated the stimulation (condition other). We ran two experiments using a between subjects design (twenty-four healthy subjects, twelve each experiment) and the same setup, but with different intensity of stimuli. In the first data collection (Experiment 1) we fixed 3 stimuli at 1 = threshold*2.5 mA, 2 = threshold*2.5+1 mA, 3 = threshold*2.5+2 mA while the frequency was stable at 200 Hz and the electric potential at 300 V. Results showed that the difference between "self" minus "other" generated stimuli was higher in the sensory electrical stimulation, indicating a sensory suppression effect. More deeply, we found that both the electrical stimulations produced a tendency to reduce the perceived sensation increasing the intensity of stimulation. On the basis of these results, we ran a second experiment (Experiment 2), as before, but with increased intensity of stimulations (1 = threshold*2.5+2 mA, 2 = threshold*2.5+3 mA, 3 = threshold*2.5+4 mA). We found that while vibrotactile and nociceptive stimulations don't change their suppression effect, sensory electrical stimulation show a great sensory suppression effect, particularly in the stronger stimulus applied. These results indicate that sensory attenuation is modulated by the kind of stimulation and by its intensity, specifically the more the intensity of an electrical stimulus is strong the more you tend to feel as less intense a stimulus produced by someone else.

That's my movement! Embodiment of a fake hand induces sensory attenuation

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Normally, a preparation for action results in a conscious intention to act. In some circumstances, the retrospective intentions to act are present and can then mobilize the same brain areas as in a prospective intention to act. For instance, it has been demonstrated that the movements of an embodied life-size virtual avatar can modulate motor parameters of the participants voluntary actions as well as their sensation of agency. To test this hypothesis, we capitalized on the phenomenon known as sensory attenuation, namely the fact that self-generated stimuli are subjectively attenuated compared to the same stimuli generated by others. Employing the Rubber Hand Illusion paradigm (RHI), we predicted that a fake embodied hand, respect to a fake non-embodied hand, should induce sensory attenuation exactly as when the own hand deliver the stimulus. We used the vertical setting of the RHI using a fake left hand filling a glove with flour; under the fake and the real left index were placed two pins connected to an electrical stimulator that produced electrical stimuli on the right subjects' hand (stimuli were fixed at threshold*2+4 mV); subjects had to rate the perceived sensation on a 1-10 Likert scale. The study was composed of three parts. In a first part, we tested all subjects with the RHI procedure (measuring proprioceptive drift and questionnaire on ownership) to check the participants experienced of illusion. In the second part, subjects received stimulations from themselves (self), seeing another person with opened (other) and closed eyes (blind), to obtain a baseline measure of subjects' suppression tendency. In the third part, we divided our sample in two groups: half of them (Group A) experienced the synchronous stimulation (as in the RHI) for one minute on the left hand to embody the fake hand and, immediately after, the fake hand (passively moved by the experimenter) clicked the button, generating the electrical stimulation on the right hand; the other half of the group (Group B) did exactly the same but they received only the asynchronous stimulation. Results show that all 32 subjects are comparable in terms of RHI susceptibility (no differences were found between groups in drift and questionnaire, that both increased only after synchronous stimulation) and in suppression tendency (all subjects perceived stimulations performed by themselves as less intense). In the experimental condition, only the Group A showed a suppression effect and positive scores at questionnaire on ownership of movement, indicating the embodiment of the fake hand. These findings demonstrates that the embodiment of a fake hand is able to induce sensory attenuation on the own hand. Since sensory attenuation arises as a consequence of one's own intended actions, this data support the idea the observation of apparent self-action results in an activation of preparation for action circuits which then give rise to the sense of agency with respect to the specific act.

Is task-switching based on domain-general or domain-dependent processes? An event-related potential study

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Several studies have shown that when participants are confronted with a task-switching paradigm in which they must repeat the same task rule as that applied in the previous trial or switch to a different one, their responses are usually slower and less accurate on switch than on repeat trials, a phenomenon known as the "switch cost". The switch cost is reduced but not eliminated even when participants are provided in advance with an instructional cue indicating which task to perform. Such a finding suggests that the switch cost could be due to the extra time needed on switch trials to reconfigure the new relevant task-set. Previous Event-Related Potential (ERP) studies have associated task-set reconfiguration processes during the cue-target interval with a larger positive component for switch than for repeat trials that is distributed over posterior scalp regions. An open debate is whether task-set reconfiguration represents an obligatory step to accomplish task-switching operations. Even more importantly, no definite consensus has yet been reached about whether task-set reconfiguration for different task-switching types would be mediated by shared or distinct processes. The present study aimed at directly addressing these issues by combining ERPs with a behavioural paradigm that orthogonally manipulated task requirements (switch vs. repeat) and cognitive domains (spatial vs. verbal) in the same set of participants (N = 48). In separate blocks of trials, they either had to perform two spatial tasks (i.e., to classify visually presented words according to their roll or pitch orientation) or to perform two verbal tasks (i.e., to classify the words based on their female/male gender status or proper/common name status). Critically, in our experimental design cue and target were combined into the same stimulus, namely, the color of each word indicated the spatial or verbal task to be implemented on any given trial. In such a way, we investigated whether task-set reconfiguration might take place even when anticipatory preparation is not afforded by the simultaneous cue-target presentation. The behavioural results showed a significant switch cost for both spatial and verbal domains. The ERP data, which were analyzed through a mass univariate approach, showed no differences between the two domains in the modulation of switch and repeat ERPs. They also revealed that switch trials were associated with a larger positivity developing in the 265-310 ms time window over left parieto-occipital electrodes and with a subsequent slow-wave modulation (350-450 ms) occurring mostly over mid-left fronto-central electrodes, which was characterized by

a more negative ERP amplitude for the switch condition as compared to the repeat condition. Overall, our data show that task-set reconfiguration can occur even when the task-switching design lacks a cue-target interval and confirm the existence of a domain-general task-switching process.

The effect of auditory feedback in an auditory Posner attention task: delay effect in ERP

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A "delay" is defined as the division of a signal in separate components, one of which is delayed, and then reintroduced into the original signal. A "delay effect" occurs when a subject hears the sound of his/her own voice that is delayed by few milliseconds. This feedback induces difficulties in the articulation of language. We analyzed the effect son attention during training with natural and delayed auditory feedbacks. If the stimulus is naturally presented without delayed latency, subjects will have no difficulty in producing verbal language. If the stimulus is presented with a delayed acoustic feedback, subjects will present difficulties in articulating language, concentrating on what they are reading, or simply pronouncing their names and surnames. This highlights the momentary interruption of an automatic process. After 7-10 minutes of delayed feedback, the subjects present habituation to the delay effect. This parameter adjusts the time between the introduction of the original signal and the reintroduction of the delayed signal. The aim of this study was to investigate ERP correlation during an auditory Posner attention task after an auditory delay effect training. We recruited a total of 20 university students (mean age 28.6). Participants had to pronounce their personal information, read a lyric and sing. The training had duration of 5 minutes. The delay time used in the experiment was 200 ms for all subjects undergoing experimental effect and 0 for those submitted in the control group. After the training, an auditory Posner attention task was administered during an EEG recording: a mono-aural pure tone pip (1.000 Hz) presented unilaterally was used both as the cue (250 ms) and as the target. Cue-target asynchrony was either 100 or 600 ms. The spatial relationship between cue and target defined two conditions: valid target (the same location as thecue) and invalid target (opposite localization of the cue). A repeated-measures ANOVA was performed on the amplitude and latency of N2 and P3. Significant results were found on the N2 component in invalid target condition. The N2 component showed slower latencies in Fp1 ($F = 7.105$, $p = 0.015$) in the delayed effect group, while Fp2 ($F = 7.901$,

p = 0.011) F8 (F = 4.877, p = 0.039) and C3 (F = 4.128, p = 0.05) showed higher latency values in the delayed effect group. Identical significant results were found in behavioural reaction times. The results of this work indicate how auditory feedback systems affect motor and auditory attentional early processes, by altering not only the task itself in language performance (voice, prosody and spoken), but also modifying subject reaction times and ERP components.

Spike-timing dependent plasticity in the fronto-parietal network revealed by simultaneous TMS/EEG

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Many studies have demonstrated the role of the fronto-parietal network in many high-level cognitive functions, such as orientation of spatial attention and working memory. However, little is known about the mechanisms of connectivity between these two areas. The aim of our study was to investigate the plasticity dynamics between frontal and parietal areas at rest by means of a Paired Associative TMS protocol (PAS) delivered during hd-EEG.12 healthy volunteers underwent two experimental sessions during which they received a Fronto-Parietal (FP) or a Parieto-Frontal (PF) PAS (ISI 10 ms, 0.2 Hz, 100 pulses). PAS effects were tested over DLPFC, PPC and M1 (as a control area) with 80 neuronavigated TMS single-pulses applied before and after the PAS protocol. Throughout the stimulation EEG was recorded from 64 channels all over the scalp. PAS effects were investigated in the time, space, and time-frequency domain. FP-PAS produced a sustained increase of DLPFC reactivity whereas PF-PAS resulted in a sustained decrease as revealed by the local mean field power. Although discontinuously, the opposite effect was observed in PPC. No significant effects were observed after M1 stimulation (p > 0.05). Results in the oscillatory domain, assessed by TMS-related spectral perturbation, showed a spike-timing dependent modulation of β-activity in the DLPFC and α-activity in the PPC. Repetitive activation of the fronto-parietal network produced opposite STDP changes in cortical reactivity, specific for the two interconnected areas (DLPFC and PPC). Such changes were stronger for the DLPFC and followed anti-hebbian rules. Specifically, a strong and sustained LTP was observed when the postsynaptic activation (parietal) preceded the presynaptic (frontal) and *viceversa*. This effect can be explained by the spatial distance of the synaptic input. Interestingly, changes in DLPFC cortical reactivity were accompanied by opposite effects on the power of local oscillatory natural frequency (i.e. β-frequency). In conclusion, we demonstrated the presence of STDP in the fronto-parietal network showing a potential relevance of local changes in the natural frequency as a marker of STDP.

Disentangling deceiving from false beliefs: an ALE meta-analysis of fMRI studies

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Deception and false belief stand on opposite sides when it comes to how reality alteration is carried out: while telling a lie crucially depends on the voluntary act to deceive, false beliefs result from memory encoding/retrieval failures independently from one's own awareness. These behaviors are relevant both when considering the social nature of human cognition and when determining whether a subject is lying or does actually believe something that is disproved by reality. Here, by using Activation Likelihood Estimation (ALE) meta-analysis of functional Magnetic Resonance Imaging (fMRI) data, we investigated the neural correlates of deception and false beliefs. Specifically, we compared brain activity in 230 healthy participants enrolled in 12 lie-detection experiments and 173 subjects who participated in 10 non-autobiographical memory retrieval studies. The voxel-based ALE meta-analysis revealed a wide network of brain regions recruited during deception as compared to truth-telling (deception > truth; pFDR < .01; 100 mm^3): bilateral insula, pars opercularis of the right inferior frontal gyrus, right middle frontal gyrus, right anterior cingulate cortex, left inferior parietal lobule and the medial section of the left superior frontal gyrus. On the other hand, cortical areas engaged during erroneous memory recovery versus correct retrieval (false alarm > hit; pFDR < .01; 100 mm^3) were: pars orbitalis of the left inferior frontal gyrus, left precentral gyrus and right anterior cingulate cortex. Most importantly, when directly comparing brain responses elicited by deception and false memories (deception > false alarm; pFDR < .05), we found an increased activity in the pars opercularis of the Right Inferior Frontal Gyrus (R IFGop). No brain regions were revealed by the opposite contrast using the same statistical threshold (false alarm > deception; pFDR < .05). The direct comparison of deception- and false memories-related brain activity aimed at revealing the neural signature of *willful* reality alteration: in this context, R IFGop may be a fundamental node in the "deception network" as the basis of processes needing to be in place when *deliberately lying*, such as content fabrication and the "cost-benefit analysis" of the chosen strategy. Further studies are needed to evaluate the role of R IFGop during deceptive behaviors on autobiographical material and to define whether or not this brain region may be a "candidate" for lie detection.

Executing and imagining transitive and intransitive gestures: electrophysiological (RP) and optical imaging (fNIRS) evidences

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Action planning and execution processes have been explored by many neuroanatomical, electrophysiological and functional studies. It is known that a complex network of neural structures is responsible for voluntary action intentionalization and production, including the Supplementary Motor Area (SMA) and pre-Supplementary Motor Area (preSMA), the Premotor Cortex (PMC), the primary motor cortex (M1), the Anterior Cingulate Cortex (ACC), and subcortical structures. Again, electrophysiological research identified specific markers of action planning processes – namely the Readiness Potential (RP) and its subcomponents. Nonetheless, the interplay between neural structures, networks and processes for the transition from motor planning and preparation to proper movement initiation and guidance is still a matter of debate, as is the relationship between structures supporting those phases. The present study then aimed at exploring cortical correlates of motor planning and production and their relationship by taking advantage of an integrated electrophysiological-hemodynamic methodology which capitalized on electroencephalography (EEG) high time resolution and functional Near-Infrared Spectroscopy (fNIRS) high spatial resolution. We compared participants (N = 15) during planning and execution or imagination of complex hand gestures. Videos depicting target gestures were presented at the beginning of each experimental trial, half of them were transitive (i.e. they implied the use of an object – such as painting with a brush) and the other half were intransitive (i.e. they did not involved object-use while still being meaningful – such as waving to greet someone). The analysis of electrophysiological markers of the planning phase revealed that comparable RPs occurred before gesture execution and imagination, with an interesting "facilitation effect" (anticipated latency) for transitive gestures in particular for motor imagination. The analyses of fNIRS markers (oxygenated haemoglobin concentration) of the execution/imagination phases revealed that while the SMA was similarly activated during execution and imagination of transitive/intransitive gestures, the PMC was particularly involved in execution processes and the posterior parietal cortex was peculiarly involved in transitive gesture execution. Finally, integrated regression analyses showed that the RP component may be deemed as a predictive factor of subsequent hemodynamic brain activity during action production and that the relationship was different across sensorimotor regions depending on task and gesture type.

Long-term empowerment effect of executive functions by multisession neuromodulation in healthy aging: follow-up evidences

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Non-Invasive Brain Stimulation (NIBS) techniques proved to be valuable tools in supporting cognitive empowerment in case of both neurodegenerative diseases and functional impairments due to cerebrovascular events. However, little research systematically explored their potential contribution to containment and prevention of physiological cognitive decline in healthy aging. Further, the majority of those studies actually focused on the effect of single stimulation sessions with limited investigation of their long-term maintenance. The present report extends previous finding concerning short-term empowerment effects of an integrated multi-session neuromodulation protocol on executive functioning by showing intervention-related long-term effects in a sample of healthy elderly people. In order to explore perceived sustainability and short/long-term intervention outcomes, we divided 23 participants into a control and an experimental group and asked them to complete a standardized neuropsychological and electrophysiological (i.e. recording of event-related potentials during an executive attention task) assessment at the beginning of the study (T0), at the end of the intervention period (T1) and after further six months (T2). The integrated intervention protocol lasted eight weeks and included three anodal transcranial Direct Current Stimulation (tDCS) sessions (15 minutes, 1.5 mA, right prefrontal placement with contralateral supraorbital cephalic reference) per week with twice-weekly executive functions tasks. Mixed effects models accounting for subject-related and time-related confound highlighted relevant performance increases in the experimental group with respect to the control one at the end of the intervention. In particular, we observed higher scores at standardized tests tapping on executive functions (abstract reasoning, cognitive flexibility and verbal generation) and enhanced automatic attention responses. Such improvements were partially maintained even at the follow-up. To sum up, the multisession neuromodulation protocol proved to be able to induce empowerment of specific cognitive abilities even in healthy aging, with interesting long-term effects. Our findings support the notion that integrated neuromodulation protocols may offer valuable intervention opportunities for cognitive decline prevention.

Functional magnetic resonance imaging by using laser stimuli in Charcot-Marie-Tooth syndrome: a case study

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Charcot-Marie-Tooth (CMT) disease is a genetically heterogeneous group of disorders. Pain is a less common symptom complained by CMT patients. In this study we evaluated the cortical activations in a patient with congenital neuropathy to observe possible variations of pain matrix area. We described the case of a 39-year-old male patient affect by CMT syndrome compared with one sex age matched Healthy Subject (HS). The nociceptive system was evaluated by Laser Evoked Potentials (LEPs). Moreover, a 3.0 T Magnetic Resonance Imaging (MRI) and fMRI (functional Magnetic Resonance Imaging) by using laser stimuli were performed. Laser stimuli were applied at dorsum of feet and hands by using a Nd:YAP laser device. Stimulus intensity was set up at 2.0J, slightly shifting the stimulation point in order to avoid stimuli habituation and skin lesions. A high-field fMRI and muscular MR were performed. We constructed 10 blocks of rest and tasks respectively, each consisting of 5 volumes. Statistical analysis was performed by using the GLM. All analyzes were corrected by Bonferroni ($p < 0.05$). The LEP examination showed an increase of latency and an amplitude reduction respect to HS. The stimulation of upper and lower limbs produced more significantly activation in insula ($p < 0.05$ correct) and anterior cingulate cortex ($p < 0.05$ correct) respect to HS. Moreover, the muscular MRI highlighted atrophy of the posterior compartment of lower limbs. The muscular echography showed an iper-echogenicity and diffuse and inhomogeneous alterations of the lower limbs muscles. The insula is a region known to play a role in the representation of bodily states, and the region comprising the posterior insula and anterior cingulate constitutes a functional area containing networks devoted to pain processing. Several activations could be due to a major sensibility of nociceptive system in CMT patient. In our case, the amplitude N2/P2 amplitude to foot stimulation was reduce than that in HS, suggesting an Aδ-fiber impairment in this neuropathy. In our patient, a reduced N2/P2 LEP amplitude suggests an Aδ-fiber decrease, mainly involving the longer axons of the lower limbs. Moreover, our results showed that the Aδ-axonal loss represents a risk factor for developing neuropathic pain. On the other hand, it is known that neuropathic pain can be sustained by a peripheral sensitization with mechanism by which nervous fibers develop spontaneous activity, lowered activation threshold, ectopic neural firing along the nerve. These further mechanisms cannot be excluded in our patient.

The premotor origin of the N2 component in Go/No-Go tasks

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In discriminative response tasks, researchers have largely debated about the meaning of the N2 component (which peaks approximately 250-300 ms after the stimulus onset) that is typically reported as larger and more anterior for no-go than go stimuli (typically referred to as the "go/no-go N2 effect"). There are two main accounts explaining the N2. The *inhibitory theory* states that the no-go N2 enhancement reflects the response inhibition by frontal areas following the no-go stimuli. Other studies did not confirm this hypothesis, and alternatively explain the N2 in terms of *conflict-monitoring*, i.e. the N2 would reflect the detection of response conflict that occurs when two or more response tendencies are simultaneously present, irrespective from being response- or inhibition-oriented. However, recent studies of the present group indicate a third hypothesis. Studying ERP activity associated to False Alarms (FA, erroneous responses to no-go stimuli), no N2 differences were found between the failed (FA) and correct (no-go) inhibition. Furthermore, it has been shown that the N2 for FA was larger than hits, and this result cannot be explained by literature about the go/no-go N2 effect. Combining ERP and fMRI measures, another study showed that, despite the presence of the typical "go/no-go N2 effect" with ERPs, the fMRI go/no-go contrast did not indicate any higher activity of cortical areas in case of no-go trials. This is against the view that the N2 component represents response inhibition or conflict monitoring following a no-go stimulus. Rather, N2 could be the expression of the premotor activity in the supplementary and cingulated motor areas that give origin to the premotor Bereitschaftspotential (BP) component. In particular, the N2 component might represent the peak of the negative activity of these brain regions. The ERP-fMRI data might also explain the aforementioned "go/no-go N2 effect". Probably, the ERP N2 component is smaller and more posterior for go than no-go trials because it is covered by the prefrontal Positivity (pP, peaking at about 300 ms after the stimulus onset, associated to stimulus-response mapping and localized in the anterior Insula), which is typically larger in go trials. In contrast, because of the smaller pP in no-go trials, a larger N2 component might emerge on the frontal areas. This hypothesis is confirmed by the aforementioned studies on FAs, where modulation of the pP was coherent to those of the N2 (FA and go trials had a different pP). Overall, the N2 enhancement in no-go trials might be (at least with equi-probable go/no-go trials), could be explained as an epiphenomenon due to a reduced masking of the late negative BP activity by the positive prefrontal activity with respect to go trials.

Highly hypnotizable subjects do not exhibit any peripersonal space

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Hypnotizability is a cognitive trait associated with physiological correlates observable in the ordinary state of consciousness and in the absence of suggestions. Subjects with high (*highs*) and low (*lows*) scores of hypnotic susceptibility exhibit differences in the sensorymotor integration. The Peripersonal Space (PPS) is a portion of space near to the body and corresponds to the space in which the subject can reach and use objects; its largeness is influenced by cognitive and emotional factors and is estimated through the line bisection test. Hypnotizability and the activity of the Behavioural Inhibition/Activation System (BIS/BAS) – which represent the individual sensitivity to frustration and tendency to look for reward, respectively – interact in a few cognitive tasks. The aim of the study was to evaluate the PPS largeness as a function of hypnotisability and of the BIS/BAS activity in right-handed subjects. Twenty-two *highs* (score > 8/12 according to the Stanford Hypnotic Susceptibility Scale, form A) and 21 *lows* (scores < 4/12), who had completed the BIS/BAS questionnaire performed 3 consecutive series of line bisection tasks on a computer screen which was automatically displaced and pseudorandomly stopped at 30 cm, 60 cm and 90 cm (3 trials for each distance) from the subjects, at eye level. The bisection error (performed minus real bisection) and time were measured. The main result was that the *highs*' bisection error was displaced toward the right side at every distance (in contrast to what occurs in the general population), whereas the *lows*' error was displaced toward the left side at 30 cm and toward the right side at 60 and 90 cm of distance (as occurs in the general population). Errors absolute values were significantly larger and bisection times were significantly longer in *highs*. The PPS largeness was modulated by BAS, whose variability accounted for the observed hypnotizability × distance interaction. Findings on the direction of the bisection error indicate that *highs* may experience all space distances as extrapersonal. Thus, theoretically they could be less vulnerable to social anxiety and related specific phobias with respect to lows and to the general population.

Interhemispheric symmetry modification related to functional recovery and motor learning in subacute post stroke patients

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Understanding the mechanisms of brain plasticity occurring after stroke is the main focus of modern neurorehabilitation that is now moving towards a "top-down approach". Cortical activity recording by means of Quantitative Electroencephalography (QEEG) can provide a numeric index sensitive to interhemispheric symmetry, the Brain Symmetry Index (BSI), that provides a generalised measure of left-right EEG power (a)symmetry, by quantifying the difference in mean spectral power per hemisphere across 1-25 Hz. The aim of this study is to investigate cortical interhemispheric symmetry modification involved in functional recovery and motor learning process after stroke. Nine subacute stroke patients (M/F: 5/4; mean age ± SD: 70.33 ± 10.7 yrs) with a cortico-subcortical lesion and a mild to moderate upper limb paresis were recruited and assessed after 45 days and after 3 months from acute event with 64-channel QEEG at rest and functional assessment (Fugl-Meyer Motor Assessment, FMMA). Two of them performed ten sessions of upper limb robotic-aided rehabilitation with a planar mobile robotic device (MOTORE, Humanware). The treatment consisted of task-oriented exercises of reaching and trajectory tracking combined with an interface that reproduces activities of daily living. The protocol was structured with a gradual increase of the intensity of trials and cognitive involvement of the patient. During every session, robotic parameters as execution time, accuracy and smoothness of movement were evaluated, as indices of motor learning. Before and at the end of the treatment patients were assessed with QEEG at rest and FMMA. The longitudinal study shows a mean trend of decrease of BSI in all frequency bands in all subjects in frontal and central areas. Patients with worse motor recovery assessed with FMMA show a significant BSI increase in Delta and Beta band in frontal and central areas. Patients with better recovery show lower BSI in the same areas and band frequencies compared with the other group and no significant changes at T2. The two patients who received robotic rehabilitation show a decrease of execution time and an increase of accuracy and smoothness of movement trajectories at the end of the treatment, highlighting a progressive retention of acquired abilities. FMMA doesn't show a significant improvement. In both patients BSI remains basically unmodified, except for an increases in frontal area only in Delta band. Our results provide evidence that brain asymmetry impairs

functional recovery in subacute stroke patients, with greater involvement of delta and beta bands in central and frontal areas; on the other hand, a good recovery is accompanied by a symmetric pattern in the same bands and areas.

Dissociable motor mapping of deceptive intentions and kinematics alterations during action observation

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Understanding other's intentions, by observing their movements, is crucial in social interactions. Previous work showed that action simulation plays a key role in detecting others' deceptive intent. Indeed, during action deception discrimination tasks, seeing an actor deceiving about the weight of an object facilitates the observers' motor activity more than seeing him acting truthfully. This facilitation for deceptive actions has been held to suggest that motor resonance is sensitive to action intentions. However, an alternative explanation is that the motor system facilitation mirrors the alteration of movement kinematics to attain deceptive vs. truthful actions. Here, we directly tested these two alternative hypotheses by using single-pulse Transcranial Magnetic Stimulation (TMS) to measure Corticospinal Excitability (CSE) from hand and forearm muscles during a weight discrimination task. Participants watched videos of an actor lifting a cube and judged whether the cube was heavy or light. The videos were taken in three conditions in which the actor was asked to lift the cube after receiving truthful information on the object weight and being asked to provide either (1) truthful (true condition) or (2) deceptive (deceptive condition) cues to the observers as well as (3) after receiving fooling information and being asked to provide truthful cues to the observer (deceived condition). This way, we independently manipulated actor's action intention and kinematics alterations. Results showed that, in keeping with previous studies, CSE increased during the observation of deceptive actions; however, a decrease of CSE was obtained in the deceived vs. the true and deceptive conditions. Importantly, while deceptive actions enhanced CSE for both muscles, perceiving kinematic alterations affected CSE in a body part specific manner. This suggests that deceptive intention is actually coded by the observer's motor system and different hierarchical levels of action representation may modulate its activity via dissociable processes.

Inhibitory control and decisional process in "new addictions": the role of reward mechanism and the effect of inter-hemispheric lateralization in a gambling task

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The term "new addictions" refers to all those phenomena that lead to behavioral dependencies, such as Pathological Gambling (PG) or the Internet Addiction Disorder (IAD). Recent data suggested that PG and IAD are associated to executive dysfunction, and hypersensitivity to immediate rewards, which are similar to those in substance abuse disorders. However, it is still not clear how the psychophysiological mechanisms underlying dysfunctional decision-making processes could affect the development of addictive behaviors in vulnerable individuals. The aim of this study was to investigate the cortical oscillations activity in healthy subjects in relation to the depressive mood, the motivational dimension and the vulnerability to Internet Addiction during a decisional risky task. To answer this question, 21 healthy subjects (aged M = 24.45, SD = 2.6) were required to perform the Iowa Gambling Task (IGT) and the Go/No-Go task (GNGt). The IGT simulates the real life decisions making; the GNGt was constructed using four different categories of background screen (neutral, control, online gambling and videogames) to elicit a gambling-like condition, while their cortical activity was registered by EEG. Then, they were given self-report questionnaires to investigate the level of mood state using the Beck Depression Inventory-II (BDI II); the dispositional sensitivity of the Behavioral Inhibition System (BIS) and the activation of the Behavioral Approach System (BAS) (BIS/BAS scale); the State-Trait Anxiety Inventory (STAI-Y); and the Internet Addiction Test (IAT). It was hypothesized that higher depressive and anxiety levels and lower inhibitory abilities to control more automatic processes could significantly correlate with Internet abuse. Moreover, the differences in the oscillation activity over the left or right hemisphere in relation to winning or losing conditions and to inhibition of control could characterise a typical profile of vulnerability in Internet Addiction. Results revealed a positive correlation between the BDI-II and IAT; the BDI-II and the STAI-Y. Thus, a depressive mood seemed to accompany people with internet abuse. The BAS-Reward scale seems to be predictive of a reduction in response times during the GNGt, when the task was played with a screen simulating an "online gambling". Subjects who received high scores on the BDI-II also had a worse performance in GNGt, and then a difficulty of inhibition of control. From the analysis of the power band it has emerged an increase of delta, theta and alpha, in the right hemisphere while choosing disadvantageous decks during IGT, and while playing

the GNGt with a "gambling" screen. This result can be ascribed to an increased of left PFC activity linked to the choice of more risky and "gambling" condition which may be considered as a biomarker of dysfunctional behavior in people at risk IAD.

Psychophysiological mechanisms in Parkinson disease with Impulse Control Disorder (ICD) during a gambling task (IGT): a fNIRS-EEG study

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Parkinson's Disease (PD) is a neurodegenerative disorder characterized by a progressive depletion of dopamine systems which leads to clinically motor symptoms such as bradykinesia, rigidity and rest tremor. Moreover, cognitive and behavioral disturbances could affect some type of PD patients with cognitive and emotional affective symptoms as anxiety and depression. Recent studies have shown that the dopaminergic therapy can induce changing in executive functioning and lead to Impulse Control Disorders (ICDs) such as pathological gambling, hypersexuality, compulsive shopping and compulsive eating. There are some risk factors and potential mechanisms for the development of ICD including personality traits, potential genetic influences and parkinson's disease-related cognitive deficits. The purpose of this study was to explore the cortical activity using two different measures such as hemodynamic response (fNIRS) and cortical oscillations (EEG) while patients performed a gambling task (IGT) which is a typical decisional risky task that includes uncertainty and reward conditions. 45 PD patients divided into 3 groups were recruited: the first composed by 15 PD patients with Pathological Gambling (PG), the second by 15 PD patients in remission of PG, and the last by 15 PD patients without ICDs. All the participants were administered a neuropsychological battery to test their cognitive state and some self-report questionnaires were used to evaluate the depression and anxiety state (BDI-II, STAI-Y), the impulsivity (BIS) and the motivational style (BIS/BAS scale). Then they were instructed to the IGT while the cortical activity was co-recorded by fNIRS and EEG, focusing on Orbitofrontal (OFC) and Dorsolateral Prefrontal (DLPFC) areas. After the task execution a metacognitive questionnaire was given to test the general self- knowledge of the cognitive strategy adopted during the IGT. Neuropsychological data showed global normal cognitive functions for all the groups, but a significant impairment in hemodynamic and EEG activity in response to more risky conditions mainly for PG, within the PFC. Moreover, this brain dysfunctional activity was related to poorer metacognition and IGT performance.

Neural correlates of action observation treatment in chronic aphasic patients

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Recent studies have shown that the systematic and repetitive observation of actions belonging to the experiential human motor repertoire without verbal facilitation enhances the recovery of verbs in non fluent aphasia. However, it is still an open question whether this approach extends its efficacy also on discourse productivity by improving the retrieval of other linguistic units (i.e. nouns, sentences, content words). Moreover, nothing is known regarding the neural substrates which support the language recovery process due to action observation treatment. In the present study, ten non fluent aphasics were presented with two videoclips (real everyday life context vs. familiar pantomimed context), each video for six consecutive weeks (Monday to Friday, weekend off). During the treatment, they were asked to observe each video and to describe it without any verbal facilitation from the therapist. In all patients, language measures were collected before and at the end of treatment. Before and after each treatment condition (real vs. pantomimed context), each subject underwent a resting state fMRI. After the treatment, significant changes in functional connectivity were found in right sensory-motor networks which were accompanied by a significant improvement for the different linguistic units in the real context condition. On the contrary, the language recovery obtained in the pantomimed context did not match any functional modification. The evidence for a recruitment of the sensory-motor cortices during the observation of actions embedded in real contexts suggests to potentially enhance language recovery in aphasia through a simulation process related to the sensory-motor properties of actions.

Pain expectancy induces freezing effects as in actual pain: evidence from corticospinal modulation during classical conditioning paradigm

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In several studies, it has been shown that pain expectancy shares common neural pathway with actual pain. In this study, by using a classical conditioning paradigm, we aimed to investigate whether the expectancy for aversive stimuli could affect the motor cortex excitability. We took advantage from the freezing effect known to accompany the actual pain; i.e., the inhibitory modulation of the motor pathway to the muscle adjacent to the painful area. Twenty five healthy volunteers (19-29 years, mean ± SD: 22.6 ± 2.43; 10 females) were undergonesingle-pulse TMS over the primary left motor cortex, while Motor Evoked Potentials (MEPs) were recorded from the Abductor Pollicis Brevis (APB) and the Abducotor Digiti Minimi (ADM) muscle of the right hand. We employed a classical conditioning paradigm in which visual and auditory stimuli (i.e. coloured squares and sounds) were conditioned by pairing aversive stimuli (i.e. electric shocks delivered to the right digit V, Unconditioned Stimuli – US), giving rise to three conditions, depending on the presented stimuli: conditioned stimuli paired with US (CS+); conditioned stimuli not paired with US (CS-); neutral stimuli (N). If the pain expectancy is able to induce changes in the corticospinal excitability, we predicted that a significant decrease in the MEPs amplitude (i.e., freezing effect), with respect to the baseline N condition, should be present not only in CS+ condition (when the actual pain was present) but also in CS- condition (when only the pain expectancy was present). MEPs amplitude in each experimental condition, expressed as percentage of the baseline, were analysed by means of a 2 × 3 repeated measure ANOVA with "muscle" (two levels: "APB"; "ADM") and "condition" (three levels: "N", "CS+" and "CS-") as within subject factors. The ANOVA results showed a main effect of both "muscle" ($F_{1, 20} = 36.7$; $p < 0.00001$), indicating greater values for ADM then for APB, and "condition" ($F_{1, 20} = 10.41$; $p = 0.0002$), indicating that the MEPs amplitude in both CS+ and CS- was significantly lower than in N condition (freezing effect). Moreover, the interaction between this two factors was significant ($F_{1, 20} = 4.73$; $p = 0.014$). This indicates that the freezing effect in CS+ and CS- with respect to N condition, although present in both muscles, was greater in APB. Our findings, in line with the notion that the human brain has a strong predictive nature, suggest that, in order for the corticolspinal modulation to occur, actual pain is not necessary; rather the pain expectancy can be sufficient.

The multidisciplinary team in the total patient care for adolescent patients with chronic pain: analgesic non-pharmacological treatments and psychodiagnostic treatments

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Over the past two decades medical practice and research have been interested in the problem of pain and in the treatment on the basis of specific pain characteristics. Studies showed that pain is a complex phenomenon, which does include physiological, cognitive, emotional and behavioural abilities: therefore it should require a complex therapeutic approach, which has to be holistic, global and personalized, especially during the "developmental age". The following paper provides observations drawn from some cases of adolescent patients (12 up to 18 year-old) with chronic pain which has a negative impact on many aspects of patients' daily life such as physical activities, school success, social and family relationships. A multidisciplinary team of doctors working together with psychologists follows the patients. The approach is global: it follows the patients from a number of perspectives, such as physiological, emotional, cognitive, relational, behavioural points of view. Moreover, the approach is also integrated: it takes care of children, but also of their parents. Patients are treated by an anaesthetist with non-pharmacological analgesic therapies (including "auricolostimolazione" and acupuncture), undergoing psycho-diagnostic treatments, which explore the following areas and/or features: cognitive abilities, coping skills, alexithymia, clinical pathologies, levels of attention, social skills and emotional or behavioural problems. Test including: YSR 11-18 (Youth Self-Report), SAFA, WISC-IV. Then two psychotherapists, one for the child and one for his/her parents, treat patients. The intensity of perceived pain is measured in all medical treatments with VAS (Visual Analogue Scale). The goal of the teamwork is on the one hand that of making the evaluation and the control of pain a part of the treatment, on the other hand that of monitoring qualitatively and quantitatively the pain itself. Another aim is that of monitoring all the parameters that can positively or negatively influence the treatment's effects, modifying them according to the needs and/or problems that may occur. The psychological assessment shows more frequently: anxiety, alexithymia, depression, distress, learning disabilities. After 5 both medical and psychodiagnostic treatments, the intensity of perceived pain decreases. An integrated medical and psychological assessment does allow doctors to (1) stimulate and promote a responsive attitude of children, (2) improve the "compliance" to the treatments, (3) be "closer" to the children both physically and psychologically, involving them and their parents in the procedure.

Caudate resting state activity predicts earning in subsequent Balloon Analogue Risk Task

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Behavioral tasks assessing impulsivity, as the Balloon Analogue Risk Task (BART) share the idea that impulsivity prevents the switching from a less efficient to a more efficient strategy. In these tests, the ability to change strategy is assessed as a function of the monetary gain. We designed an fMRI study to assess if gains at BART correlated with the Hurst Exponent (HE) measured during RS acquired before the task. HE measures the complexity of time series in terms of its predictability. Higher HE describes a more rigid brain activity, less influenced by external inputs. Thirty-six healthy, drug-free volunteers (16 female, mean age ± SD: 25 ± 5 yrs) were recruited. A RS Echo Planar sequence (300 time points, 27 3.5-mm-thick axial slices – 1-mm gap – TR/TE = 1640/40 ms, FA 90°, FOV= 24 cm, res. = 94 × 94) was obtained on a 3T SiemensMRI Scanner. High-resolution anatomical images also were acquired. After the acquisition, subjects played a modified version of the BART inside the scanner. In the BART, a balloon is displayed on the MRI screen. The balloon can be inflated by pressing a left hand held button. For each button press, the balloon inflates and the subject accumulates money. Alternatively, subject may choose to bank the gain at any time, by pressing a right hand held button. If the balloon pops, the gain is lost. Thus, each inflation increases gains but also the risk of popping. Three blocks of ten balloons each were presented. Each inflation corresponded to a gain of 10 cents of Romanian Leu (ROL). Balloons had different maximum number of inflations before popping which were randomized in each block. After each inflation, the value reached by the balloon was displayed on the screen. The total gainwas updated after each balloon. At the end of the task, subjects received the earned cash. After volume registration and movement de-trending, HE was calculated with the discrete second-order derivative approach implemented in the Matlab *wfbmesti* function. Forgroup analysis, after Talairach transformation, we performed a whole brain linear regression where total gain was used to predict HE. Clusters with a $p < 0.02$ and a volume > 450 µl (corresponding to a 0.05 FWE) were considered significant. HE in the bilateral caudate nuclei inversely correlated with gains. The present findings showed that proneness to impulsivity is predicted by caudate nuclei RS activity. Specifically, the lower HE, the lower is the impulsivity. Reflecting a less rigid brain activity, low predictability may represent a neural cor-

relate of the ability to change strategy and modulate reward seeking according to the changing environmental conditions. Our results also have wider implicationsas they show that it was possible to predict the behavioral performance of the individuals.

Parietal cortex involvement in visual perceptual learning: a rTMS investigation

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Practice-induced visual perceptual learning is thought to reflect the plasticity of sensory brain regions. The hypothesis that changes in early visual areas may depend on top-down modulation from higher level brain regions by attentional mechanisms is still debated. We used a causal approach by repetitive Transcranial Magnetic Stimulation (rTMS) to evaluate the role of primary visual cortex (V1) and Posterior Parietal Cortex (PPC) in visual perceptual learning. Twelve healthy volunteers performed a forced-choice orientation discrimination task of gabor patches (consisting of 500 trials in five blocks) without any intervention or immediately after a conditioning inhibitory 1 Hz rTMS protocol delivered over the V1, the right PPC, and the vertex (control area), in four different days. Conditioning inhibition by 1 Hz rTMS over the V1 produced an overall worsening of the performance accuracy but no effect in the learning rate, as measured by the slope of the learning curve. The learning rate was lower after right PPC inhibition compared to the other conditions when evaluated during the first two blocks (200 trials) where occurred most of the learning. These preliminary findings suggest that higher level brain regions may be involved in the mechanisms underlying perceptual learning.

Cholinergic modulation of neural stimulus representation in early visual cortex

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Pharmacological manipulation of cholinergic activity alters behavioral performance during shifting selective attention tasks, preferentially on maintenance with no effect on the attention shift *per se*. Cholinergic modulation has direct effects on stimulus representation, and these effects may account for changes in behavioral performance. Here we used fMRI to assess the effects of cholinergic manipulation on neural representation of stimuli during a shifting selective attention task. Specifically, in early visual processing regions, representational geometries were used to map the distances among multivoxel response patterns of the attended stimuli. We hypothesized that cholinergic enhancement and inhibition would differentially affect the task components. Two groups of 9 ("enhancement" group – ENH) and 11 ("inhibition" group – INH) healthy adults participated in two distinct randomized, double-blind, placebo-controlled fMRI (3T) studies. In separate sessions, subjects received an i.v. infusion either of placebo (PLA) or drug (DRUG, i.e., physostigmine – PHY – in the ENH or scopolamine – SCOP – in the INH). The task comprised two superimposed images of Faces (F) and Houses (H) that were presented side by side. Subjects performed a matching task as they attended to either the F or H stimuli, and were cued periodically to shift attention. To assess the effect of drug on the maintenance of the attention, we mapped the hemodynamic response patterns of the attended stimuli in early visual cortex using the first trial following a shift in attention as reference frame (thus responses to last trials were plotted based on the first trial as the reference axis). Similarly, to assess the effect of drug on the process of shifting attention, we mapped the attended stimuli using the last trial as reference frame. Representational measures within these reference frames were derived. Repeated measures ANOVAs were performed to assess group (INH and ENH), session (PLA and DRUG), stimulus (F and H), and trial succession effects. As results, PHY increased similarity and reduced variability of stimulus representation relative to PLA, while SCOP did the opposite ($p < 0.05$). Moreover, PHY enhanced the stimulus representation by increasing its specificity (e.g., faces trials became more face-like) relative to PLA, while SCOP obtained opposite effects ($p < 0.05$). Finally, no trial succession effects were found, indicating that cholinergic modulation did not influence shifting of attention *per se*. These results demonstrate that enhancing cholinergic activity increases the similarity among representational patterns of the attended stimuli in visual processing regions, while impairing cholinergic activity led

to opposite results. Moreover, the cholinergic modulation directly affects the neural representation of the visual percept of task-relevant stimuli or attended features in a manner consistent with previously reported behavioral effects.

Advanced Distributed Learning and ERP: interaction in augmented reality, haptic manipulation with 3D models and learning styles

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The Advanced Distributed Learning (ADL) is a learning process mediated by new technologies. The ADL also makes use of Augmented Reality, which takes place through processes of virtual manipulation. The experimental research on Augmented Reality markers and 3D objects focuses on the possibilities of interaction and manipulation of virtual forms in reality, that allows us to touch and interact with objects that do not exist but that are observable through a screen. Literature shows that there are different modules within the occipitotemporal cortex that receive both visual and somatosensory inputs and it explains how these can be integrated in the learning process. These cortical modules can be active in the evaluation of the various aspects of surface properties of objects, such as the 3D shape, as well as in visual and tactile movements. The purpose of this work is to analyze ERP components (P1, N2, P3) variations, during two different kinds of learning training (T): the same objects are manipulated either in Augmented Reality or during the condition of real haptic manipulation and the variations due to different learning styles are investigated. 12 university students were recruited for the study (mean age 23.11). The subjects were evaluated through a 4 scales style learning test: Visual Verbal (VV), Visual non Verbal (VnV), Kinesthetic (K), Analytical (A). The subjects performed a training lasting 5 minutes consisting of haptic manipulation of 3D models, obtained through modeling a 3D Blender 2.74 and manipulation in Augmented Reality, presented through Dune® Aurasma models. After each training the subjects had to perform a recognition task of the same stimuli (presented in 2D), during an EEG recording. A General Linear Model was computed to investigate research hypothesis. Statistical Analysis reveals significance values in ERP components analyzed. N1 showed significant values in Analytic Learning (p = 0.007), Training (p = 0.00) and interaction between A*TL (p = 0.014). N2 showed significant value in Visual non Verbal Learning style (p = 0.00), Training (p = 0.01) and interaction VnV*T (p = 0.00). P3 showed significant value in Visual Verbal Learning style (p = 0.01). The subjects with high scores in Analytic Learning style show higher amplitude in the Pz channel, in P1

component. The subjects with high scores of Visual Non Verbal Learning style show higher amplitude in the Centrals, Occipitals and Parietals Channels, in N2 component. The subjects with Visual Verbal Learning present higher amplitude in Frontals, Centrals, Parietals, and Occipitals Channels, in P3 component. We can conclude that learning styles are involved in perceptual levels during recognition tasks and according to the prominent style, processing involves different ERP components and different brain areas. The learning style affects more these variations when the mode of training is through Augmented Reality, where the visuomotor process is prevalent.

Sensory stimulation during slow wave sleep always primary activates sensory areas: a high-density EEG study

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During Non-Rapid Eye Movement (NREM) sleep, is the human cerebral cortex really insensitive to external stimuli or are they otherwise processed? We have recently shown that the bistable cortical response evoked by peripheral sensory stimuli (N550 and P900 of K-Complex) is induced in fronto-central cortical areas by an early positive wave (P200), which originates in primary sensory areas and then travels across the cortex in a posterior-anterior direction. The purpose of this work is to characterize the spectral activities of the P200 and to compare them with those of the P900 and of the pre-stimulus baseline. For each evoked KC, we have performed spectral analysis by using FFT on 300ms time-windows, one before the administration of the sensory stimulus, one centered on the peak of the P200, and one on the P900. The first window characterizes the baseline of EEG activity. We have found that: (1) the P200 is a real excitation that is characterized by a significant increase of beta/gamma activity (30-45 Hz) compared to both baseline and P900; (2) the P900 is mainly characterized by a significant increase of sigma activity (12-16 Hz) with respect to both baseline and P200. In conclusion, our results show that sensory stimulation during NREM sleep induces excitatory bumps (P200), similar to activities sustain-

ing perceptive and/or integrative functions during wakefulness. The P900 is a cortical late response, induced by thalamic spindling. We hypothesized that P200 is a pure sensory excitatory wave mainly due to glutammatergic thalamo-cortical volleys starting from core thalamic nuclei. Probably, the role of wake-like activities of P200 is to open activity-dependent K+ channels, in order to induce the downstate (N550) and subsequent upstate (P900) that characterize the bistable response of the cerebral cortex during NREM sleep. On the other hand, P900 represents the interplay between a re-entry from matrix thalamic cells and cortical circuits, and yields the reported high levels of synaptic and firing activity.

Neuroesthetics: the role of reward mechanisms and preferences during Leonardo's museum exploration

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The present research aimed at detecting the visitors' emotive engagement and neuroesthetics experience during museum spatial exploration. The main purpose is to compare visitors' behavior within two different museum spaces: the "Leonardo room" is characterized by linear map and ancient and historic artifacts; differently, the "Spatial room" represents the modern museum, strongly interactive, with videos, games and multimedia artifacts. Also, we have compared the visitors' emotive responses to artifacts evaluated as more positive and negative between the two spatial areas. Implicit (brain oscillations and hemispheric lateralization effect) and explicit (visitor preference behavior) measures were considered in order to define the cortical network related to the reward mechanisms that were supposed to be frontally left-lateralized. Indeed, brain oscillations (delta, theta, alpha, beta) and lateralization effect (Log-transformed-Asymmetry, LTA) were monitored within the prefrontal area when 18 visitors (7 women and 11 men) participated to the study: they were asked to freely explore for 10 minutes each area and to express their preference on them. Mainly frontal alpha band power revealed a significant decrease (cortical activity) in all visitors during the "Leonardo room" exploration evaluated as more interesting for historic link to Leonardo da Vinci's works, compared to "Spatial room". In addition, it was observed in general a more emotive engagement for men; in fact, a left DLPFC decrease of alpha activity was observed in men compared to women in response to artifacts considered as more positive, involving and interesting. It is supposed to be related to the topics represented in the museum (e.g. artifacts: models of military engineering, spacesuits, rockets). Left DLPFC was responsive to higher rewarding condition, predicting the preferred artifacts. Therefore, a strong relationship was revealed between explicit and implicit measures based on reward mechanisms.

The "alphabet" of human hand movements: a kinematic-EMG-fMRI study on the neural correlates of postural synergies

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The human hand offers a vast movement range and adaptability (i.e., a high number of *degrees of freedom*) to perform different motor acts. The concept of "synergy" has been proposed as a way used by the nervous system to simplify the control of hand postures, while maintaining the ability to flexibly adapt to a wide variety of objects and task conditions. While the concept of synergies has been useful in describing kinematic and neurophysiological observations, their neurobiological correlates in the human brain have not been investigated. In the present study we employed novel encoding techniques to determine whether regional brain activity during grasping movements could be predicted by the combination of hand synergies, comparing also kinematic and electrophysiological models on the basis of their ability to predict brain signals. Nine healthy right-handed volunteers (4 M, 5 F, age 25 ± 3 yrs) participated in three experimental sessions. Hand posture was recorded with a motion capture system (PhaseSpace©), muscle activity was measured with EMG (five channels) and brain activity was measured with fMRI at 3 Tesla. Participants shaped their hands as if they were grasping 20 different common-use imagined objects that were presented visually for 2.5 s; the movement was performed after a 5 s interval. Each movement was repeated 5 times. The kinematic and EMG data were used to compute postural and muscle synergies from either joint angles or EMG signal features, using principal component analysis. The same paradigm was performed in fMRI; a multiple linear regression analysis was used, with the matrices of kinematic and EMG synergy weights as encoding model. The results were accuracy values that describe the success of each postural model and a map with the voxels whose activity was modulated by the motor act being performed. The encoding procedure led to a better performance for the kinematic than the EMG synergy model (mean 68.0 ± 6.9%, min 59.2%, max 82.1%, $p < 0.05$). The group map identified the voxels with

successful encoding performance in a well-defined network of hand-related regions: bilateral precentral, supplementary motor and supramarginal areas and left inferior parietal and postcentral cortex. This study identified some regions, consistently engaged across participants, which are involved in controlling the end-postures of grasping and specifically modulate the pattern of hand muscle and joint movements associated to the target objects. In the present study, we showed that the cortical network controlling hand postures encodes specific high-level representations of motor acts through postural synergies. Moreover, the maximum encoding accuracy could be obtained with the model based on synergies rather than the ones based on somatotopic digit position or muscular activity. These results therefore open interesting insights on the ability to decode task-specific patterns of neural responses from motor control and action representation networks.

A cortical and sub-cortical parcellation clustering by intrinsic functional connectivity

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Network analysis of resting-state fMRI (rsfMRI) has been widely utilized to investigate the functional architecture of the whole brain. Such analysis can divide the brain into several discrete elements (nodes) connected by links (edges) representing the relation between two elements. The brain cortical and subcortical areas can be segmented or parcelled into several functional and/or structural regions. The connectome analysis of human-brain structure and functional connectivity provides a unique opportunity to understand the organisation of brain networks. However, such analyses require an appropriate definition of functional or structural nodes to efficiently represent cortical regions. In order to address this issue, here we propose a robust parcellation method based on resting-state fMRI, which can be generalized from the single-subject level to the multi-group one, considering the input data of a single subject and constructing multi-resolution graph elements. We combined voting-based measurements to divide the cortical region into sub-regions in order to obtain the whole brain parcellation. Our parcellation relies on majority vote and poses spatial constraints within a hierarchical agglomerative clustering framework to define parcels that are spatially homogeneous. We used rsfMRI data collected from 40 healthy subjects and we showed that our purposed algorithm is able to compute

stable and reproducible parcellations across the group of subjects at multi-resolution level. We find that, even though previous methods ensure on average larger overlap between parcels and regions in AAL atlas, the method proposed herein reduces inter-subject variability, especially when the number of parcels increases. Our high-resolution parcels seem to be functionally more consistent and reliable and can be a useful tool for future analysis that will aim to match functional and structural architecture of the brain.

NREM sleep transient events in fronto-temporal dementia

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Fronto-temporal Dementia (FTD) is increasingly becoming recognized as a major cause of early onset (< 65 years) neurodegenerative dementia. Although sleep disorders significantly impair patients' and caregivers' quality of life in neurodegenerative diseases, polysomnographic data in FTD patients are scarce in the literature. Aim of our study was to investigate sleep microstructure in FTD, by means of Cyclic Alternating Pattern (CAP) and to compare these variables with cognitively intact healthy elderly and patient with Alzheimer disease. A groups of ten behavioral variant FTD patients (6 M, 4 F; mean age 61.2 ± 7.3 years; disease duration: 1.4 ± 0.7 years) and to compare them with 20 cognitively intact healthy elderly and 10 patient with Alzheimer's Disease. Sleep in FTD patients was altered at different levels, involving not only the conventional sleep stage architecture parameters (total sleep time, single stage percentage, NREM/REM cycle organization), but also microstructure. FTD subjects showed CAP disruption with decreased slow wave activity related transients (A1 index, n/h: 14.5 ± 6.8 vs. 38.8 ± 6.6, $p < .001$) and increased arousal-related fast CAP components (A2 index 22.9 ± 8.2 vs. 11.6 ± 3.7, $p = .006$; A3 index 41.9 ± 20.7 vs. 13.0 ± 6.5, $p = .002$). When compared to AD, FTD showed had several sleep parameters similarly or even more affected by neurodegeneration, but in a much shorter time span. Peculiar alteration of A1 index in FTD has been reported. Several significant correlations between sleep variables and neuropsychological tests were found. Sleep impairment in FTD may be specifically related to the specific frontal lobe involvement in the neurodegenerative process. The pattern of alterations seems

somewhat peculiar, probably due to the anatomical distribution of the neurodegenerative process with a major impact on frontal lobe generated sleep transients, and a substantial sparing of the posterior cortex related phenomena.

Cortical responses to emotional film clips: an EEG investigation

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Film stimuli are a powerful tool to elicit emotions, allowing a multimodal stimulation that determines the emergence of an affective state as it occurs in everyday life, thus this method represents a suitable ecological choice for studying brain activity elicited by different emotions. Using a standardized set of 18 two-minute excerpts, we investigated brain electrical response elicited by six categories of film clips, namely Erotic, Fear, Sadness, Compassion, Scenery and Neutral. Thirty-eight undergraduates (19 females) watched the film clips in randomized order while their brain activity was recorded by means of 38 EEG channels. After each film clip they had to evaluate emotional valence and arousal with the Self-Assessment Manikin, and other affective scales. After artifacts correction, electrodes were clustered in nine region of interest, and spectral power was computed for alpha (8-13 Hz) and High-Beta (21-30 Hz) frequency bands. Analysis of variance was performed for each band considering Film category, Caudality (Anterior vs. Central vs. Posterior) and Laterality (Left vs. Central vs. Right) as within group factors. Alpha band, here considered as a reverse index of cortical arousal, showed that over the central and the posterior central clusters the emotional categories prompted the maximum differentiation of the brain responses, with the most arousing categories, Erotic and Fear, producing the greatest alpha inhibition. Within similar categories often confused in the literature, brain activity elicited by Sadness was greater than that evoked by Compassion clips. Unlike alpha more sensitive to arousal, EEG Beta band was sensitive to valence, showing that the aversive categories (Fear, Sadness and Compassion) produced significantly larger activation compared to pleasant-neutral clips, in bilateral temporo-parietal EEG sites. Using sLORETA, the main generator of the observed alpha responses was located within the parietal lobe (BA 7) and the main generator of the beta activity was found within the superior and middle temporal gyri (BA 21-22). The temporal activation elicited by aversive emotions may reflect the influence of deep structures (i.e. amygdala and hippocampus) over cortical regions involved in audio-visual integration processes boosted by the emotional content of the stimuli. Taken together the present findings show how emotions modulate activity within brain regions specialized in multimodal perceptual integration and in emotion-related action preparation, highlighting the potential role played by these structures to the generation of emotional experience and behavioural response.

Causal modulation of the neural interactions during the planning phase of prehension movement: a TMS-fMRI approach

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The neural substrates subtending prehension, our ability to reach and grasp objects, comprise two parieto-frontal pathways. Specifically, the dorsomedial pathway connects the occipito-parietal cortex (Superior Parieto-Occipital Cortex – SPOC, Superior Parietal Lobule – SPL) to the frontal lobe (dorsal Premotor area – PMd), while the dorsolateral pathway connects the inferior part of the parietal lobe (anterior Intraparietal Sulcus – aIPS) with the ventral portion of the frontal lobe (ventral Premotor area – PMv). Both pathways are involved in the planning and execution of prehension. Nevertheless, it is yet unclear which is their specific role and how information is transferred within and between the regions within these two pathways. To investigate this issue, we adopted a combination of techniques: 1 Hz repetitive Transcranial Magnetic Stimulation (rTMS) and functional Magnetic Resonance (fMRI). Offline rTMS was applied over left SPOC as it is reciprocally connected with the dorsomedial and dorsolateral pathways. Furthermore, it has been shown to be modulated by visual feedback. Participants (N = 14) performed prehension movements towards an object while lying in the MR scanner. We manipulated visual feedback by asking subjects to keep their eyes either closed (blind grasp) or opened (visual grasp) when executing the action. The other experimental manipulation consisted in performing the task after offline 1 Hz rTMS stimulation over left SPOC or after sham stimulation over the same site. Our results show an effect of TMS stimulation, which induced task-related modulations of the activity within the network. In particular, we found that TMS induced an inhibition in the activity of SPOC and pre-cuneus bilaterally when participants planned a movement with their eyes open. In contrast, TMS induced an increase in activity in pre-Supplementary Motor Area (pre-SMA) and anterior portion of the Inferior Frontal Gyrus (IFG) during the same condition. Our results suggest that areas in the frontal lobe can support the planning phase of prehension when areas traditionally engaged in this task are perturbed.

Facilitation in visual search for reversed letters following r-TMS of the left parietal cortex

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Search asymmetries have been described in visual search tasks for letters among mirror – reversed letters and *viceversa*. Thus, it is harder to find the letter "N" among its mirror reversals "И" than *viceversa*. Noting that this reversed letter effect involves both a processing of task irrelevant information and a linguistic association, we explored whether the right Posterior Parietal Cortex (PPC) and/or the left PPC play a role in the reversed letter effect. Sixty healthy right-handed Italian subjects (15 males, 45 females; mean age: 24 ± 3 years) were randomly assigned in two groups, according to the hemisphere stimulated: right PPC (N = 30) and left PPC group (N = 30). The task required search for a uniquely tilted, oblique bar. All the oblique bars were embedded in an object shape "N" that contained familiar verbal information or "И" which was the mirror reversal of "N". The target oblique bar was always tilted in the opposite direction to the other oblique bars. Display was viewed at a distance of 55 cm on a white background. The fixation stimulus was a black cross at the display center. Subjects performed the task in baseline and after repetitive Transcranial Stimulation (rTMS). We counterbalanced the order of these two sessions between subjects. The words "letters" or "N" was never mentioned. Subjects were asked to press a left or right button, as fast as possible, with the index or middle fingers of the right hand, respectively to indicate whether the target was in the left or right half of the display. Each session (baseline and rTMS), contained 80 stimulus displays, with 40 trials for each stimulus type (target-in- N and target-in-reversed- N). The trials from the two stimulus type were randomly interleaved in each session. rTMS trains at 1 Hz frequency and 600 s duration were applied using a MagStim Rapid 2 magnetic stimulator and a figure-of-eight coil (diameter: 70 mm) over two scalp sites, corresponding to P3 and P4 positions of the 10-20 EEG system. Two separate ANOVAs were conducted on the accuracy and the averaged RTs, with stimulus type (target-in- N vs. target-in-reversed- N) and session (baseline vs. rTMS) as within-subject factors and hemisphere (right vs. left) as a between-subject factor. Value of $p < 0.05$ was considered as significant. The results revealed that rTMS on right PPC had no effect in the task performance. In contrast, rTMS on the left PPC speeded up the performance on finding letter "N" among its mirror images but not when searching for the mirror image "И" among "N" s. We suggest that the observed

facilitation is related to letter processing subserved by the left PPC. Impairing the letter form recognition with rTMS reduces the top-down interference by task irrelevant linguistic information in our task, which requires only low-level visual feature (orientation of oblique bars) discrimination.

Attentional dysfunctions after hippocampal stroke: evidence from event-related potentials in a case report

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The hippocampus has traditionally been related with long-term, declarative or episodic memory. Recently, this neural area has been also involved in attentional processes. We here present results of a psychophysiological assessment in a patient with unilateral hippocampal stroke. A 42-year-old man experienced an antero- and a mild retrograde amnesia with complete inability to learn new information, due to an acute ischemic lesion in the left hippocampus. His long-term recall was intact. The clinical picture has been spontaneously recovered within five hours, with the exception of the recall of the event, while he underwent the psychophysiological evaluation consisting of a P300 oddball paradigm (with counting and motor task) and a CNV motor task. The patient correctly performed required tasks. No significant difference emerged in P300 parameters between the patient and controls for both counting and motor response. For P300 task with motor response, N2d latency was significantly longer in the patient than in controls (Fz: $p = 0.03$; Cz: $p = 0.03$; Pz: $p = 0.02$) as well as the N2d amplitude was lower in the patient than in controls (Fz: $p = 0.06$; Cz: $p = 0.05$: Pz: $p = 0.04$). During the same task, RTs were significantly longer in patient than controls (patient: 537.4 ms; controls: 294.1 ± 19.5 ms; $p < 0.001$). No significant differences emerged for total CNV and W1-CNV areas between the patient and controls. The W2-CNV area was significantly lower in the patient than in controls (Cz: $p = 0.03$; Pz: $p = 0.003$). Latencies of N2d/post-S2 (Fz: $p = 0.04$; Cz: $p = 0.02$; Pz: $p = 0.05$) and P3d/post-S2 (Fz: $p = 0.04$; Cz: $p = 0.05$) components were significantly longer in the patient than in controls. RTs were similar between the patient and controls in CNV task. The psychophysiological abnormalities we observed in this patient suggest that hippocampus may play a role in the attentional processing of the stimulus and may influence the inhibitory control during the premotor activity related to a goal-directed act. It is known that different areas of the prefrontal cortex, particularly the anterior cingulate cortex, the dorsolateral prefrontal cortex, and the supplementary motor area are active during response conflict. Reasonably,

the alterations in ERPs parameters related to inhibitory control observed in our patient are associated to the interruption of the hippocampal projections towards the prefrontal cortices more related to the executive control of cognition.

The role of cerebellum in the attentional processing of the stimulus: evidence from an event-related potentials and transcranial direct current stimulation study

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The functional domain of the cerebellum extends beyond its traditional role in motor control. In recent years this structure has increasingly been seen as playing a crucial role also in cognitive performance and attentional processes. Attentional processing consists of a set of processes that manage the flow of information through the nervous system and appropriately allocate attentional resources to relevant stimuli. The aim of this study was to investigate the role of the cerebellum in attentional processing of the stimulus using a P300 Novelty task. We studied the effects of transcranial Direct Current Stimulation (tDCS) delivered over the left cerebellar hemisphere on the P300 components in healthy subjects. Fifteen healthy subjects underwent a cathodal, anodal and sham session and recorded a P300 Novelty task prior and after tDCS session. Only cathodal cerebellar tDCS significantly reduced the amplitude of the N1 and P3 components for both the target and novel stimuli. Moreover, N1 latency for all the stimuli was shorter after the cathodal tDCS session than after the sham or anodal sessions. These results showed that, because of a possible functional cerebellar inhibition, only cathodal tDCS have perturbed P300 parameters thus supporting the role for the cerebellum in the attentional processing of the stimulus. Specific networks involving the frontal and parietal regions are related to attention and the cerebellum is as a subcortical structure that may interact with cortical brain areas, there by controlling attentional processes. In particular, we speculate that the cerebellum acts indirectly by regulating and managing the activation and inhibition levels of the cortical areas that work in the attentional networks.

The sensory suggestibility modulates individuals' susceptibility to the rubber hand illusion

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Simultaneously stroking a visible rubber hand with a person's unseen hand cause the feeling that the fake hand is part of one's own body. This intriguingly phenomenon, termed Rubber Hand Illusion (RHI), is widely used for studying the sense of body ownership. The subjective experience of the RHI, however, largely varies between participants. Actually, little is known about the factors influencing individuals' differential susceptibility to the RHI. The illusion involves multisensory integration of visuo-tactile-propioceptive information, as well as cognitive processes (i.e., incorporating the rubber hand into one's own body representation). These processes can be influenced by the individuals' sensory suggestibility. Thus, this personality trait would be crucial in determining sensitivity to the RHI. The present study investigates whether the degree of sensory suggestibility determines the extent to which the individuals experience the RHI. Based on the Sensory Suggestibility Scale (SSS), 74 healthy participants were assigned to the "low", "mid" or "high" suggestible groups. The RHI was assessed after synchronous and asynchronous stroking. We used a self-report questionnaire as subjective measure of illusion, and the proprioceptive drift as objective measure of illusion. Both objective and the subjective measures revealed that the "high" group was higher susceptible to the RHI than the "low" group. Crucially, the statement specifically assessing the feeling of ownership on the rubber hand, revealed that the "high" group felt stronger RHI after synchronous stimulation compared to the "low" group. The same statement also significantly correlated with SSS total score, indicating higher sensory suggestibility was associated to stronger feeling of ownership. This study clearly demonstrates that sensory suggestibility strongly contributes to participants' experience of the illusion. The role of individuals' sensory suggestibility should be considered more carefully in future studies adopting the RHI paradigm.

Emotional coping modulates physical performance in mountain ultra-marathon race

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Under extreme conditions, including those exerted by extreme environments and/or exercise, human body is pushed to its limits. Competitions such as ultra-running race are close to the limits of human performance, from both physiological as well as psychological points of view. Thus, exercise physiologists are very interested in analysing physical and emotional consequences of sports where runners compete over very long distances. The Tor Des Geants® (TDG) is a peculiar model for studying mind/body interactions since it is the only endurance race (1 week) combining long distance and fatigue with emotional coping styles. Identifying the effects of strenuous exercise on anxiety and mood; in particular how the individual strategy of behavioral coping affects the physical performance under extreme conditions. A group of experienced ultra-marathon runners, performing the mountain Tor des Geants® ultra-marathon: 330 km trail-run in Valle d'Aosta, 24.000 m of positive and negative elevation changes, was monitored. Well-trained athletes were tested one week before TDG (pre-race), in the middle of the race, and after the race (post-race). Neuropsychological evaluation will be conducted by means of a standardized psychometric battery to assess emotional function: mood, Profile of Mood State (POMS); evaluation of anxiety-state, Self-Rating Anxiety State (SAS); evaluation of anxiety-trait, State-Trait Anxiety Inventory (STAI). Non-verbal behaviors, recorded through the Ethological Coding System for Interview (ECSI), were analyzed offline and grouped in categories to evaluate ethological profile. This individual psychological aspect varies according to the environment and reflecting emotional and affective states. All statistical analyses were conducted only on the 11 athletes that finished the race. Post-race compared to pre-race shows: (1) lower values of tension and confusion (POMS; $p < 0.001$); (2) higher values of state-anxiety (SAS; $p < 0.001$); (3) greater control of stressful stimuli (ECSI Flight; $p < 0.05$) and (4) higher emotional arousal (ECSI Relaxation; $p < 0.05$). Higher anxiety levels (SAS, STAI-Y; $p < 0.05$) and higher emotional arousal (ECSI Relaxation and Affiliation; $p < 0.05$) in pre-race were associated to a better sportive performance. The main result of this study is that basal higher levels of anticipatory anxiety and emotional arousal allow athletes to finish the competition in a shorter time, supporting the idea that emotional hyper-reactivity favors both mental control and physical activity in extreme conditions. Finally, this study depicts TDG as a suitable model for exploring the interaction between performance and anxiety/mood management.

A common space for action: visual and aurally affordances

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How can we handle objects by relying on auditory information only? How do we represent distinct object features (e.g., location, form, affordance, etc.) when visual input is unavailable? Previous studies consistently indicated that viewed objects afford suitable actions, even in the absence of any intention to act, and that this link is spatially constrained. We previously developed a spatial alignment effect paradigm to demonstrate that objects afford suitable actions only when they are visually presented within the action space of an agent. Nonetheless, whether this holds just for vision or whether the link between object and action depends on spatial constraints independently from the sensory modality that conveys all these pieces of information to the brain remains an open question. To assess this issue, we designed a series of behavioral experiments in 65 (34 ± 14 years, 37 males) sighted and 11 (42 ± 12 years, 5 males) congenitally blind subjects. Across conditions, participants had to pantomime a reach-to-grasp movement towards objects visually or aurally presented in a congruent (with affordance) or incongruent condition and located within or outside the subject reachable space. Reaction times were entered in a Linear Mixed Effect (LME) repeated-measure model to determine significant spatial alignment effects (i.e., decreased reaction times when participants execute a motor act which is congruent with that afforded by a perceived object). In both sighted and congenitally blind individuals, object features evoked actions when the object was visually or aurally presented within a reachable space only (significant Congruent × Location interactions, $p < 0.05$). In addition, we examined the same spatial alignment effect when an aurally presented object was located next to either to the perceiver or another individual. We found that the spatial alignment effect also occurred whenever the object was presented within the reaching space of a potential actor, regardless of whether it was placed within the participant's own or the other's reaching space, consistent with findings from our previous visual study. Altogether, these results demonstrate that sighted and congenitally blind individuals do not differ in mapping objects on to their own action space presented either visually or aurally. Of note, this action-oriented object perception can be modulated by the presence of another potential actor. Thus, the individual spatial representation of objects that affects the link between actions and objectsis independent from the sensory modality through which the position of objects in respect to the agent is perceived and does not require visual experience.

Visuo-motor learning differently modulates cortical topology of sleep slow oscillations and of fast rhythms expression during NREM sleep: a high-density sleep EEG study

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Memory benefits of NREM sleep and the slow/fast rhythms coordination appears to convey the consolidation of brain plasticity due to the acquisition of new information occurring during wakefulness. We studied NREM sleep modulation as a function of a visuo-motor learning task in 7 healthy volunteers (2 females). We used as control condition a similar motor task, however not requiring the learning of new motor patterns. The two tasks were performed in different days (1 week of separation) and both before and after the night we recorded sleep EEG. Also, a week before the experiment, participants spent a night in the laboratory, as adaptation to the experimental condition. The two sleep recordings were performed with high density EEG (128-electrodes HydroCel Geodesic Sensor Nets and GES300-EGI). EEG data analysis took into account two markers of the thalamo-cortical entrainment: the Sleep Slow Oscillations (SSO) and sleep spindles. For both graphoelements with estimated morphological and topological characteristics. We have identified a differential behaviour of both SSO and sleep spindles regarding wave amplitude and topology of detections. For SSO, the learning task increases wave detection in the motor/premotor areas of the dominant hemisphere and increases fast rhythms grouping in the SSO upstate in the visuo-motor integration areas. For spindles, the learning task increases frontal spindle density, and shift the peak amplitude to the central areas. Results indicate that visuo-motor learning increases the entrainment within thalamo-cortical circuits related to areas involved in the task.

Facial feedback effect explains the autonomic impairment in PD for emotional recognition

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Parkinson's Disease (PD) is a degenerative neurological disorder of the central nervous system with a strong impact on both social and emotional level. Parkinson patients typically present with emotional processing impairment in emotional experience and emotion recognition. However, it is not yet known whether these patients have lost the capability to feel the emotions intrinsically, to modulate to emotional experience associating subjective response with physiological modulations, or to decipher emotions in others. The present research aims at investigating the contribution of central, peripheral and facial feedback measures in PD patients when they processed emotional cues using a multilevel approach, comparting self-report (appraisal), autonomic (Skin Conductance Response, SCR) and motor electromyographic (EMG zygomaticus and corrugators facial muscles) measures. The integration of these measures allowed firstly a direct comparison between the explicit appraisal of emotions (with specific reference to the two parameters of valence and arousal) and the autonomic responsiveness to emotions. Secondly the role of EMG (zygomaticus and corrugators muscle) in determining the central and peripheral modulation was explored. Indeed the facial feedback model supposed that the autonomic facial response by facial muscles may affect both the emotional appraisal and the physiological modulation. 20 patients have been selected and 34 healthy volunteers (HC), matched for age and education. PD patients observed and evaluated affective pictures that were chosen from International Affective Picture System (IAPS). These pictures concerned four types of stimuli: 10 pleasant – low and high arousal; 10 unpleasant – low and high arousal, 5 neutral. PD patients seemed to not adequately answer to the emotional categories which were considered salient in standard conditions (HC). Indeed, there was an autonomic impairment for a category-specific emotion (negative and high arousal). Particularly, patients have revealed an inadequate sensibility (reduced SCR) only for negative emotional condition. In parallel EMG behavior was disrupted (reduced corrugators activity) in response to negative high arousal emotional cues. However, PD patients were able to correctly categorize the emotional cues based on their valence/arousal, probably due to a "gap" between this central process and the autonomic system activity. Then, the regression analysis pointed out the predictive role of the corrugators activity to explain the impaired autonomic response: a reduced corrugators mimic was linked to a reduced peripheral responsiveness toward the negative and high arousal emotional stimuli.

Neural coding of action planning with and without visual feedback

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The fronto-parietal and occipito-temporal cortices show action-related preparatory responses for grasping and reaching movements. What remains unclear is whether the role of these areas is related to the visual representation of the object that is dynamically shaped in the context of the upcoming action or to the anticipation of somato-motor consequences of the planned action. To answer this question, we used a slow event-related fMRI paradigm that independently manipulated vision of the object (Vision or No Vision) and action type (Grasp or Move hand). Movements consisted of either grasping the object with a whole hand grip or moving the hand close to the object. Importantly, the interaction with the object was required in the Grasp but not in the Move hand condition. Sixteen right-handed human participants performed delayed movements with and without visual feedback using their dominant hand. At the beginning of each trial an auditory cue instructed participants whether or not to close their eyes and the action to be performed at the end of the trial. A delay of 10 seconds was followed by the go cue. The delay phase before movement initiation was the focus of our analyses. We used multi-voxel pattern analyses to decode movement intentions during the planning phase of the movement, specifically object-directed grasp and non-object directed actions. We hypothesized that brain areas involved incoding action-related object properties would show abovechance decoding accuracy between Grasp and Move hand in the Visual condition. In addition, we hypothesized that brain areas involved in coding the anticipation of somato-motor consequences of an action would show above chance decoding accuracy between Grasp and Move hand across Vision and No Vision conditions, as the anticipation of somato-motor consequences is present for both movement types regardless of the level of visual information. We found that bilateral premotor area, primary motor area, anterior intraparietal sulcus, the superior parietal occipital sulcusand the caudal intraparietal sulcus in the left hemisphere showed above chance decoding accuracy between Grasp and Move hand in Vision conditions as well as across Vision and No Vision conditions. In addition, bilateral medial Intraparietal Sulcus (mIPS) and Lateral Occipital area (LO) showed above chance decoding between Grasp and Move hand in the Vision condition only. The overlap in the fronto-parietal network between activity patterns predicting visual processing and somato-motor anticipations suggests that these areas coordinate different aspects of the action plan. The pattern of activity in the mIPS and LO suggests a crucial role of these areas in the visual processing of action-related properties of objects regardless of the somato-motor anticipations.

Looking at emotions: a psychophysiological investigation on affective processing

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Our emotional reactions to stimuli depend on appetitive and defensive motivational states activated, respectively, in contexts promoting and threatening our survival. The affective space is defined by valence (pleasant-appetitive vs. unpleasant-defensive) and arousal (the degree of motivational activation), whose relative influence on psychophysiological responses to emotion is debated. We tackled this issue by measuring Pupil Diameter (PD), Heart Rate (HR) and Skin Conductance (SC) to affective stimuli orthogonally varied on valence (negative, neutral, positive: V-, V=, V+) and arousal (A-, A+). To minimize perceptual and semantic-lexical confounding effects, we used a carefully controlled set of affective words on which 48 participants executed a lexical decision task (implicit affective processing). Another currently open question concerns the underlying causes of the observed huge inter-individual variability in psychophysiological responses to emotion. We tackled these issues by investigating the influence of participants' personality traits and baseline autonomic state on their physiological responses and explicit affective processing. To do this, we selected a group of participants (IA) with high scores on interoceptive awareness (the conscious perception of bodily signals) and low scores on emotional susceptibility, the bent to experience discomfort/vulnerability when facing affective stimuli, and a group with the opposite profile (ES). We also recorded their resting-state autonomic activity and asked them to provide affective ratings on stimuli. ANOVA on PD revealed a valence × arousal × group effect: in line with their personality profile, IA group had greater PD for V+A- and all arousing words, while ES group had greater PD to all but the V=A- words. SC showed a very similar pattern of results. Instead, for the HR, a valence × group effect was found: only IA group showed a valence effect: a greater HR deceleration for V+, followed by V- and V= words. Further analysis revealed linear effects of both personality traits and baseline autonomic state on physiological responses. This confirms previous findings of a PD-HR dissociation suggesting the sympathetic nature of PD responses. Finally, the two groups differently experienced emotions: IA group rated V- words as less arousing and V+ and, especially, V+A- words as more positive and arousing; this would explain their greater physiological responses in this condition. ES group, instead, showed dissociated implicit and explicit affective processing: despite they accurately rated arousal of V+A- and V-A- words, their physiological response to them was exaggerated and

not distinguishable from that to arousing words. Taken together, these results provide first insights on the complex interplay among physiological systems, personality traits and intrinsic autonomic state, suggesting the importance to consider all these aspects in the investigation of the explicit and implicit affective processing.

Empathy for pain in patients with fibromyalgia assessed through laser evoked potentials

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Mirror neurons allow our brain to correlate the observed movements with the own ones and to recognize their meaning. Empathy is defined as the ability to have a direct and experiential understanding of the mental states of others, especially in pain. It depends on a mirror mechanism that encodes the sensory experience directly in emotional terms. Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome, associated with a large set of symptoms, characterized by dysfunction of neural circuits responsible for perception, transmission and processing of nociceptive afferents. The aim of this study was to evaluate the empathy for pain in people with chronic pain through the examination of cortical evoked responses induced by laser stimulation, and vision of laser stimulation of other individuals, in a population of patients with FM and healthy controls. We evaluated 13 female patients whit FM compared with 13 female controls. All the subjects were submitted the evaluation of the Empathy for Pain Scale (EPS) and the Toronto Alexitymia Scale-20 (TAS-20). The recordings were called "twins" and performed in pairs. We registered Laser Evoked Potentials by stimulating the dorsum of the hand in three conditions: (1) "CLOSE" by the interposition of a panel between the subjects; (2) "HAND SIDE BY SIDE" we in turn we delivered a sequence of laser stimuli over the hand of both the subjects and we asked to observe the other person's hand while this was stimulated; (3) "RANDOM SEQUENCE" we randomly stimulated the hand of both the subjects. We found a reduced N2P2 amplitude in patients compared to controls. An empathic cortical response, registered as a N2P2 complex following the vision of the painful stimulation of the other, was present in 76.9% FM, 84.6% controls. The amplitude of this evoked potential was significantly reduced compared to the real stimulation, both in fibromyalgics and in controls. Patients with FM showed higher scores on scales of empathy and alexithymia. We found a positive correlation between TAS-20 and EPS-tot, and a positive correlation between EPS-tot score and N2P2 amplitude following the real stimulation, in both groups. There was

a statistically significant relationship between EPS-tot score and the cortical response of empathy, especially in the close condition. This study confirmed the presence of a cortical evoked potential for pain of the others, assuming the activation by mirror neurons of cortical areas to the development of the cognitive-related pain. A greater degree of empathy assessed by clinical scales seems to be related to increased cortical activation. The magnitude of the cortical recruitment elicited by painful stimuli is greater in subjects with high empathy scores, suggesting a greater availability of attentional resources dedicated to the development of their own and other pain.

Psychological and genetic correlates of controversial moral choices in professional insurance brokers

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The hypothesis that genetics, in addition to education, plays a role in modulating human moral behavior has recently become an issue of great interest in cognitive neuroscience. Recent findings by our group showed that a genetic driven augmentation of dopamine availability increases the utilitarian behavior in female subjects, maybe by reducing their emotional counterpart during the decision making process. To examine the relationship among genes, education and moral behavior, here we studied insurance brokers, as they are professionally trained to make rational choices and to constantly suppress their emotional involvement. After signing an informed consent, 120 male professional brokers were asked to answer a number of moral dilemmas, all requiring to sacrifice the life of one person in order to save more people. They also completed psychometric scales investigating their levels of empathy, leadership and impulsivity. Finally, they provided a saliva sample for genetic testing. As dopamine has been linked to crucial behavioral aspects that influence moral decision making, such as executive functions, reward, empathy and altruism, five functional polymorphisms, COMT rs4680, DRD4 uVNTR, DRD4 rs1800955, SLC6A3 3'-VNTR and ANKK1 rs1800497, involved in the regulation of dopaminergic neurotransmission, were genotyped. The same battery of data was collected from an independent control group of male university students. In both groups of subjects, leadership correlated positively with perspective taking and negatively with personal distress. All subjects showed average levels of empathy, but, in brokers, con-

trary to the control group, empathy and moral reasoning acted independently, that is, their empathetic abilities did not affect their utilitarian choices. Interestingly, in brokers but not in the control group, utilitarian choices were positively associated with impulsivity when deciding to sacrifice persons with reduced life expectancy (terminally ill or very old subjects). Furthermore, contrary to the control group, brokers judged these choices as morally acceptable. The genetic analysis revealed that brokers with both DRD4rs1800955 CC genotype by itself and in association with the A1 allele of ANKK1 rs1800479, engaged more often in utilitarian actions. This association was not observed in the control group. Our findings suggest that leaders may beable to understand the perspective of others without being influenced by their own negative emotional states. Moreover, brokers compared to naive people, are more able to quickly evaluate cost-benefit ratios in making moral choices. Interestingly, genetics influences brokers' utilitarian behavior by modulating the activity of dopamine receptors (DRD4 and DRD2).

Effects of cranio-spinal tDCS in the treatment of cognitive and motor symptoms in early Huntington's disease

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Transcutaneous Direct Current Stimulation (tDCS) is a new and safe technique for modulating central nervous system excitability. We assessed changes in early Huntington's Disease (HD) following tDCS by evaluating Unified Huntington Disease Rating Scale (UHDRS). No study exists to date about treatment of motor and cognitive symptoms in early HD with tDCS. For our study we used a constant current programmable electrical stimulator (HDCStimTM, Newronika, Italy) connected to a pair of rectangular electrodes. tDCS electrodes were thick (6 mm) rectangular pieces of saline-soaked synthetic sponge (7 × 5 cm, 35 cm^2). We applied current at a density of 0.071 mA/cm^2 and delivered a total charge density of 85.7 mC/cm^2, therefore below the threshold values for possible tissue damage. Electrodes were applied over the thoracic spinal cord (T9-T11) and parietal cortex of right hemisphere, respectively as anode and cathode. Anode was applied over the thoracic spinal cord (T9-T11), while cathode was positioned over the right parietal cortex. The stimulation consisted in a daily session of treatment during 5 days, of 20 minutes (2.0 mA) each

one. The patient was 37 years old with a family history of HD and the motor and cognitive symptoms appeared two years ago. The clinical evaluation was performed before tDCS (T0), after 5 days of treatment (T1) and after 2 weeks from the last session (T2). At T0 were evaluated UHDRS: motor function (17) and behavior section (25). At T1 we assessed changes in scores of motor function (12) and behavior section (18) and also at T2 for motor function (13). We have shown for the first time significant effects of tDCS both on motor and behavioral symptoms in early HD. The configuration we used likely reduces the abnormal peripheral afferent input, possibly restoring at the same time the balance of interhemispheric communication by interfering with right parietal hyperactivity. This is also the first study using tDCS for the treatment of hyperkinetic movement disorders.

Control of action in the ipsilateral dorsal premotor-motor circuit

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The ability to with hold a forth coming action and to release it when appropriate requires the unfolding of several distinct processes, ranging from the basic sensory capacities, to the memory and the storage of a sensorimotor rule, and finally to the access of that rule by the motor system. Various studies with monkeys suggest that the dorsal Premotor Cortex (PMCd) could play a pivotal role in the control and in the preparation for arbitrary instructed actions. In the present work, we investigate whether the PMCd could be a good candidate for processing this task in humans. Since a rich pattern of connectivity is present in nonhuman primates between the PMCd and the primary motor cortex (M1), by analogy similar functions and connections between the PMCd and the M1 are hypothesized in humans. However, these features have not been functionally demonstrated mainly because of the technical difficulty of applying the Transcranial Magnetic Stimulation (TMS) dual-coil paradigm, which is the technique that is commonly used for this purpose (i.e. cortico-cortical connectivity), to two cortical regions in such spatial proximity. Therefore, how to investigate hypothesis regarding the role of PMCd in the control of action in humans is still a tricky issue. Nevertheless, in our precedent work, by moving the target from the hand-related M1 to the mouth-related M1, we provided evidence for an ipsilateral PMCd-M1 circuit, defining a specific region in the PMCd that gives origin to premotor-motor connections, resulting in a specific short-latency inhibitory effect of the PMCd on the M1. In the present work, we adopted a dual-coil TMS paradigm during a simple reaction time task. In the first experiment, sixteen participants were asked to match and time their action with the onset of an instructed arbitrary visual cue, in a way in which it was possible to catch the involvement of this circuit in the sensorimotor transformation concerned with

the control of action by means of the TMS modulation. Dual-coil TMS over the ipsilateral PMCd-M1 circuit revealed a powerful, highly replicable and consistent modulation of the corticofacial excitability and a time locked behavioural effect due to the double stimulation during a specific portion of the foreperiod. In the second experiment (twelve participants), it was shown, by means of the same technique, that the control of the forth coming action carried out by the PMCd-M1 circuit is consistent and effective, independently from the duration of the foreperiod itself. This is indeed a first step toward the investigation of a cortical circuit concerned with the ability primates exhibit while they are preparing and eventually releasing an instructed action in an efficient manner as well as at the right time.

Effects of mental fatigue on attention network test: contributions from ERPs

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Mental fatigue refers to the effect that subjects experience during and following prolonged periods of cognitive activity that requires work efficiency, and may lead to temporary deterioration of attentional functioning and response readiness, even with increased number of errors. The aim of the study was to investigate the effects of mental fatigue on attentional performances combining Attentional Network Test design and ERPs, in order to better define them from a neural networks' efficiency perspective, according to the Posnerian model. Twenty healthy subjects were enrolled and randomly assigned to two groups: a fatigue group (10 subjects) that performed 1h of a continuous performance of mental arithmetic task, and a control group (10 subjects) that performed 1h of leisure activity; prior and after, subjects performed the ANT, while EEG activity was recorded. RTs were analysed according to the subtraction method requested by ANT; CNV amplitudes were analysed according to the different types of cue provided by the task, N1 and P3 latencies and amplitudes to the targets were analysed according to the cue in order to evaluate the ERPs responses related to the alerting and the orienting networks; moreover, N2 and P3 amplitudes to the target were analysed according to the target type, in order to evaluate the "executive" ERPs response. Alerting, orienting and executive networks' efficiencies were comparable between groups, while accuracy declined only after mental effort (p = 0.016); mean overall reaction time shortened after ANT repetition only in the control group (p = 0.01). Regarding ERPs related to alerting and orienting networks, only after mental fatigue a decreased CNV amplitude bordered on significance (p = 0.085) was found, with no differences between cues, while in the control group CNV remained stable. Mental fatigue did not exert any effect on the N1 and P3 amplitudes and latencies. On the opposite, ERPs related to the executive network (N2 and P3 elicitated by incongruent and congruent conditions) were

influenced by mental fatigue: during the ANT following the mental work load, N2 and P3 amplitude to the incongruent stimuli were significantly reduced (respectively $p = 0.016$ and $p < 0.001$), while in the control group they did not change; similarly, in the fatigue group the P3 amplitude to the congruent condition did not increase after repeating the task ($p = 0.77$), while it was higher in the control group after ANT repetition ($p = 0.054$). Our data showed that mental fatigue modulated ERPs related to the executive network, besides affecting generically the behavioural performances to the task. Alerting and orienting seemed to be preserved by the effects of cognitive fatigue. The results fit in well with the theoretical model implicating the frontal basal ganglia circuitry as the core substrate of mental fatigue.

Can "pain matrix" be convinced to feel more pain? Looking for a neurophysiological marker of nocebo effect

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To investigate whether the expectation of feeling more pain modifies Laser Evoked Potential (LEP) amplitude and laser-pain rating. Twenty subjects were recruited: 10 in a Verbal Suggestion Session (VSS) and 10 in a Conditioning Session (CS). At time 0, LEPs were acquired from 31 scalp electrodes to right and left hand stimulation. At time 1, Vaseline was applied on the right hand and subjects were informed that they were receiving a hyperalgesic cream. In VSS, LEPs were recorded using the same stimulus intensity as in the baseline. In CS, LEPs were recorded initially to a stimulus of surreptitiously increased intensity, in order to make the subjects believe that the hyperalgesic treatment worked. Then, Vaseline was applied again and LEPs were recorded at the same stimulus intensity as in the baseline. In VSS, laser-pain rating was increased after treatment. In both VSS and CS, the fake treatment did not produce any increase of both N2 and P2 amplitudes. However, in VSS the N2/P2 habituation was significantly lower to right than left hand stimulation. No topographical modification was observed. Our results suggest that the expectation of feeling more pain increases the laser-pain rating, but not the LEP amplitude. Nevertheless, the reduction of the physiological LEP amplitude habituation represents the neurophysiological marker of the nocebo effect.

Motion area V5 is sufficient for discrimination of the orientation of moving stimuli but not for their conscious perception

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Hemianopia is a visual field defect characterized by decreased vision or blindness in the contralateral visual field of both eyes following a unilateral lesion along the post-chiasmatic visual pathway. Despite this loss of vision, some unconscious visual abilities ("blindsight") could be present in the blind field. The probability of finding this phenomenon can be increased by presenting moving stimuli in the blind field as those stimuli can activate subcortical pathways that convey visual information to extrastriate visual areas (e.g. the motion area V5), bypassing the primary visual cortex. Therefore, the aim of this project was to assess the role of area V5 in yielding conscious or unconscious perception of moving visual stimuli. To do that we tested one hemianopic patient with a right lower quadrantanopia, in behavioral experiments as well as in a 3T-fMRI session including Retinotopic Mapping (polar angle), V5 Localizer and DTI (performed to compare the structural connectivity and the integrity of white matter fibers, e.g., optic radiation). We assessed fMRI activation of V5 by contrasting full field moving random dots with full field static random dots to evaluate cortical activation due to the pure moving condition. We found that this patient showed activation of extrastriate visual areas including V5 when presenting moving visual stimuli, despite no activation of dorsal V1 when presenting the stimulus in the blind quadrant. Interestingly, he performed above chance, albeit unconsciously, only in an orientation discrimination task with moving but not static stimuli presented in the blind area. In conclusion, this preliminary result in a single case provides evidence that in the absence of V1 the presence of V5 activation is necessary for above-chance performance with moving stimuli but is not sufficient for perceptual awareness. This has relevance for understanding the neural bases of perceptual awareness.

Cortical reorganization and clinical outcomes after stroke: a longitudinal evaluation

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Since early days after stroke, the brain undergoes a complex reorganization to allow compensatory mechanisms that promote functional recovery. Cerebral networks reorganize their structural and functional neuroanatomy in a dynamic manner over time. Characterize specific neurophysiological markers of motor recovery after stroke could improve clinical decision making. At this regard, the aim of this study was to track the time-course of motor cortical reorganization, in stroke patients, and to individuate the neurophysiological markers associated to positive clinical outcome. To this aim, a multimodal approach that integrates Transcranial Magnetic Stimulation (TMS) with electroencephalography (EEG), and clinical measures was applied longitudinally following stroke. Seven patients in the sub-acute phase of ischemic cortical and/or subcortical stroke were recruited and evaluated within 20 days (T0) and after 40 (T1), 60 (T2) and 180 (T3) days after stroke. For each time-point, cortical reactivity (in terms of local mean field power) and cortical oscillations (in term of event related spectral perturbations) changes, evoked by 80 single TMS pulses, were assessed over the motor cortex of the affected and unaffected hemisphere, combining TMS-EEG. These measurements were paralleled with behavioral motor and functional disability changes assessed by behavioral and clinical evaluations (Fugl-Meyer Assessment of motor recovery, Berg Balance Scale and Stroke Specific Quality of Life Scale). Repeated measures ANOVA and Friedman test were used to evaluate changes over time of all measures. Our data showed specific cortical oscillatory activity changes in the alpha band, in a specific time point (T2) of the longitudinal evaluation only in the affected hemisphere. Stroke patients showed a significant increase in evoked alpha oscillations that occurred within the first 180 msec after TMS, as highlighted by spectral perturbation analysis. Notably, these changes occurred at 60 days after stroke, indicating that crucial mechanisms of cortical reorganization occur in this short-time window. These changes coincided with the amelioration of clinical and behavioural outcomes. Alpha evoked oscillations increase resulted a good biomarker of motor functional recovery. For the first time, this study demonstrates the possibility to track longitudinally the cortical changes following stroke, by means a multimodal approach. Specifically, the study of motor cortical changes in stroke patients may contribute to characterize the neural mechanisms underlying motor disabilities and their recovery. These findings could allow, not only to identify neurophysiological

markers of stroke pathophysiology, but also to provide new insight into how and when neuromodulatory interventions could drive neuroplasticity in a functional direction.

Monitoring attention skills and psychophysiological correlates in a sample of Special Forces operators: a pilot study

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Attention is one of the most complex and pervasive cognitive function. Information-selection, focusing and concentration are indeed crucial skills that underlie other cognitive functions and continuously mediate the relationship between an individual and the environment. According to Posner and Petersen model, attention components are supported by three main neural subsystems: the alerting network, which grounds on the noradrenergic activity of brainstem arousal systems along with right hemisphere structures mediating sustained vigilance; the orienting network, involved in directing attention focus and including posterior parietal structures, superior colliculus and pulvinar; and an executive network, mediating conscious control and awareness and including medial prefrontal and cingulate cortices. The integrated activity of such systems regulates behavioural and physiological responses to the environment and can be trained. The fine tuning of aforementioned attention skills and networks becomes particularly critical for people involved in cognitively and physically stressful or high-risk activities, such as military and security operators, as critical is the evaluation of their functioning. While selective and more complex attention skills may be easily assessed by well-known response times tests including different stimuli and more or less effortful tasks, such practice is not part of standard monitoring examinations. The present study, then, aims at investigating the potential of such measures for the assessment of psychophysical performance in military operators. Further, it aims at investigating the relationship between simple attention measures and psychophysiological alertness/stress responses during and outside tactical activities so to investigate their predictive value. 69 operators took part in an initial evaluation step, which included a series of standardized Response Times (RT) computerized tests tapping on focused and spatial attention skills and on inhibition and response control abilities. Preliminary findings interestingly highlighted that military participants did not present the expectable decline of attention perfor-

mances with age, but presented instead significant negative correlations between age and attention-related RT, i.e. older operators showed better performances. In addition, a first series of single-case analyses highlighted positive associations between RT and specific subcomponents of heart rate variability indices, hinting at a link to sympathetic/parasympathetic regulation. We suggest that those findings may be accounted for by the role of continuous psychophysical training.

Making error: why did it happen and how to fix it? Electrophysiological signs from the brain

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ERP studies investigating error processing typically adopted response-locked approaches to describe the brain activities following erroneous response, that is the error-negativity (Ne) and the error-positivity (Pe) components. After error commission, the accuracy improvement and the response slowing are usually reported as the main post-error behavioral adjustments; however, ERP literature about processes predicting such adjustments is lacking. The main goal of this study was to investigate the preparatory brain activities leading to False Alarms (FAs, i.e., erroneous response to non-target stimuli) and post-error adjustments in a visual discrimination task. To this aim, we adopted a stimulus-locked approach and a large signal segmentation (2 seconds), allowing to investigate the pre-stimulus and pre-response components. From a large database of subjects involved in an equi-probable Go/No-Go task, we selected only those (N = 36) who made a relevant number of FAs. In a first analysis, brain activity of the correct (inhibited or responded) trials was compared to that of the FA trials. Results showed that the FAs were not explained by the pre-stimulus components (prefrontal negativity, pN, and Bereitschaftspotential, BP), nor by the perceptual processing components (P1 and N1). At the opposite, significant differences emerged at level of the prefrontal positivity (pP) component, peaking about 300 ms after the stimulus onset (corresponding to 100-150 ms before the motor response). The pP in FA trials was larger than No-Go and smaller than Go trials, suggesting an erroneous processing of the Stimulus-Response (S-R) mapping. In a second analysis, the ERPs of post-error trials were compared to post-correct trials (i.e., trials following correct Go and No-Go). Results showed significant effects at level of the two pre-stimulus preparatory components. The pN and the BP were respectively enhanced and reduced in post-error trials when compared to post-correct trials. Further, at behavioral level the performance of post-error trials was characterized by significant accuracy improvement and response slowing. Overall,

the novel result of the study indicates the S-R mapping process (reflected by the pP component) as the main mechanism predicting the erroneous response. As consequence of error, different neurocognitive adjustments emerged in the preparation of the subsequent trial, i.e. greater top-down attentional control (enhanced pN component) and reduced excitability of the premotor areas (reduced BP component): these brain adjustments were respectively associated to the accuracy improvement and the response slowing on the post-error trial.

Voluntary inhibitory control and impulsivity in Parkinson's disease with and without levodopa-induced dyskinesias

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Levodopa therapy is the most effective treatment for Parkinson's Disease (PD) motor symptoms, however, some complications such as Levodopa-Induced Dyskinesias (LIDs) and impulsive behaviors frequently occur in combination with its use. This suggests the emergence of a behavioral disinhibition parallel to LIDs that could be ascribed to alteration of the prefrontal functionality. The present study was aimed to investigate whether PD patients with LIDs were more impulsive in comparison with PD patients without LIDs according to a self-report index and voluntary inhibitory performance. To this goal, two matched samples of PD patients with (N = 8) or without LIDs (N = 8), evaluated by the Barratt Impulsivity Scale-11 (BIS-11), performed a stop signal task in baseline condition and following experimental manipulations. In fact, to stress differences between groups their performance to the stop signal task was tested also under the effects of a supramaximal Levodopa intake combined with the application of continuous Theta Burst Stimulation (cTBS) over the right inferior frontal cortex or in sham condition. The results showed similar performances between groups to the stop signal task in baseline, albeit the PD with LIDs Group resulted clearly more impulsive than the PD without LIDs Group according to the BIS-11 total score. Following the combined effects of prefrontal cTBS and supramaximal Levodopa intake, Go reaction times were prolonged in all PD patients with respect to all others conditions. Moreover, the analysis of the Stop Signal Delays (SSDs) revealed that patients belonging to the PD without LIDs Group were more able to manage longer delays to the stop signal task following

supramaximal Levodopa intake in absence of a stimulation effect. No modulation of Stop Signal Reaction Times (SSRT) or Stop Respond RTs was observed according to both experimental factors. The present results suggest that is possible to improve the motor initiation control in PD patients combining supramaximal Levodopa intake with prefrontal cTBS, but the effect of one of these interventions is not appreciable alone. Furthermore, according to SSDs analysis, PD without LIDs Group resulted the one susceptible of the improving effect of Levodopa intake, proposing a better integrity of dopaminergic network respect to PD with LIDs Group. In conclusion, the present findings suggest a marginal role of voluntary control of action and reactive inhibition in PD patients, while confirming the hypothesis of the emergence of a behavioral disinhibition in patients with LIDs.

Temporal dynamics of action affordance: an ERP study on everyday objects

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The present study aims to tap the electrophysiological correlates of action affordance. Previous researches have mainly focused on the evaluation of action affordance perception using as stimuli different category objects (e.g. living-non-living or tools-non tools) and/or tools dissimilar in their function or use. The novelty of our study concerns the evaluation of the same common use objects which differ only in the dimension of perceived action affordance (elicited by the design). Experimental stimuli were three couples of pictures representing everyday objects previously selected by a rating procedure. In particular each couple of items contained a high- and a low-affordance rated object. Twelve healthy volunteers (6 males and 6 females, mean age 23.3) were tested using an oddball paradigm where the couples of high- and a low-affordance objects were used both as standard and target stimuli in two different randomized oddball-procedures. EEG was recorded during the all experiment trough 28 electrodes (10-20 system). Event-Related Potentials (ERPs) time locked to the item presentation were averaged (-200-1000 ms) separately for each channel as a function of the level of affordance (high or low affordance) and the category of the stimulus (target or standard stimulus). Results showed that early in the time course high and low-affordance objects elicited an activation that differs in latency, amplitude and scalp distribution. Specifically, the N200 component had minor latencies and enhanced amplitude for high-affordance vs. low-affordance objects in the standard condition. Since typically the N200 amplitude is enhanced when the motor response inhibition it is more difficult, we may hypothesize that the motor inhibition for high-affordance requires minor effort compared to low-affordance objects. Thus, our data may suggest that high-affordance objects facilitates motor control, probably due to a higher activation of automatic attentional

resources. In keeping whit this, high affordance tools may foster a neural activation allowing a facilitated access to relevant information during the interaction with the surroundings.

The role of affective awareness in a social categorization task: behavioural and autonomic data

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Affective neuroscience research posits that non-conscious stimuli evoke emotion states and physiological indexes also when individuals are not visually aware of them. In this study we tested in 34 Italian participants whether subliminal and supraliminal affective priming may influence the attribution of faces to a social group. Participants' face temperature (peri-orbital region and nasal tip) during the task was measured by means of functional Infrared Thermal Imaging (fITI). This technique allows skin temperature recording by tracking changes in facial temperature with high thermal resolution. The emotional visual stimuli used for the affective priming were taken from the International Affective Picture System and the neutral faces employed in the social categorization task were taken from three validated face sets. To prevent visual stimuli to be consciously perceived, we employed the forward and backward masking technique: the target image was presented for 33 ms and it was preceded and followed by visual masks created by scrambling the target itself. During the supraliminal block the target image was presented for 500 ms. In the subsequent social categorization task, participants were asked to report whether the neutral face belonged to an in-group (i.e., Italian) vs. out-group (i.e., Romanian) individual. We fit behavioral and thermal data in a mixed model logistic regression predicting the probability of categorizing the face as in/out-group. A significant two-way interaction between negative valence and temperature (200-600 ms time bin) was present. In the negative subliminal condition the increase in orbital temperature, indexing the engagement of the ANS sympathetic division, predicted out-group categorization, while its decrease, indexing the engagement of the ANS para-sympathetic division, predicted in-group categorization. By contrast, in the negative supraliminal condition, the increase in orbital and nose temperature predicted the categorization of faces as in-group, while its decrease predicted out-group categorization. In keeping with assimilation and contrast effects in priming research, target categorization in the subliminal block was valence-driven, whereas in the supraliminal block, target categorization was opposite respect to the valence of the prime. As an emotional

regulation index, we computed the difference in orbital temperature when categorizing the face as out-group vs. in-group in the negative supraliminal condition. The difference was negatively correlated with the frequency of in-group choices suggesting that higher sympathetic activity may underpin the aversion to include strangers in one's own social group. Inclusion behavior seems to be affected by differences in emotion regulation: the tendency to transfer priming-driven affective reactions to unrelated social decisions is in fact more pronounced in individuals who show stronger increases of peri-orbital temperature when facing threat-related stimuli.

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

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

Event related potentials recorded by intracerebral electrodes

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In patients presenting with symptomatic drug resistant epilepsy, preoperative evaluation by means of intracerebral electrodes provides an opportunity to explore the neural generators of the Event-Related Potentials (ERPs). We studied 5 pediatric patients with drug resistant epilepsy. Intracerebral electrodes were implanted in frontal, temporal, and parietal lobes at different sites, depending on seizure types. Auditory and somatosensory ERPs were recorded from the intracerebral electrode contacts. The analysis was addressed to the electrode contacts where an inversion of the neurophysiological component polarity was observed or where the potential amplitude was maximal. The auditory P300 component was consistently recorded by the lead contacts located in the hippocampus with a clear phase reversal in the posterior hippocampus. The auditory mismatchnegativity (MMN) showed huge amplitude in the insularcortex, while the somatosensory N140 amplitude was maximal in the frontal lobe. Our results confirm the role of the hippocampus and the frontal lobe in the building of the P300 and N140 potentials, respectively. Moreover, they suggest the involvement of the insula in the MMN generation.

Decoding speech: multivariate classification of the Italian vocalic system through fMRI

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Human communication is based on the interplay between its acoustic and motor components to drive effortless, socially mediated acquisition and fluency. Previous evidence of a highly organized "cortical phonology" was obtained through intracranial recordings using synthesized syllables and through fMRI with natural voice though with a simplified phonemic set. We hypothesize that all the phonemes of a language are mapped discretely onto the cortex, despite their fine sensorimotor features (i.e., frequency structure, muscle synergies). Thus we collected and classified

fMRI data during listening, covert and overt articulation of the Italian vocalic system [i][e][ɛ][a][ɔ][o][u] voiced naturally and repeated 6 times within each trial type, with a slow event-related design comprising 10 GRE-EPI sequences in 11 adult right-handed Italian monolingual speakers (8 F; mean age = 26.8 ± 5 yrs) on a GE 3T scanner (TR 2.5 s; 2 × 2 × 2 mm; 37 axial slices, partial coverage). A listening-only trial was administered in 2 runs with 2 s stimulus presentation and 8 s ISI. 6 listening-plus-repetition runs were administered as well, with trials comprising 2 s acoustic stimulus presentation, 8 s ISI, 2 s repetition of the stimulus and 8 s ISI, equally divided between covert and overt repetition (3 + 3). All runs and stimuli were randomized within and across subjects. BOLD scans were preprocessed in AFNI, while T1-weighted images were nonlinearly aligned to MNI space in FSL. A 3-voxel-radius searchlight classifier was run on single-subject data from each trial type to compute rank accuracy (Acc) related to vowel discrimination. Single-subject data were subjected to a permutation test, retaining those regions whose accuracy was associated to a *p-value* < 0.05, uncorrected for multiple comparisons. The searchlight discriminated phonemes during listening in left Broca's Area (BA), insula, left/right Superior Temporal Sulcus (STS), left/right Premotor Cortex (PMC) and right ventral Prefrontal Cortex (vPFC); during covert articulation in left BA, left insula, left/right STS, left/right PMC, right vPFC; during overt articulation in left BA, left insula, right STS. Thanks to the perceptively salient nature of vowels (acting as syllabic peaks of sonority, enabling word differentiation), their cortical signature emerged at each stage of speech processing in specific regions. Interestingly, PMC, part of the human mirror neuron system, is linked to inner, but not outer, speech deficits in lesion studies: thus, our finding suggests that this area may act as the functional bridge between perception and motor control of speech, allowing for a continuous phonological rehearsal.

A P300 clustering of old patients stimulated in an immersive virtual reality scenario with Oculus Rift

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The loss of autonomy is a problem that increases with age. In this study we investigated cognitive status of elderly patients in order to define new approaches in the

design of living environments which may allow to obtain an adaptable system in terms of the deficit measured. Cognitive status was evaluated by Mini Mental State examination and through the registration of the Event-Related evoked Potentials (ERPs) P300 by means of a visual oddball paradigm. Through Oculus Rift 30 elderly subjects aged over 50 years and 18 control subjects aged between 20 and 39 years were immersed in a virtual reality in order to simulate a home environment. The target stimulus was assigned to the bathroom door that was illuminated whit white, red and green light; the frequent standard stimuli were all the other rooms. In an analysis time of 0-800 ms, we measured a positive component (P300) to isolate neural activity associated with target stimuli. In control subjects we didn't find any differences in P300 latency and amplitude after the different colors of the stimulation. For the elderly group, after white and red color of stimulation we found a significant P300 latency increase compared to the control group. When the stimulation color was green, some subjects of elderly had a response time comparable with that of the control group. These results may suggest that the latency of P300 signal elicited by oddball stimuli is strictly dependent from their colors and correlates with age. The virtual reality environment and the relative colored stimuli provided by our project seem to be feasible, sustainable and then useful to implement an innovative framework to learn how it is possible to reach a personalized design of living environment in general. In particular, we suppose that patients with different grading of cognitive impairment could take advantage to be hosted in houses or hospital rooms where the color of doors or other forniture of vital interest, could be customized by using commercial equipment provided by a domotic controller.

Repetitive transcranial magnetic stimulation of the posterior parietal cortex for the treatment of focal dystonia

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Symptoms in Focal Hand Dystonia (FHD) are associated with deficient cortical inhibition, leading to alterations in the topography and response properties of somatosensory and motor brain areas. It has been shown that inhibitory low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) over contralateral Premotor Cortex (PMC) may ameliorate FHD symptoms. However, no significant clinical improvement has been observed. On the basis of preliminary findings showing biased spatial attention in FHD and beneficial effects by 1 Hz rTMS over contralateral Posterior Parietal Cortex (PPC, i.e. a site that plays a crucial role in spatial

attention) we explored whether the parietal site might be a more effective site for rTMS treatment than PMC in ameliorating dystonic symptoms. We thus compared the effects of a weekly three days treatment over PPC with those of a three days treatment over PMC in two dystonic patients. Patient 1 (P1), a 41-year-old right-handed man, suffered by complex focal dystonia of the right hand, while Patient 2 (P2), a 43 year-old right-handed woman, suffered by a severe form of focal dystonia of the left lower limb that subsequently spread to the upper left and then upper right limb. Weekly three days sham stimulation over PMC constituted the control condition. One Hz rTMS at 90% of resting Motor Threshold was applied over the left hemisphere in P1 and over the right hemisphere in P2. There was a minimum interval of 2 weeks between subsequent treatments. Clinical and behavioral evaluation of upper limbs comprised the patients' self-estimation of dystonic symptoms, hand writing (using the right hand), finger tapping (using right and left hands), and the use of everyday objects (using right and left hands). Findings show that rTMS over PPC induced longer term beneficial effects than rTMS over PMC, in both patients, on the finger tapping task performed with the hand contralateral to stimulation. In P1 beneficial effects were also evident on the other tests (all performed with the right dystonic hand, contralateral to stimulation). The lack of evident effects in P2 on the other tests might be explained by the hand used to perform the task (hand writing was performed with the hand ipsilateral to rTMS stimulation) and by a ceiling effect due to the mildform of dystonia affecting the upper limbs. This preliminary study provides some evidence that rTMS over contralateral PPC may induce longer term improvement than over contralateral PMC on manual dexterity of contralateral hand in focal dystonia. Future double-blind placebo-controlled studies on groups of patients are needed to further explore the effectiveness of rTMS treatment over PPC in focal dystonia.

Autonomic activity and outcome in patients with severe disorder of consciousness

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Diagnosis and early prognosis of Vegetative State/Unresponsive Wakefulness Syndrome (VS/UWS) as well as its differentiation from Minimally Conscious State (MCS) still rest principally linked to the clinical observation of responsiveness. Heart Rate Variability (HRV) has been proposed as useful predictor of outcome in brain injured patients. The incidence of established clinical indicators of responsiveness also has been proven correlated to measures of HRV. A correlation between Low Frequency (LF) spectra values, severity dysfunction and outcome has been reported. We tested the trend of % of Low Frequency (%LF) in 26 patients (13 females), diagnosed as VS/UWS in according with current criteria, by mean of 5 min of ECG

recording. The first session was performed within 10 days of the hospitalization in the semi-intensive care unit, and with an interval of 10 days for a total of 4 HRV measurements for each patient. The results were tested by mean of Generalized Linear Model for repeated measures. The results showed a significant variation in %LF values in the time (p = .018) with a significant difference between the several phases of assessment (p < .05 after Bonferroni correction). Comparing the different outcomes (VS/UWS vs. MCS) a significant result was observed only in the group whose patients were later diagnosed as MCS (p = .004) with a significant increasing between the first and last assessment of %LF (p = .002). The results showed how the autonomic activity by HRV analysis can help in the prognosis of DoC patients.

The representation of word classes in the brain: an MVPA study

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This study assessed the cortical signature of the word classes of noun, verb and adjective through a multivariate, searchlight-based classifier, by testing whether word class-specific information is represented independently of both relationality (the only necessary semantic property of verbs) and word features such as imageability, concreteness and familiarity. fMRI (GE 3T) was used to examine neural activity in 15 (5 F; age: 29 ± 4 years; years of education: 18 ± 2) right-handed native Italian healthy volunteers while they performed a match-to-sample task. Stimuli were Italian verbs (e.g., *cadere* "to fall", *costruire* "to build"), nouns (e.g., *nesso* "link", *tavolo* "table") and adjectives (e.g., *simile* "similar", *sottile* "thin"), matched for form and lemma frequency, length in letters and number of core arguments of verbs. They were also balanced for relationality and rated for familiarity, imageability and concreteness by an independent group of 94 subjects. Three stimuli and a probe, always from the same word class, were visually presented for 1.5 s each, with a 6 s inter-trial interval. Subjects were asked to respond whether or not the probe stimulus was semantically related to one of the three preceding stimuli. After standard preprocessing with AFNI, the scores of the three independently controlled features were regressed out for each stimulus. Residual BOLD response was then used in a multi-class searchlight-based classifier, whose accuracies were tested as significantly

different from chance by a permutation test. Familiarity, imageability and concreteness significantly correlated with neural response within a well-known language network ($R^2 = 0.10$; $p < 0.05$, corrected for multiple comparisons). Search light analysis performed on word classes ($p < 0.05$, corrected for multiple comparisons) revealed distinct brain regions in the left hemisphere selectively engaged by verbs (posterior middle temporal gyrus, inferior frontal gyrus), adjectives (antero-lateral-temporal lobe), nouns (antero-medial-temporal lobe). This study identified selective functional brain correlates of the distinct word classes of verb, adjective and noun within a left-lateralized language network. These results provide the first robust indication of the neural underpinning of nouns and the first evidence on the representation of adjectives as grammatical category, thus making specific contributions also to the study of conceptual combination processes associated with the left antero-lateral-temporal lobe. Moreover, these data confirm the most consistent neuroanatomical findings from previous studies on verb-selectivity and provide new evidence on how word class-specific information is represented in the brain when stimuli are controlled for crucial semantic features of verbs, as opposed to other word classes, and the effect of familiarity, imageability and concreteness is ruled out.

Neural correlates of fatigue in multiple sclerosis: a diffusion tensor imaging and transcranial magnetic stimulation study

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Fatigue is a common and specific symptom in neurological diseases described as an overwhelming feeling of extreme exhaustion, and it concerns the inability to sustain a force or work rate during exercise, often defined as "objective fatigue". Many patients displaying symptoms of physical and mental fatigue have no profound weakness, persistent or progressive cognitive decline or failure of peripheral neuromuscular function. This particular type of fatigue has been termed neurasthenia, frequently reported by patients suffering from Multiple Sclerosis (MS). The pathological substrate of behavioral deficit in MS is not entirely understood and may reside both in grey matter involvement and white matter injury, with derangement of white matter tracts architecture. In order to investigate the role of connectivity alterations in the development of fatigue and behavioral impairment in MS patients, we examined 19 MS patients combining neurophysiological paradigm by means of Transcranial

Magnetic Stimulation (TMS), cognitive assessment and Magnetic Resonance Imagining (MRI) with Diffusion Tensor Imaging (DTI) based tools. DTI is a noninvasive MRI techniquethat can be used to probe the structural integrity of white matter through quantitative parameters, such as Fractional Anysotropy (FA). We were able to reconstruct the anterior thalamic projectionsand the cortical-striatetracts, finding lower FA values in the right hemispheres, which results in weaker connectivity in patients compared with controls. In addition, we analysed the thalamic and basal ganglia volume, showing a significant atrophy of striatum and thalamus in fatigued patients, correlated to the neurodegenerative process of the striatum-thalamus loop. We assume that fatigue and cognitive impairment could be related to micro-structural impairment of white matter tracts of the cortical-subcortical-cortical loop.

Visual spatial attention modulates brain electrical response in hemianopic patients with left or right brain lesion: a SSVEP study

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Hemianopia is a visual defect characterized by decreased or absent vision in one hemifield contralateral to a lesion along the post-chiasmatic visual pathways. Steady State Visual Evoked Potentials (SSVEP) is a technique where a flickering visual stimulus is presented and a continuous sequence of oscillatory potential changes is elicited in the visual cortex. This technique can be very useful to detect residual unconscious responses to visual stimuli presented to the blind hemifield of hemianopic patients. The aim of this study was to evaluate the effect of visual spatial attention on brain electrical activity in the blind visual field of right or left hemianopic patients. We carried out two SSVEP experiments, a passive stimulation and a spatial attention task in one left hemianopic patient (CL), one right quadrantanopic patient (GA) and a control group. A 2° flickering black and white sinusoidal Gabor grating was used as stimulus. During passive stimulation the grating was presented with a reversal rate of 12 Hz in each of 4 quadrants (flickering one at a time). Participants were to fixate a central point. Results in the passive condition showed clear sinusoidal waveforms modulated to 12 Hz with a contralateral (with respect to the flickering stimulus) topography in posterior electrodes. Comparisons between the patients and the control group showed a deficit in the frequency power in the blind visual

field in GA while in CL the deficit was observed in both blind and intact lower visual fields. In the spatial attention task the same stimulus was presented with a reversal rate of 11 Hz in the lower left and 13 Hz in the lower right fields. Participants were asked to attend either to the right or to the left quadrant and to press a button when the stimuli changed their orientation. Behavioral results showed a marked deficit in both patients in both blind and intact visual fields but worse in CL than GA. In all participants SSVEP analysis revealed larger frequency power in attended than unattended conditions mainly in the contralateral topography. GA showed no differences in the effect of attention in comparison with the control group in the blind visual field while in the intact visual field a larger frequency response than in the control group was observed. In contrast, in CL there was a deficit in the blind visual field for both attended and unattended conditions while the response in the intact visual field was similar to that of the control group. All in all, we conclude that attention can modulate brain electrical activity in the blind visual field of hemianopic patients even in absence of behavioral response and awareness of the stimulus.

Is error monitoring a graded or an all-or-none process? An EEG study in immersive virtual reality

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In immersive virtual reality, merely seeing an avatar from a first-Person Perspective (1PP) induces the feeling of being the owner (Ownership) of the artificial body and of controlling its actions (Agency). Recent findings from our laboratory show that observing from a 1PP execution errors in the avatar's actions elicits typical electrocortical signatures of error monitoring as the Error Related Negativity (ERN) and the Medial-Frontal Theta (MF-Theta) band power synchronization. Whether error-related EEG signals reflect a discrete or a continuous process of error monitoring remain still debated. Here we aimed to investigate whether the mere observation of two different magnitude, erroneous reach to grasp actions performed by an embodied virtual limb seen from a 1PP, induces different ERN amplitudes and MF-Theta power synchronization in the onlooker's brain. EEG was recorded in twenty-two healthy adults immersed in a virtual scenario (CAVE system) and in a one-to-one scale virtual body seen from a 1PP. Participants observed correct or incorrect reach-to-grasp a glass actions performed by the right avatar's limb. Small or large deviations could occur in incorrect trials consisting in right-ward arm-path deviations from to be grasped glass. At the end of the avatar's actions participants verbally rated how much they experienced Ownership and Agency over the virtual arm by uttering a number on a 7-points Likert scale (where 1 and 7 indicate no and maximal owner-

ship/agency, respectively). Results showed that the magnitude of avatar's errors did not modify rating scores of Ownership but reduced rating scores of agency. Moreover, ERN was elicited by observation of both small and large incorrect grasps with higher amplitude in the latter than the former condition. Similarly, the MF-Theta was synchronized for incorrect grasps only with ampler values in the large incorrect grasps. In addition, higher level of Ownership predicted ampler ERNs in the large incorrect grasps. These findings expand previous knowledge on the link between sense of ownership and agency, mere observation of a virtual body from a 1PP and electro-cortical signatures of error monitoring. The error monitoring EEG signatures seem linearly affected by the magnitude of the arm-path deviations suggesting that the processing of kinematic errors is continuously active when monitoring errors in the actions of others and that. Moreover, EEG signatures of error processing may reflect the analogical processing of the conflict between intended and actual responses suggesting that error monitoring occurs according to a fine-grained graded process.

Neuromodulation of insight processes by the means of non-invasive brain stimulation: a tACS and tRNS study

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Insight process, also called the "Eureka" or "Aha!" experience, is defined as an unexpected and sudden realization of the solution to a problem, popping in mind after an unconscious elaboration of problem's items. Tightly linked with creativity and fluid intelligence, insight often represents the way in which many scientific discoveries emerge to consciousness, e.g. Newton's gravitation law and floatation's principle of Archimede, but it also represents a crucial element for everyday problem solving abilities. The aim of the present study was to enhance insight capability in healthy

subjects by means of transcranial Electrical Stimulation (tES). Thirty-one healthy participants were asked to solve an insight task (Compound Remote Associates test, CRA) while receiving transcranial alternating current stimulation (tACS, at 10 Hz and 40 Hz) and transcranial Random-Noise Stimulation (tRNS, 100-500 Hz) over right parietal (10-20 system = P4) and temporal (10-20 system = T8) lobes. Before the first stimulation session, subjects performed an extensive neurocognitive assessment including fluid intelligence, IQ and executive functions tasks, together with a psychological evaluation. Participants also performed a functional MRI acquisition to correlate the behavioural response to tACS-tRNS with fMRI resting-state pattern before the neuromodulation intervention. Finally, electroencephalography (EEG) was also recorded before each stimulation block. Results revealed a frequency-dependent effect for tACS stimulation respect to Sham condition. Specifically, 40 Hz-tACS on P4 induced an increase of 45% in accuracy in most difficult items and an increase of 40% in medium difficulty items; stimulation over T8 caused an improvement of 28% in accuracy for difficult trials. 10 Hz-tACS stimulation on P4 led to reaction time decrease (-28%) in correct answer of medium difficulty items, while the same stimulation over T8 caused a decrease (-25%) of correct answers provided by subjects on easy trials. As for tRNS, when applied on T8 it enhanced accuracy (+28%) in most challenging items, while stimulation of P4 caused a decrease of reaction time for correctly solved medium difficulty trials (-27%). No improvement was found with stimulations of left hemisphere both on the prefrontal (F3) and parietal lobes (P3). The present results show the involvement of right parietal and temporal regions in insight-problem solving, and possibly suggests distinct neurophysiological substrates for the effects of tACS and tRNS, which differently affect performance in terms of reaction times and accuracy. We hypothesize that this differential effect could reflect two steps of insight problem solving: the inhibition of common representation of the problem (mediated by alpha oscillations) and the following discovery of new association(s) suddenly emerging to consciousness (promoted by gamma activity).

Cortical inhibition of laser-pain and laser evoked potentials by non-nociceptive somatosensory input

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Although the inhibitory action that tactile stimuli can have on pain is well documented, the precise timing of the interaction between the painful and non-painful stimuli in the central nervous system is unclear. We aimed to investigate this issue by measuring the timing of the amplitude modulation of Laser Evoked Potentials (LEPs) due to conditioning non-painful electrical stimuli. LEPs were recorded from 31 scalp electrodes in 10 healthy subjects after painful stimulation of the right arm (C6-C7 dermatomes). Non-painful electrical stimuli were applied by ring electrodes on the second and third finger of the right hand. Electrical stimuli were delivered at 50 ms, 150 ms, 200 ms, and 250 ms Inter-Stimulus Intervals (ISIs) after the laser pulses. LEPs obtained without any conditioning stimulation were used as a baseline. As compared to the baseline, non-painful electrical stimulation reduced the amplitude of the vertex N2/P2 LEP component and the laser pain rating when electrical stimuli followed the laser pulsesat +150 ms and +200 ms ISIs. Since at these ISIs the collision between the non-painful and painful input is likely to take place at cortical level, we conclude that the late processing of painful stimuli is inhibited by the processing of non-painful stimuli within the cerebral cortex. Moreover, our results do not provide evidence that non-painful inputs can inhibit pain at a lower level, including the spinal cord.

Remote control of a humanoid robot through brain computer interface in healthy and spinal cord injured people

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The efficient control of our body and the successful interaction with the environment are possible through the integration of multisensory information. Advancements in Brain Computer Interface (BCI) may allow people with sensorimotor diseases to actively interact in the world through the control of remote surrogates. Crucially, the understanding how multisensory signals contribute to control external devices is still meager. Recently we tested the role of human footstep sounds as auditory feedback in facilitating the use of a remote BCI-controlled surrogate during a pick-and-place navigational task (BCI-users and Humanoid robot located in Rome-Italy and Tsukuba-Japan respectively). In particular, a synchronous auditory feedback with the humanoid's real footsteps reduced the time required to complete the task. In a new study we tried to replicate this preliminary finding in a novel group of healthy subjects and a small sample of Spinal Cord Injured (SCI) people. Participants were asked to complete a similar navigational task controlling a remote robot by means of a steady state visual evoked potentials BCI system. Participants observed the remote environment from the robot's perspective through a head mounted display. Body-related (human footsteps) and non-human (computer-beep) sounds were used as synchronous/asynchronous auditory feedback. Performance measures (object placing accuracy and time required to complete the pick-and-place scenario) and subjective reports about the experience of observing a remote environment from the robot's point of view were analyzed. Healthy participants had better placing accuracy when the human footstep sound (synchronous and asynchronous), relative to a computer-beep sound, was paired with the humanoid footsteps. On the contrary, SCI people demonstrated more difficulty in steering the robot during asynchronous auditory feedback conditions. Importantly, subjective reports highlighted that the BCI mask overlaying the remote environment with the flashing stimuli did not limit the observation of the scenario and the feeling of being in control of the robot. Pairing visual information with body-related auditory feedback may improve the way in which BCI-users control a remote device. Moreover, the fact that SCI people presented more difficulty in completing the task suggests that our understanding about the structural and functional brain changes following a spinal lesion may be crucial for improving the flexibility of BCI systems. Overall, our data seems to suggest that

sensorimotor-related information may help BCI-users to control external devices and further studies are required to understand how the contribution of residual sensory channels could improve the reliability of BCI systems.

Skin temperature modulations underlying the feeling of ownership over a virtual hand

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Observing a virtual body from a first-Person Perspective (1PP) typically induces an illusory Feeling of Ownership (FO) over the virtual body or its parts. Studies demonstrate that FO is indexed not only by subjective reports but also by changes of autonomic reactivity (e.g. heart rate, skin conductance, and skin temperature measured with standard thermometers). In the present study, we combined Immersive Virtual Reality and thermal imaging to explore whether the FO over a virtual limb affects the skin temperature of the participant's real limb. Twenty-four healthy participants placed their hands on a table in a fixed position and wore an Head Mounted Display through which they saw from a 1PP a virtual body having same dimension and position of their real one. While the virtual body's left limb was occluded by a virtual panel, the right one could appear as: (1) a normal limb, (2) a limb with the hand detached because of a missing wrist, (3) a wooden block and (4) a wooden block with the extremity detached because of a missing piece of wood. Participants observed each condition in four separate sessions each lasting 3 minutes. Participants were asked to focus their attention on the virtual right limb and, at the end of each session, to answer a 12-items questionnaire concerning the strength of the perceived ownership over the virtual right hand by means of a 7-point rating scale. Finally, during each session participants were asked to report when they started to feel the illusion of FO. During the whole session the skin temperature of both experimental (right) and control (left) hand was continuously recorded by a high-sensitivity Infrared Thermal Camera. Observation of the full limb condition (1) brought about the highest level of FO and a significant reduction of skin temperature of both hands compared to the other observation conditions (2, 3, 4). Moreover a negative correlation was observed between subjective ratings and skin temperature suggesting that the higher the FO over the normal limb the lower the skin temperature. Finally, the analysis of the skin temperature over time in the condition 1 revealed that the

modulation started after ~35 seconds from when participants started to feel the illusion (mean: 44.3 sec). These results demonstrate that the illusory ownership over a virtual hand, elicited by a mere passive observation, is reflected in a modulation of the autonomic mechanism underlying the skin temperature regulation.

Methods in detecting interictal epileptiform discharges using magnetoencephalography: a preliminary experience

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Magnetoencephalography (MEG) is an essential neuroimaging tool for presurgical evaluation in patients affected by intractable epilepsy. Interictal MEG recordings were performed in patients affected by drug resistant partial epilepsy. We used a CTF MEG™ 275 system combined with a 3 layers Magnetically Shielded Room (MSR). High spatial sampling density was guaranteed by 275 individual sensor channels (axial gradiometers), while a SQUID design engineered to maximize signal-to-noise ratio assured a white noise level of sensors lower than 10 fT(rms)/√Hz. A 64 channel EEG (56 unipolar channels, 8 bipolar channels) sub-system was included in the equipment. We recorded MEG and scalp EEG simultaneously in order to collect at least 20 minutes of eye closed multimodal spontaneous data. The sampling rate for data acquisition was set to 1200 Hz. Scalp EEG was recorded from 21 electrodes (monopolar channels) placed according to the International 10-20 System. Advanced Continuous Head Localization technology (CHL) was used to ensure a more precise localization of brain activity. We tested a small sample of patients diagnosed with epilepsy (N = 3) before they underwent neurosurgical intervention. First, we located EEG epileptiform discharges (spikes, polyspikes and sharp waves) with a band pass filter of 1.6-30 Hz. Then, we used a standardized scheduled method to identify MEG interictal epileptiform discharges by reviewing solely the 275-channel MEG waveforms band pass filtered between 10 and 70 Hz, and a time line of 0.75 sec/cm. Finally, we selected interictal spikes using both MEG and EEG, simultaneously, in order to better visualize epileptiform activities. Instead of averaging spikes for dipole source localization, we analyzed individual spikes to obtain the extent of the possible epileptogenic zone. We selected the earliest spike peak showing a reasonable magnetic field topography for dipole source analysis and we marked it with a cursor. When continuous spikes occurred we selected just the events with a temporal distance higher than 1 second. For each spike, ECD (Equivalent Current Dipole) analysis was done in a 100 ms window (50 ms before and 50 ms after the peak of spikes). Dipole sources locations were classified in two groups: cluster and

scatter. Cluster occurs when 6 or more dipoles are adjacent within 1 cm or less; scatter occurs when there are fewer than 6 dipoles (regardless of the distance between them) or when there are dipoles located at a distance greater than 1 cm (regardless of the number of dipoles). We were able to detect MEG dipole clusters in 2 out of 3 patients, suggesting that those epileptogenic zones might require surgical ablation. MRI showed focal cortical dysplasia in only 1 out of 3 patients. Further investigations are needed to confirm these preliminary results.

A new method for sham-controlled acupuncture in experimental visceral pain

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This study aimed to investigate the validity of a new method for sham acupuncture in experimental visceral pain. Fifteen subjects underwent a sequence of either sham stimulation or acupuncture followed by visceral experimental pain stimulation. Experimental pain was induced by rectal stimulation with an inflatable balloon. The balloon was distended until the pain threshold was reached. Before and after intervention, an electroencephalogram (EEG) was recorded for 2.5 minutes to explore central effects of acupuncture. Only 5 participants (36%) were able to indicate the correct sequence of sham and acupuncture (p = 0.4; compared to chance level). A significant increase in balloon volume was observed after sham acupuncture (p = 0.049) and acupuncture (p = 0.046). However, the change in rectal balloon volume was not different between groups (p = 0.6). No differences in EEG spectral power distributions between sham stimulation and acupuncture were seen (all p > 0.6). The presented sham procedure provides a valid method for blinding of "sham acupuncture" and may be used in future blinded controlled trials of acupuncture for visceral pain.

Two-in-one: inter-brain hyperconnectivity during cooperation by simultaneous EEG-fNIRS recording

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Hyperscanning is a quite recent paradigm in neuroscience which consists in the simultaneous recording of the cerebral activity of two or more subjects involved in interactive tasks. This measure allows to explore inter-personal brain mechanisms underlying and generated by social interactions, when participants are continuously modifying their own actions according to the partner's ones. Previous studies showed that this mutual adaptation results in interactional brain synchrony to which all members contribute; accordingly, these mechanisms are involved only during interactive social relations and cannot be captured by conventional single-subject recordings. However, hyperscanning research recurred to either electrocortical or imaging techniques to explore the temporal dynamics or the brain networks involved in interactive behaviors but, to our knowledge, there are no previous attempts to acquire both measures jointly. Thus, the aim of the present study was to investigate the cognitive processes underlying the execution of joint cooperative actions performed by couples of subjects by means of a multi-method hyperscanning technique. We aimed at assessing to what extent cortical synchronization, in both electrophysiological (by EEG) and hemodynamic (by fNIRS) components, could emerge between two brains during cooperation. Also, we intended to explore arousal-related peripheral responses during the task. To explore these issues, 14 participants paired as 7 dyads were recorded with dual-EEG and dual-fNIRS setups while they were engaged in an attentive task finalized to engage cooperation. After a resting period which served as control condition, the task was sub-divided in 8 blocks with a pause halfway assessing the goodness of the cooperation scores. Thus, inter-brain activity coherence over the prefrontal regions was calculated between the two participants across blocks. We found that the coherence between the two signals varied across blocks in accordance to the perceived degree of cooperation. Such differences point toward a modulation between the two subjects' brain activity as a function of the task, with respect to control conditions. This work represents the first use of dual-EEG/dual-fNIRS setups for simultaneous measurements of brain-to-brain coupling and endorses the use of hyperscanning techniques for social interactive studies in naturalistic environments.

Combined EEG/EMG evaluation during a novel dual task paradigm for gait analysis

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Little knowledge is available about neural dynamics during natural motor behavior and its perturbation in aging and neurological diseases. In the present study, we aimed to evaluate electroencephalography-electromyography (EEG-EMG) co-registration features of rest and walking in basal condition and under cognitive tasks in normal subjects, in order to characterize a "normal gait" and to define the possible paradigm to detect abnormal behavior. We realized EEG-EMG co-registration in 17 healthy subjects in different conditions: (1) sitting; (2) standing; (3) walking. A P300 acoustic oddball paradigm was performed during (4) standing condition and (5) during walking. The 10-60 and 60-90 Hz frequency range EMG analysis of the four muscles examined (left and right tibial, left and right gastrocnemius) confirmed a significant increase of EMG activity in the four muscles in walking condition compared with standing and sitting conditions (Bonferroni: walking vs. seated and standing $p < 0.0001$). This EMG activity was not modified in the performance of the cognitive task during walking. The P300 amplitude increased during walking compared to standing condition (ANOVA: $F = 7.52$, $p = 0.008$), while there were no significant changes in latency. The EEG analysis showed a reduction in the μ-rhythm during execution of the cognitive task in static condition and a significant increase in temporal-frontal derivations under dynamic conditions. These variations were not age related. A coherence analysis between EEG and EMG rhythms showed a cross-correlation between 7-12 Hz EEG rhythm and the frequency spectrum of the agonist and antagonist muscles during walking, which was reduced while performing cognitive task of P300 paradigm. The P300 component amplitude increases during physical activity. The negative correlation between age and P300 component vanishes during gait. The spectral width of the total alpha rhythm appears reduced in the course of P300 in a static situation, this is likely a phenomena of desynchronization related to cognitive task. During gait, the activity is canceled, suggesting a state of "idling" of cortical areas previously involved in the target stimulus recognition process. The movement encourages cognitive activity, offsetting the age-related deficits. Although apparently the cognitive task does not alter the muscle recruitment, it produces a strong cortical activation and reduces the coherence between cortex and effector, in a more evident way in older subjects. More evident results could be outlined performing the same analysis on subjects with impaired mobility.

Functional connectivity under painful stimulation in migraine

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In previous studies migraine patients showed some abnormalities of pain related evoked responses, as reduced habituation to repetitive stimulation. In this study we aimed to apply a novel analysis of EEG bands synchronization and directed dynamical influences under painful stimuli in migraine patients compared to non migraine healthy volunteers. Thirty-one migraines without aura outpatients (MIGR) were evaluated and compared to 19 controls (CONT). The right hand was stimulated by means of 30 consecutive CO2 laser stimuli. EEG signal was examined by means of Morlet wavelet, synchronization entropy and Granger causality, and the statistic results embedded into a scalp model. The vertex complex of averaged Laser Evoked Responses (LEPs) showed reduced habituation compared to controls. In the pre-stimulus phase enhanced synchronization entropy in the 0.5-30 Hz range was present in MIGR and CONT between the bilateral temporal parietal and the frontal regions around the midline. Migraine patients showed an anticipation of EEG changes preceding the painful stimulation compared to controls. In the post-stimulus phase, the same cortical areas were more connected in MIGR vs. CONT. In the totality of patients and controls, the habituation index was negatively correlated with the Granger Causality scores. A different pattern of cortical activation after painful stimulation was present in migraine. The increase in cortical connections during repetitive painful stimulation may subtend the phenomenon of LEPs reduced habituation. Brain network analysis may give an aid in understanding subtle changes of pain processing under laser stimuli in migraine patients.

Human-human and human-animal interactions: ERPs measures and empathic concern

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Empathy commonly refers to the emotional concern aroused by the affective state of another living person and its importance in creating meaningful social bonds led to the publication of a large amount of papers with the intent to explore brain mechanisms underlying these salient social interactions. Despite the great majority of studies focused on human-human contexts, we do not establish relations with only other humans, but also with non-human animals. The aim of the present work was to explore brain responses (Event-Related Potentials, ERPs: N300 and P300) involved in empathic resonance mechanisms between humans (human-human, HH) or between humans and animals (human-animal, HA) taking into account the specific role of DLPFC in response to interactions with different emotion valence (positive vs. negative). The second aim of this research was to explore the direct relation between the cortical response to high impact emotional contexts and the personality empathic profile as assessed by Balance Emotional Empathy Scale (BEES) and Interpersonal Reactivity Index (IRI). To verify these effects, a 16-channel portable EEG-System was used to record the electrocortical activity of 15 participants (7 females, 8 males) while passively viewing the affective interactions. Results showed that both HH and HA interactions elicited significant N300 and P300 peak amplitude increasing in response to positive and negative compared with neutral interactions. However, N300 was mainly related to valence effect, with increased peak amplitude for negative patterns (negativity bias), irrespectively from condition, and distributed over the frontal sites (left and right DLPFC). P300, instead, was modulated by the relevance of the interactive context independently from the valence effect and was frontally and parietally distributed. Finally a significant relation was found between emotional empathy trait (BEES) and N300 peak amplitude. These results are discussed in light of the significance that different species-specific and species-aspecific relationships have in establishing meaningful empathic responses.

EEG and autonomic response to pleasant touch: an insight in healthy subject and in patients with disorders of consciousness

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Touch is central to human social life. It is one of the first approach in primates, to communicate emotions. Different studies have been performed to prove that touch can convey more positive emotions than other modalities; nevertheless very little is known about emotions in patients with Disorders of Consciousness (DOC). Could they feel emotions? What kind of emotion can be perceived and what are the modalities to convey emotions? Here we focused on affective touch. The aim of this study is to characterize the autonomic and EEG response to affective touch (caress) in healthy subject, and to find out if the same or other responses could be detected in patients with DOC. We recorded autonomic parameters (electrodermal response EDA, heart rate variability HRV, Breath) and EEG in 32 healthy participants and 4 patients with DOC. Psychological tests were administered to healthy subjects. The whole experiment was divided into two consecutive phases: the automatic caresses with a device developed by the Faculty of Engineering and the human caresses provided by an operator at the same velocities and forces levels. Throughout the experiment, there were three phases of resting sessions with a duration of two minutes: the first at the beginning of the protocol, another between the automatic caresses and the human caresses and the last at the end of the manual stimulation. In the two phases of emotional stimulations six combinations of different velocities and forces were suitably randomized, with a pre-stimulus and a post-stimulus interval of 35 seconds each. The presentation of the six kinds of caress-like stimuli was randomized among subjects. Regarding EEG results, for healthy subject two distinct patterns were observed: concerning the robotic caress we found a suppression of the oscillation over the contralateral somatosensory cortex during caresses performed with the lower force and the highest velocity in alpha and beta bands. This phenomenon has already been described previously as the well known suppression of low frequency alpha/beta (μu) oscillations in electrodes over the left somatosensory cortex contrololateral to the stimulation. The manual caress didn't modify significantly EEG activity. Interestingly for the highest force both the robotic caress and the manual one induced a decrease in EEG oscillation activity ipsilateral to the stimulation in alpha band but not in gamma. This could be due to an increase of the arousal, as the highest force is not comfortable for the subject. The analysis of the autonomic parameters confirmed the trend observed. In fact LF/HF ratio increased proportionally to the velocity of the caress, this is due to an increase of the sympathetic activity and a

decrease of the parasympathetic activity (increase of the arousal) and the statistical analysis of the psychological test confirmed it. Regarding patients, the main finding is that the manual caress at the lower force produced an increase of the EEG power in the alpha band in three out of four patients. That could be explained as a relaxation due to the pleasantness of the caress.

Three-chord harmonic sequences with unexpected out-of-key endings: are they suitable stimuli for eliciting N400 responses?

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Music-elicited N400 responses are usually obtained by using musical targets consisting of short musical excerpts in combination with word primes. The N400 obtained in response to those stimuli is believed to reflect the processing of extra-musical meaning, with reference to the relationships between concepts conveyed by music and words semantics. The aim of this study was to verify whether a completely musical stimulus (i.e., with music as prime and music as target) is able to elicit N400 responses as well. For this purpose we employed a new stimulus composed of the minimum number of chords necessary and sufficient to enable the subject to predict a plausible closure of the sequence (priming) and, at the same time, to provide him/her with the closing chord of the sequence (target), either congruous (probable closing) or not (improbable closing) to the tonal context. Subjects had to discriminate and recognize the irregular targets (i.e., the out-of-key endings of the sequence) according to a classic odd-ball paradigm. ERPs components were extracted from 19-channels EEG traces recorded from eight healthy subjects. The statistical reliability of ERP components was assessed by means of non-parametric Wilcoxon test. Moreover, both the corresponding surface electric fields (2D scalp-maps) and cortical current densities (sLORETA) were studied. In all subjects participating in the study, together with the classical ERAN, N5, and P600/LPC components, a N400 wave was also obtained. We deem that this is a true N400, given the complete overlapping of polarity, latency, and topographic distribution to the classic N400 waves. Furthermore, our chord-primed chord-elicited N400 seems to share with the word-primed music-elicited N400 certain generators that are located on the posterior part of both the right medial temporal gyrus (BA 21/37) and the superior temporal gyrus (BA 22). This suggests that even chord-primed chord targets can convey extra-musical meanings.

Selective attention impairment in amyotrophic lateral sclerosis

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Aim of this study was to evaluate attentional control mechanisms in Amyotrophic Lateral Sclerosis (ALS) using an auditory Event-Related Potentials (ERPs) paradigm. Fifteen mild to moderate ALS patients and 15 healthy controls were administered a brief neuropsychological test battery and an ERPs paradigm assessing selective attention. Four types of auditory stimuli were presented in random order: short standard (200 Hz, 200 ms), long standard (200 Hz, 500 ms), short deviant (1000 Hz, 200 ms) and long deviant (1000 Hz, 500 ms). Participants had to respond to the long deviant stimuli only. During the task the electroencephalogram (EEG) was recorded. The N200, P300 and Re-Orienting Negativity (RON) ERPs components were analysed. Compared to controls ALS patients showed reduced amplitudes and delayed latencies of N200, P300 and RON suggesting an alteration of the cognitive processes involved in change detection resulting in a reduction of the allocation and re-orientation of attentional resources. The ERPs results support the hypothesis that ALS involves extramotor cognitive functions including auditory attentional processing at all processing stages, early (200 ms) and late (300-600 ms). Altogether the data obtained in this study support the hypothesis that ALS is a multisystem disease with extra motor involvement of cognitive functions and provides further evidence that the ERPs represent an effective tool for evaluating and monitoring cognitive functions of ALS patients requiring only minimal motor responses.

Impaired self-confidence in motor monitoring by tDCS of the right premotor cortex

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The monitoring of motor performance is fundamental for optimal motor control and learning. Computational models of motor control suggest the existence, in the human brain, of a "comparator" mechanism, dedicated to action monitoring, which detects the congruence between the intended and the actual movement. In this study, a double-blind, sham-controlled experiment in healthy right-handed participants (N = 14), we aimed at interfering with the activity of such a comparator by means of cathodal transcranial Direct Current Stimulation (c-tDCS), delivered to the Premotor Cortex (rPM) or to the Posterior Parietal Cortex (rPPC) of the right hemisphere. Participants performed a 2-digit sequence motor task with their left – non-dominant – hand, while receiving single-pulse Transcranial Magnetic Stimulation (spTMS) over the right primary motor cortex, contralateral to the performing hand. By evoking involuntary muscles twitches in the contralateral left hand, spTMS was used to disrupt, trial-by-trial, the participant's motor response during the task. At the end of the task, monitoring and awareness of motor performance was assessed by a questionnaire. c-tDCS to right PM, but not sham or parietal c-tDCS, impaired the participants' ability to reliably evaluate their motor performance, making them self-doubting about their judgements at the questionnaire. Moreover, the correlation between the errors induced by sTMS to M1, and the participants' report of having committed more errors, was positive and significant, after both sham and PPC c-tDCS; conversely such a correlation was not significant, after rPM c-tDCS. In line with computational and neuropsychological models of motor control and awareness, the present findings support the existence of a mechanism in the right PM, which monitors and compares intended vs. actual movements, evaluating their congruence. Motor monitoring becomes less efficient after c-tDCS to the rPM, impairing the participants' ability to reliably evaluate their motor performance.