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**The functional role of ventral Premotor Cortex in motor monitoring of voluntary actions: an fMRI study during mechanic limb immobilization.**

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# Neuropsychological Trends

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Abstracts  
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SYMPOSIA ABSTRACTS

**Social brain and recurrent connections**

**Avenanti A.**

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Our social life crucially depends on the ability to process emotional signals from other people. The Superior Temporal Sulcus (STS) is a key brain region for the visual analysis of facial and bodily movements. Yet, it is unclear how the human STS interacts with the primary visual cortex (V1) to support the ability to recognize emotional expressions. Here, we tested the hypothesis that functional connections from the STS to V1 are causally essential for emotion recognition. To establish the timing of such connections, in a first TMS/EEG coregistration study, we recorded TMS-evoked potentials (TEPs) induced by STS stimulation. Thus, TEPs reflected the activation spread propagating from STS to functionally connected regions. TEPs over occipital electrodes were maximal at ~200 ms from the TMS pulse, suggesting this late TEP component reflected a complex and indirect pathway from STS to V1. Based on this temporal information, we developed a novel cortico-cortical Paired Associative Stimulation (ccPAS) TMS protocol aimed at inducing Hebbian associative plasticity between the right STS and V1. In a series of ccPAS experiments, we administered pairs of TMS pulses over these two regions to repeatedly activate the pathway between them. In a critical ccPAS condition, the first TMS pulse was administered over STS followed by another pulse over V1. The two areas were stimulated with an optimal inter-stimulus interval of 200 ms (derived from the TEPs experiment), so to enhance the synaptic efficiency of the STS-to-V1 pathway. Participants were tested in an emotion recognition task or a difficulty-matched gender recognition task. In different experiments, task performance was acquired before and after the critical STS-to-V1 ccPAS protocol or other control ccPAS conditions. We found that the critical ccPAS protocol aimed at strengthening reentrant connectivity from STS to V1 (but not in the opposite direction) enhanced the human ability to visually recognize emotional expressions. No changes were detected in the gender recognition task. The enhancement in emotion recognition followed the temporal profile of Hebbian plasticity and was observed only when the optimal ISI of 200 ms was used, not when TMS pulses were delivered at an ISIs of 0 or 100 ms or when sham ccPAS was administered. Thus, plastic changes were critically dependent on both the direction and timing of connectivity; if either of these requirements was not met, perceptual enhancement did not take place. We therefore provided novel causal evidence that STS-to-V1 backward connectivity is functionally malleable and causally essential for accurate emotion recognition. Although the stimulated STS-to-V1 pathway is likely indirect, our study suggests this pathway is functionally specific as performance improved only in the emotion recognition task. These findings have implications for theoretical models of emotion recognition and visual perception.



## **Motor cognition in healthy and pathological aging: a study on motor imitation in Alzheimer's Disease**

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Alzheimer's Disease (AD) is the most common form of dementia that causes a decline of intellectual functioning that interferes with daily life activities. Although in the early stage of AD pathological alterations in the medial temporal structures may account for the memory impairments, in mild and moderate stages a significant loss of volume could be observed also in frontal and parietal lobes, areas involved in the link between action and perception. The coupling between action and perception, mechanisms known as motor resonance, is crucial to allow humans to efficiently communicate with other people and to interact with the environment, a function that is markedly deficient in AD. Despite these alterations, in a recent paper we showed that after the observation of an abstract moving stimulus the motor response of AD patients was automatically influenced by its features, suggesting the preservation of motor resonance mechanisms, expressed in the form of automatic imitation. Nevertheless, when AD patients face more challenging tasks, which encompass high-level processes of motor cognition, such as the voluntarily imitation of the features of an observed movement, the cognitive deficits resulting from the disease might negatively affect patients' response. Aim of the present study was to investigate whether voluntary motor imitation, i.e. a volitional mechanism that involves observing another person's action and translating this perception into one's own action, was affected in AD patients. Further, we tested whether this ability was modulated by the nature of the observed stimulus by comparing the ability to reproduce the kinematic features of a human demonstrator with that of a computerized stimulus. AD patients showed an intact ability to reproduce the velocity of the observed movements, particularly when the stimulus was a human agent. This result suggests that high-level cognitive processes involved in voluntary imitation might be preserved in mild and moderate stages of AD and that voluntary imitation abilities might benefit from the implicit interpersonal communication established between the patient and the human demonstrator.

## **Blink-related EEG: a look into consciousness**

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The reason why we blink (on average about 15 times per minute, at rest) still eludes in part our understanding, but certainly goes beyond the simple moistening of the cornea, since a lower number of blinks would be enough. The Blink Rate (BR) undergoes a maturation process from birth to adulthood, which is parallel to the development of the CNS and the awareness of self and world. Situations requiring visual attention significantly reduce the BR. During reading or watching films, the BR is reduced compared to resting, but single blinks cluster into defining moments, such as reading pauses or scene changes. It is as though the subject minimized the chance of losing some essential information by avoiding blinking and then recovered in moments when important information is absent. Moreover, it is known that blinking reflects the change in the attentional

focus. It allows the disengagement from a target (either visual or mental), the shifting and the engagement on a new one. Therefore, two successive blinks define a time span where attention and related processing are active. Thus, each blink closes the previous attentional span and opens the next one, acting as a pacemaker of the segmentation of cognitive processes, which are characterized by alternating phases of attention/processing and short-term memorization. The blink certainly represents a moment of discontinuation of the information flow, but also contains within itself the element to overcome that interruption (i.e. memorization), while also serving as a connecting element between a before and after. It is interesting to note that attention and short-term memory are considered basic elements of primary consciousness. In fact, attentional focus displacements enable the interaction between subject and environment, while subsequent memorization allows us to keep trace of these interactions, thus ensuring the continuity of the stream of consciousness. Compared to conventional analysis of the resting state EEG, where recordings are usually performed with eyes closed or epochs invalidated by blink artifacts are discarded (thus paradoxically losing the activity of interest), the analysis of EEG modulations associated with spontaneous blinking introduces a new dynamic element (i.e. the blink) to be considered as an anchor point for both time- and phase-locked analyses. Cortical sources of multi-band blink-related oscillations have been recently localized in the precuneus, which is considered responsible for the representation of self in relation to the outside world and candidate as a possible interface between self and out-of-self. Interestingly, the spectral parameters of these oscillations showed a close relation with levels of consciousness in patients with disorders of consciousness and have been able to differentiate at group level patients with minimally conscious state from those with unresponsive wakefulness syndrome.

## Temporal aspects of action observation in sport

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The processing of time-dependent features of movement has a crucial role in predicting whether the outcome of a complex motor sequence is consistent with its ultimate goal or results instead in an execution error. Recently we investigated in a group of swimmers whether the ability in predicting the temporal outcome of sport motor actions is influenced by the motor skills learnt. Further, we also studied the effect of observation of temporal errors in the action execution on the observer's motor system. This was done by investigating how different spatio-temporal patterns in the execution of a soccer action can affect corticospinal excitability in soccer experts and novices. In the first study, 30 swimmers, 30 water polo players, 30 rhythmic gymnasts, and 30 control subjects, were recruited for the study. The experimental session consisted of watching a video showing a swimmer doing two laps in crawl style. This video was presented on a computer screen for 36 times. Each time the video was interrupted after a variable interval from its onset by a dark window of variable duration (3, 6 and 12 s) randomized across trials. During the dark interval, subjects were asked to indicate when the subject in the video reached the poolside by clicking on any button of the laptop keyboard. We found that for the 3 s dark interval the absolute value of timing error, representing the temporal prediction, was significantly

lower in swimmers with respect to the other groups. In the second study, 16 soccer players (Soccer\_Group) and 10 novices (Novice\_Group) were recruited and asked to watch two videos representing a correct soccer action, where a pass was performed with the correct timing, and a delayed action, where the pass was delayed with respect to the play development. Corticospinal excitability during Action Observation (AO) at different time-points was assessed by means of transcranial magnetic stimulation for the right tibialis anterior, a muscle involved in the observed movement. During observation of the correct video, in the Soccer\_Group corticospinal excitability, recorded at the moment the ball was passed, was significantly higher than that recorded after the pass. On the contrary, in the delayed video, the Soccer\_Group showed a significantly higher corticospinal excitability about 800 ms before the ball was passed than that recorded at the beginning or at the end of the action, i.e. when the pass was really performed. No statistically significant differences were reported for the Novice\_Group in the different time-points for both videos. All these results confirm that the observer's motor experience strongly influences the temporal prediction and the corticospinal excitability during the observation of well-known actions. Further, motor experience, likely through a mechanism of temporal prediction, affects the activity of the neural system underpinning AO, inducing an increase of corticospinal excitability when the action is expected and not when it is actually observed.

## Neuroenhancement of memory in aging: the potential of transcranial Direct Current Stimulation

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Normal aging is associated with progressive changes in cognitive functions especially in processing speed, working memory, and in particular episodic memory which displays the largest degree of age-related modification. Cognitive decline, particularly memory loss, is of considerable concern to older individuals because of the possible progression to pathological conditions such as amnesic mild cognitive impairment and Alzheimer's Disease. In humans, non-invasive brain stimulation techniques like transcranial Direct Current Stimulation (tDCS) are well-suited to explore brain plasticity across the lifespan. In previous research in the field of memory changes due to aging, tDCS was applied for two main purpose: to test the involvement of a cortical region in memory function in older adults as compared to young participants and to investigate whether tDCS could modulate memory formation and learning, an issue of relevance for preventive interventions on memory decline. Studies of our research group showed that anodal tDCS applied during the encoding phase, after the consolidation process or in the retrieval phase strengthened episodic memories in healthy older adults, an effect indicated by enhanced delayed recall compared to placebo stimulation. Moreover, growing body of literature indicates long-lasting benefits on memory performance in older adults after repeated tDCS sessions combined with cognitive training, but the neuronal mechanisms underlying the effect of this intervention remains largely unexplored. The potential of neuroenhancement with tDCS is particularly promising for use as a cognitive enhancer to improve failing memory due to age and prevent disease, since no adverse effects have been reported in healthy subjects and in patients. Larger randomized controlled studies in combination with other neuroimag-

ing techniques are highly needed to test the effects of tDCS on aging brain structure and to establish the real-world impact and duration of cognitive enhancement.

## **I know what you will do: action anticipation in elite athletes**

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Sounds offer a rich source of information about events taking place in our physical and social environment. However, outside the domains of speech and music, little is known about whether humans can recognize and act upon the intentions of another agent's actions detected through auditory information alone. Recently through several studies we indicated how intention could be inferred from the sound an action makes, and in turn, how this information is used to prospectively guide movement. We showed that increased levels of practice or experience heighten the ability to tune into relevant sensory information that specifies a future course of action and enhance the level of action representation. It is supposed through these mechanisms that expert sports players are able to better predict the consequences of an action. Whilst evidence has shown that motor resonance through vision allows elite athletes to infer the consequences of a motor act, in the same vein we show that athletes are able to use the information embedded in the sound of an action to infer intention and that action-relevant experience enhances this ability. This result suggests that action intention can be perceived through the sound a movement makes and that the ability to determine another person's action intention from the information conveyed through sound is honed through practice. These findings sustain that idea that sound contains relevant information about an action-related event that not only facilitates the re-enactment of the listened-to action in quite a sophisticated manner but also allows for the extraction of key dynamic kinematic features. Indeed it is the dynamic and kinematic information embedded in the sound of a human action that supports the perception of the actor's intentions. It is the experience itself that shapes and refines this perception, allowing for the extraction and elaboration of relevant movement based information in the early stages of the movement so that the participant can act in an anticipatory way.

## **Electrophysiological markers and cognitive profile in aging: implications for screening and intervention**

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The aging process is associated to a complex ensemble of structural and functional changes. Focusing on the aging brain, the most reported modification has to do with the progressive atrophy of prefrontal cortices. The decrease in cortical volume is accompanied by a gradual (and greater) decrease of white matter density in anterior portions of the brain and by a progressive reduction of the functionality of the dopaminergic system. Those findings lead to the development of the frontal lobe hypothesis, which states that age-related cognitive and behavioral changes are due to the gradual decline of

frontal brain structures. At the same time, functional data highlighted how older people show peculiar compensatory activity involving prefrontal regions when they are engaged in cognitive tasks, thus keeping acceptable performance levels notwithstanding neural losses. Within this scenario, the development of markers able to mirror and track functional decline across physiological and pathological aging processes is one of the most relevant challenges. Traditional paper-and-pencil assessment procedures, indeed, may not be sufficiently sensitive to discriminate small cognitive difficulties occurring, for example, in prodromal phases of degenerative diseases. Oscillatory and event-related electrophysiological measures, instead, are thought to be valuable candidates, them being sensitive to changes in cognitive and functional states, easy to record, non-invasive, and cheaper than alternative instrumental markers based on biochemical, metabolic or neuroimaging methods. Even though most of recent research focused on early pathological signs of Alzheimer Disease and/or Mild Cognitive Impairment, age has been classically associated to decrease in alpha band power and to progressive slowing of EEG rhythms even in healthy elderly people, as well as to prolonged latency of the N2 event-related component, lack of habituation of the P3a component, and reduced/late P3b deflections, mirroring altered information-processing and allocation of attention resources. In addition, in a recent study integrating cognitive-behavioral (standardized neuropsychological tests and computerized reaction times tasks) and electrophysiological (28-channels resting and task-related EEG-ERP) assessment in a sample of healthy old people, we observed relevant correlations between alpha reactivity during eyes open/closed resting and performances at a reaction times task, potentially marking differences in information-processing efficiency. Present and literature evidence point out the potential of EEG-ERP measures to help sketching a finer and more complete picture of cognitive-functional profile even in healthy elderly, and data on age-related changes of oscillatory cortical activity may be deemed as potential targets for future intervention via transcranial alternating current stimulation or neurofeedback techniques.

## Reward-based plasticity of visual selective attention

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Intelligent behavior is critically warranted by selective attention, which allows focusing of limited processing resources on relevant information, and grants its access to perceptual awareness and behavioral guidance. Processing priority can be assigned bottom-up on the basis of stimulus features, or top-down on the basis of behavioral goals. Recent studies however have challenged this dichotomous view of attentional control, showing that attention is also highly vulnerable to other types of information. Studies conducted in our laboratory over the last decade provided crucial findings supporting a new perspective on attentional functioning and eventually contributing to the rise of a new field of research within cognitive neuroscience of attention. In particular, we showed that attention is strikingly affected by the learned associations between the selection of specific visual objects or locations in space and the rewarding consequences obtained in return. When the attentional selection of an item or a spatial location is systematically associated

with biased reward contingencies, significant adjustments will appear in their attentional priority, leading for instance to an increased priority of items and locations that – when selected in the past – have led to more rewarding outcomes. After reviewing our main findings I will highlight the results of very recent investigations which provide an insight on the possible neurobiological bases of these effects by exploring the impact of inter-subject variability. We asked whether reward-based attentional learning would be accounted for by specific predictors, notably traits that are linked to reward processing, but also by gender. The latter interest was motivated by recent reports that reward sensitivity differs across genders, thus implying that the effects of reward signals on attention may differ across genders as well. In a protocol designed to investigate reward-based changes in the attentional priority of spatial locations, we found that while attentional deployment was overall crucially influenced by prior rewards, the effects of reward history were markedly affected by gender. Specifically, while males exhibited the expected pattern of results, with greater priority developing for locations associated with higher reward, females showed an opposite trend. Critically, both the extent and the direction of reward-based adjustments were further predicted by personality traits indexing reward sensitivity, indicating that not only male and female brains are differentially sensitive to reward, but also that specific personality traits further contribute to shaping their learning-dependent attentional plasticity. These results contribute to a better understanding of the neurobiology underlying reward-dependent attentional learning and cross-subject variability in this domain.

## Creativity in neurological disorders

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Creativity is the ability to come up with new, original solutions to problems. There are two basic ways we can think about the possible solution. These two types of thinking are called divergent thinking, when multiple related ideas for a given topic or solutions to a problem are generated, and convergent thinking that involves finding the one “right” solution to a problem. Though several brain areas are activated during creativity process, neuroimaging studies showed that neural activation related to creativity task involved bilateral inferior temporal gyri, left insula, left parietal lobule, right angular gyrus, as well as regions in the prefrontal cortex. Similar to other highly mental functions, it is assumed that creativity emerges from fundamental cognitive operations related to specific brain organization, characterized by cognitive processes such as working memory, sustained attention, planning, cognitive flexibility, mentalizing and abstraction. Artistic changes have been described in several neurological disease such as Frontotemporal Dementia (FTD), Parkinson's Disease (PD) and Alzheimer's Disease (AD). Different studies demonstrated that all dimensions of the creativity process were impaired in patients with FTD behavioral variant whereas patients with semantic dementia showed enhancement of artistic creativity. Furthermore, PD patients, who take dopaminergic medications, showed enhanced creativity, because dopaminergic treatment could induce a reduction of latent inhibition and an enhancement of novelty-seeking behavior, leading to a better performance in creativity task. The art produced by neurological patients reveals that when brain damage is

localized or diffuse, or when neurodegenerative brain disease is present, artistic depictions of the imagination are still possible. Creativity was found to play an important role for dementia patients in terms of diagnosis and rehabilitation strategies.

## Attention orienting in the presence of social stimuli

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In recent years, research has shown that individuals presented with a face showing a task-irrelevant averted gaze, tend to produce covert shifts of attention in the corresponding direction. Despite gaze is an important social signal, only few studies have addressed the possible modulations of gaze cueing as a function of social factors. In the first part of the talk, I will present results from recent behavioral investigations with human participants in which my colleagues and I have manipulated different social aspects related to the identity of the cuing face and the identity of the participants. Overall, the results strongly support the notion that social variables such as status and group membership can affect gaze cueing to a large extent, although these effects are likely context-dependent. In the second part of the talk, I will also discuss recent data showing how social attention, measured by means of the gaze-cueing technique as well as with a “social inhibition of return” paradigm can be impaired in clinical populations suffering from disorders that are known to have a heavy impact on social cognition abilities.

## Sleep unconsciousness is paradoxically induced by fragments of wakefulness

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How the brain becomes unconscious is still under debate. During non-REM sleep, the phenomenon of the neuronal bistability, which comprises a phase of total stillness named “down state”, plays a pivotal role in maintaining physiological unconsciousness by preventing integration of information. In the context of EEG signals, a cycle of bistability is called Sleep Slow Oscillation (SSO), in which the down state corresponds to its negative peak. Recently, we have shown that a positive bump of wake-like activation precedes events of spontaneous SSOs in humans, suggesting it may act as a trigger of a bistable behavior. Further, we have demonstrated that such evoked SSOs (i.e. sensory K-Complexes) elicited in healthy humans during non-REM sleep show an early excitatory bump that, traveling over the cortex, favors cortical proneness to a bistable behavior, mainly in the fronto-central regions. In this line, our studies on the fractal dynamics of EEG signals indicate that the functional connectivity induced by the traveling bump breaks down during both



shallow and deep non-REM sleep as compared to wakefulness, resulting in the formation of parallel and segregated neuronal activities that impairs the integration of information necessary for conscious unitary scenarios. In conclusion, our results naturally lead to rethink the features and the functions of SSOs, regardless these may be spontaneous or evoked. We propose that, during sleep, information travel pertains to the positive bump occurring before the down state. The higher proneness to bistability in the fronto-central regions is crucial. Half a second of diffuse electrical silence induced by excitatory activity may prevent consciousness due to the breakdown of large-scale functional connectivity.

## **Towards an objective assessment of the capacity for consciousness**

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Validating brain-based indices of consciousness in behaviorally unresponsive patients represents a general challenge due to the lack of a gold standard to assess test accuracy. Here, we address this problem of circularity by first validating a recently proposed metric – the Perturbational Complexity Index (PCI) – in a benchmark population who could confirm the presence or absence of conscious experience through subjective reports and then by applying the same index to patients with Disorders of Consciousness (DOC). The benchmark population encompassed 150 healthy controls and communicative brain-injured subjects in various states of unconsciousness, disconnected consciousness, and conscious wakefulness. Receiver Operating Characteristic (ROC) curve analysis was performed in order to define an optimal cutoff discriminating between the conscious and unconscious conditions. This cutoff was then applied to a cohort of non-communicating patients (39 Minimally Conscious, MCS, and 43 Vegetative State, VS, patients). We found an empirical cutoff that discriminated with 100% sensitivity and specificity between the conscious and the unconscious conditions in the benchmark population. This externally validated cutoff resulted in a sensitivity of 94.7% in detecting MCS and allowed identifying a number of unresponsive VS patients (9 out of 43) with high values of PCI, overlapping with the distribution of the benchmark conscious condition. Given its high sensitivity and specificity in the benchmark and MCS population, PCI offers a reliable, independent stratification of unresponsive patients, which has important physiopathological and therapeutic implications; specifically, we argue that the high-complexity VS subgroup may retain a capacity for consciousness that is not expressed in behavior.

## **Web-mediated addictions: from Internet Addiction to Gaming Addiction**

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A growing number of studies is focusing on the behavioral Addiction to Video Games (VGA), which appear to have some similarities – in terms of development and consequences – to others forms of addiction (gambling and substance-related). Research



about this topic, however, has been so far hampered by a lack of a standard definition of this disorder before the publication of DSM-5. APA has decided to include in the DSM-5 the diagnosis of Internet Gaming Disorder (IGD), focusing on the addiction to Internet-connected gaming activities. The diagnosis of Internet Addiction (IA), on which much of the last 15 years scientific debate of the field of new technologies has been focused, has been left out of DSM-5. Thus, at the moment, the prevalence of both IGD and IA and their characteristics are unclear. The existing body of research on the topic, on the whole, has established a fairly consistent correlation between both IA and VGA (including IGD) to several adverse outcomes, especially in childhood and adolescence: depression, anxiety, social phobia, conduct problems, lower academic achievement, and Attention-Deficit / Hyperactivity Disorder (ADHD). Given the above considerations, one of the questions that needs additional research is how similar are the pathological uses of VG or the Internet, and how a diagnosis of one disorder is related to the diagnosis of the other. The study here presented provides some information relevant to this question, as the aims of the research were to investigate the differences between sub-clinical problematic VG use and Internet use, and clear IGD and IA in terms of gender, amount of time spent gaming, preferential coping strategies, adjustment problems, interpersonal relations. We administered a survey containing measures about the abovementioned variables to 474 Italian students recruited in the three main regions of the country (age range 9-19;  $M = 13.86$ ). Results show that 14.6% of participants had a sub-clinical problematic use of VG, while those with a clear IGD were 1.7% ( $n = 8$ ); 19.2% of them showed a sub-clinical problematic Internet use, while full-criteria IA was found in 9.3% of them. IA appears to be related to worse interpersonal relations in each domain (parents, peers, teachers), to worse coping strategies, to higher scores in aggression and attention problems and to worse problems of VGA. The same can be said for VGA: addicted users show higher scores in IA, worse coping strategies (lower active and support seeking), worse interpersonal relations (mostly with female peers and teachers), social problems and attention problems. Also, they spend more time using Internet than non-problematic VG users. To conclude, there seem to be a close relationship between IGD and IA both in terms of characteristics and consequences of the diagnosis. This result need more investigation, considering that it is difficult to distinguish these phenomena because of their partial overlap, based on the online games' large diffusion.

## Personality and cognitive biases discriminating late adolescents as regular gamblers

Pace U.

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Psychological literature on gambling has stressed that regular players may have different degrees of risk. This may also depend on personal characteristics related to aspects of personality and decision-making styles. In the present study, we hypothesized that late adolescent pathological gambler' attitudes would differ radically from those of low-risk and problematic gamblers, as a function of cognitive and personality biases, such as sensation seeking, magical thinking, and decision-making styles. Two hundred twenty-eight late adolescents, regularly attending bingo halls, aged between 19 and 21 years,

completed measures on aforementioned psychological variables. Results confirmed our hypotheses, since data have shown that peculiar decision-making styles and characteristics of personality discriminate late adolescent pathological gamblers from other players attending bingo halls.

## **Guilt and reward shape the neural correlates of spontaneous deception**

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Previous research suggests that deciding whether to lie to another individual involves a moral dilemma between the temptation to deceive to get a personal reward and the desire to follow social norms of moral conduct (social reward). A failure to achieve the social reward of honesty is very often associated with a subsequent sense of guilt. Consistent with this, guilt aversion has been considered one of the strongest motivator for honesty. On the other hand, sensitivity to primary reward is considered a promotor of dishonesty. Neuroscientific studies have shown that higher activity of insula (an area related to guilt) during resting state predicts lower deceptive behavior, while higher activity in the nucleus accumbens when reward is anticipated predicts higher rates of dishonest behavior. In a previous study, we showed that the act of lying was associated with decreased motor readiness, an ERP component linked to motor preparation and that this reduction was weaker in participants who report to feel low guilty for lying (i.e. manipulative people). In this study, we tested the effect of personal reward and social reward (guilt aversion) on the motor readiness to lie. We employed the ‘temptation to lie card game’ an experimental paradigm where participants could spontaneously choose whether to lie (egoistically or altruistically) or not to other players. We manipulated personal reward by modulating the economic reward magnitude available on each trial and the social reward by modulating the level of guilt associated to each decision (through the employment of low versus high social ranking opponent players). Our findings show that guilt and reward seem to act as opposing forces on the decision to deceive: guilt decreases the probability to make egoistic lies and increases the probability to make altruistic lies, enhancing honest behaviour. On the other hand, reward magnitude increases the production of egoistic lies and decreases the production of altruistic lies, pushing participants toward dishonest behaviour. Moreover, personality traits related to moral cognition (i.e. manipulation, impression management and moral disengagement) significantly modulate deceptive behaviour, confirming the importance of both situation and personal disposition. Moreover, we found reduced Lateralized Readiness Potential (LRP) amplitude and reduced Mu suppression (as measured by time-frequency analysis) for egoistic lies in the high guilt versus the low guilt condition. Surprisingly, LRP reduction was found when participants were lying in the high vs. low reward condition suggesting that even if participants were more tempted to lie in this condition (as showed by the behavioural results), the motor preparation of this response was cortically inhibited. Our findings confirm the importance of personal and social rewards in shaping interpersonal deception and provide critical evidence for a role of cortical motor preparation in implementing (im)moral actions.

## Physiological response to physical activity: physical and brain fitness as integrated adaptations

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The benefits to health that derive from regular physical activity are many and well documented. An active lifestyle lowers the risk of developing various chronic diseases (e.g. coronary heart disease, hypertension, type 2 diabetes) and lessen the functional decline due to ageing. Physical fitness is considered an integrated measure of the efficiency of the body functions. It can be defined as a set of measurable attributes related to the ability to perform physical activity with vigour. Each component of physical fitness (mainly cardiorespiratory fitness, muscular strength and endurance, flexibility and body composition) can be improved, regardless of age. The adaptive responses that occur in the body when an individual augments his/her level of physical activity bring about an increase in physical fitness, according to a dose-response relationship. Better performances are reached, generally coupled with a feeling of “energy” and well-being. Good levels of physical fitness have been demonstrated to be associated with improved cognitive functions across the lifespan and would help in preventing cognitive decline and dementia. Regular exercise has been shown to promote the growth of cerebral blood vessels and neurogenesis and to enhance communication across synapses. Consistent with these findings structural imaging studies have confirmed an association between physical activity and grey matter volume, being larger in active people compared with sedentary. During acute exercise concentrations of Brain-Derived Neurotrophic Factor (BDNF) have been found to augment. Brain plasticity could be enhanced and executive functions, learning and memory processes could result improved. It has been recently shown that acute effects of dynamic aerobic exercise boost learning process both in visual and motor domain in young healthy subjects. Modifications in cognitive processes may develop over time as the adaptation to repeated individual bouts of exercise. The association between physical fitness and brain health has been proposed to be mediated in part by the beneficial effects of regular exercising on cerebral blood flow and its regulation. High levels of cardiorespiratory fitness have been reported to be associated with augmented cerebral blood flow at rest and with improved cerebrovascular reserve, that means an enhanced ability of cerebral vessels to respond to increased metabolic demand and neural and chemical stimuli. As in other circulatory districts, aerobic physical activities would enhance endothelial function, decrease oxidative stress and vascular inflammation and increase blood flow due to vasodilation, recruitment of capillaries and growth of new capillaries. The consequent elevated levels of growth factors would promote neurogenesis and synaptogenesis. The more efficient neuro-vascular coupling would contribute to induce an increase in cognitive performances.

## Genes, brain and behavior: is there a Functional Frontal Fragility condition?

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The first observations of severe changes in personality and behavior in individuals that had suffered lesions of the anterior portion of the brain, have prompted investigations in the neural mechanisms that subtend impulse control, modulation of aggression and social behavior in humans. For the sake of simplicity, human behavior can be considered as the resultant of instinctual/emotional factors on one hand and critical reasoning on the other. When this balance becomes defective, either because of emotional dysfunction and/or impaired critical ability, individuals may express abnormal behaviors, including some that fail to respect societal norms and laws. While Free Will is undoubtedly awidely debated and complex concept, in the forensic context it can be defined operationally as the ability (to decide) not to act automatically in response to an impulse; that is, from a criminal law perspective, as the capacity to do otherwise. Overall, responsibility requires the integrity of multiple emotional, cognitive and behavioral abilities. Patients with the behavioral variant of Frontotemporal Dementia (bvFTD) offer a valid model to investigate moral responsibility and the underlying neural bases. As a matter of fact, these patients invariably show a progressive loss of the ability to control their instincts and impulses, to modulate their behavior, to respect moral laws, along with a dramatic affective flattening. We argue that the co-occurrence of peculiar neurobiological and environmental factors may result in a condition of Functional Frontal Fragility, even in individuals who do not present any bvFTD. Indeed, allelic variants of gene involved in neurotransmission, by modulating individual susceptibility to childhood aversive environmental factors, may increase their likelihood to develop behavioral dyscontrol as adults. Moreover, morphological and functional abnormalities often are found in frontal and limbic areas of antisocial individuals. Recently, we showed also that inhibition of automatic behavioral responses – that is, the ability to do otherwise – is compromised after prolonged sleep deprivation due to local sleep phenomena in frontal cortical areas. We conclude that any condition that leads to a frontal impairment with a causal link with behavioral dysfunction should be considered relevant from the forensic/legal perspective, even in the absence of a full-blown clinical picture, like bvFTD.

## Neuroimaging of the placebo effect

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Several lines of evidence indicate the key role of expectation and learning in placebo analgesia, both in experimental and in clinical settings. Understanding the modulation of brain activity during anticipation, contextual learning and pain perception is therefore an important step, bearing theoretical and practical implications, in explaining how externally reinforced stimuli interact with individual traits to induce placebo analgesic responses. These issues have been extensively investigated over the last few years by neuroimaging studies. A first aim has been to map the brain centres involved in triggering and shaping placebo analgesia. Functional Magnetic Resonance Imaging (fMRI)

and positron emission tomography studies detected medial and lateral prefrontal foci active during anticipation of analgesia. Some of these foci showed increased activity over time during placebo conditioning, suggesting a learning-related process, and/or were positively correlated with the magnitude of the placebo analgesic effect. Accordingly, placebo analgesia is reduced by experimental manipulations (e.g. transient inactivation by transcranial magnetic stimulation) or clinical conditions (such as Alzheimer's Disease) affecting prefrontal areas. The prefrontal cortex appears therefore as a key structure in placebo conditioning and anticipation of analgesia, modulating a complex cortico-subcortical antinociceptive network involving the rostral anterior cingulate cortex and the periaqueductal gray. A second aim has been to establish whether placebo analgesia is accompanied by modulation of pain-related circuits in the central nervous system. Reductions in noxious-evoked fMRI signal increases have been detected in the dorsal anterior cingulate, thalamus and insula, as well as in the amygdala and striatum. These findings suggest direct placebo effects on brain regions involved in processing nociceptive information, and more generally in emotional mechanisms. A third aim has been to identify personality traits and neural signatures predicting placebo responsiveness, or related to different mechanisms of placebo analgesia. For instance, during anticipation of analgesia, subjects characterized by high hypnotic susceptibility show increased activity in the right dorsolateral prefrontal cortex and reduced functional connectivity of this same region with brain regions related to emotional and evaluative pain processing; the opposite pattern of fMRI activity and functional connectivity is found in subjects with low hypnotic susceptibility. These and other results suggest that different mechanisms can be involved in placebo responsiveness, depending on individual cognitive traits.

## **It's not all in your car! The efficient brain of professional car racers**

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Selected individuals may achieve very high levels of skills and performance in fields ranging from arts to sport activities as a consequence of intensive training and maybe of genetic predisposition. Recently, brain functional studies indicated that skill acquisition in different perceptual, motor or cognitive domains is associated with both a reduced utilization of resources and an improvement in information processing, thanks to a better communication between task-related brain areas. Altogether, these observations support the hypothesis of an improved “neural efficiency” in skilled individuals. Our group particularly focused on investigating brain structural and functional correlates associated with exposure to extreme training and competing conditions, like those involved in professional car racers. Formula 1 pilots are indeed exposed to demanding conditions and require exceptional skills in terms of visuo-spatial processing, motor control, decision making and sustained attention. As compared to ordinary drivers, highly trained racing-car drivers undergo both “quantitative” and “qualitative” modifications – i.e. a reduced activation in driving-related cortical areas and increased regional correlations – that favor an improved “neural efficiency” in the brain of these highly skilled athletes. Driving-related areas also present an increased gray matter density, likely reflecting an association between the functional and structural plastic brain modifications that support top racing

performance. Interestingly, studies exploring age-related functional changes during distinct cognitive tasks revealed complementary findings of a “neural (in)efficiency”, as older individuals often recruit a greater volume of brain cortical areas and show a reorganization of associated functional networks. Of note, the achievement of a greater neural efficiency in specific behavioral activities may contribute to improve resistance to cognitive fatigue. In fact, recent investigations showed that brain areas or networks that are intensively “used” during prolonged task practice may show brief periods of local, temporary deactivation (“local sleep”) that negatively impacts behavioral performance. Future studies will test whether the reduced resource consumption associated with neural efficiency could favor an increased resistance to cognitive fatigue during long tasks.

## **Brain mechanisms to regulate reactions to social exclusion**

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Social exclusion is an experience that most humans face daily. Social exclusion, especially when prolonged, can change the brain, undermine health, and reduce life expectancy. Mostly relevant to these negative outcomes, however, is how people respond to it. To date, one of the chief contributions of neuroscience to the understanding of social exclusion is that it is truly, and automatically, a painful experience. Nevertheless, social pain’s automatic components in the brainstem, anterior cingulate and insular cortices, are counterbalanced by the controlled, regulatory function of the prefrontal cortex. In particular, the right Ventrolateral Prefrontal Cortex (rVLPFC) is a brain region that appears to be critical for the regulation of social pain. The present set of experiments tests the hypothesis that modulating the cortical excitability of the rVLPFC may regulate emotional and behavioral responses to social exclusion. Participants received transcranial Direct Current Stimulation (tDCS) over the rVLPFC in anodal, sham (Study 1 and 3) and cathodal (Study 2) modality. Five minutes before the end of the tDCS stimulation, participants were randomly assigned to a manipulation of inclusionary status (i.e. Cyberball). In Study 1 and 2, feelings of social pain and negative emotions were assessed. In Study 3, behavioral aggression was measured. In Study 1, we found that anodal tDCS over the rVLPFC decreased pain following social exclusion. In particular, anodal tDCS but not sham stimulation reduced pain unpleasantness and hurt feelings in excluded participants whereas no effects of tDCS stimulation emerged for included participants. In Study 2, we found that cathodal tDCS over rVLPFC led to reversed effects, increased feelings of social pain, hurt feelings, and negative emotions resulting from social exclusion. Crucially, in this study, cathodal stimulation was applied over a control region (the right posterior parietal cortex) and no effects on people’s emotional reactions caused by social exclusion were found. Finally, in Study 3, socially excluded participants given anodal stimulation were less aggressive than those given sham stimulation. Among socially included participants, no aggression differences emerged between the anodal and sham stimulation. Crucially, excluded participants who received anodal stimulation were no more aggressive than included participants. Overall, these studies suggest that the rVLPFC plays a key role in regulating responses to social exclusion and that it is possible to up-regulate and down-regulate reactions to social exclusion by modulating cortical

activity of the rVLPFC. These modulatory findings fit well with the critical role of the VLPFC in self-regulation and inhibition of many other impulses such as gambling, substance abuse, and poor financial decisions.

## Moral judgment as an intertemporal choice

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Humans frequently make moral judgment, namely, they decide whether implementing an action is right or wrong based on principles and values shared with other members of the social community. Moral choice is often intertemporal, since it requires taking into account payoffs of both short- and long-term consequences of action. For instance, in the “footbridge dilemma”, the short-term gain of killing one person is the saving of five lives, but it competes with the anticipation of having remorse for breaking moral rules in the long-term. In the present study we explored the relation between these two domains – moral judgment and intertemporal choice – in Italian healthy young adults. Moral judgments included personal dilemmas, where violations involved one’s own agency, and control impersonal dilemmas, where violations did not involve one’s own agency. Hypothetical monetary intertemporal choices involved larger-later reward against smaller-immediate or smaller-sooner reward. As main finding, reduced time to accept personal violations was accompanied by increased preference for immediate monetary gratification (i.e. participants were more impulsive). We suggest that, once a common mechanism of anticipating consequences and emotions associated with action is less efficient, individuals are unable to make long-sighted choices. They are thus less willing to wait longer for more convenient reward, and they are unable to envision future negative consequences of making personal immoral action in the immediate present. Further cognitive and neural mechanism underlying this process, as well as the relation with other cognitive functions will be discussed.

## Neural and psychophysiological correlates of basic and social emotions recognition

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Affective blindsight refers to the uncanny ability of patients with cortical blindness following destruction of the primary visual cortex (V1) to discriminate reliably the emotional content of stimuli they cannot consciously perceive because projected in the blind portion of their visual field. Therefore, such clinical condition offers a valuable opportunity to investigate and compare emotion recognition with and without awareness and reveal the psychophysiological and neural properties characteristic of each mode of perception. Here we present several novel evidence related to these issues. First, emo-



tional expressions projected to the blind field elicit spontaneous facial reactions and psychophysiological changes, as indexed by facial EMG and pupil dilation respectively, that are faster and more pronounced than the reactions triggered when the very same stimuli are displayed to the patients' intact visual field. Noteworthy, not all types of expressions can be discriminated without awareness, but only biologically primitive expressions (e.g. basic emotions like fear or anger). Conversely, facial expressions of so-called social expressions (e.g. guilt or arrogance) do not trigger differential psychophysiological responses and cannot be discriminated without awareness. This pleads in favor of an evolutionary perspective, which argues that only biologically hardwired emotional signals can access phylogenetically ancient subcortical neural structures, such as the amygdala and superior colliculus, that are pivotal for emotion perception without awareness. As this neural network for non-conscious emotion perception seems to draw on the magnocellular visual system, which is tuned to low spatial frequencies, we examined in a combined fMRI / behavioral study the causal role of these factor. We presented broadband, low and high spatial frequency filtered fearful and neutral facial expressions to patients with affective blindsight, who were asked to guess the emotional content of the stimuli. Above chance recognition was possible for broadband and low frequency faces and was associated with activity in the superior colliculus, pulvinar and amygdala. Conversely, correct discrimination dropped to chance level for high frequency stimuli and activity in such subcortical structures was suppressed. Lastly, in vivo tractography (DTI) shows that these subcortical structures have direct anatomical connections in the intact human and non-human brain and that such connections are strengthened in patients with affective blindsight.

## Visuo-spatial modulation of pain

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Cognitive theories of pain suggest that nociceptive inputs are elaborated by a multi-sensory processing system that prioritizes stimuli that are meaningful for the integrity of the body and integrates them into multi-frame representations of the body and the proximal space, with the ultimate aim of protecting the body. Relevant for this aim is the ability to localize nociceptive stimuli because it allows the detection of which part of the body is potentially threatened. Interestingly, it has been shown that the role of the representation of space is crucial for the perception of nociceptive stimuli. Indeed, studies with patients suffering from hemispatial neglect have suggested that the ability to detect, perceive and report nociceptive stimuli is critically dependent on spared representation of peripersonal space. Furthermore, the existence of a peripersonal frame of reference to map the position of nociceptive stimuli also supports the existence of multimodal interactions between nociceptive inputs and sensory inputs from other modalities, for example vision. Previous studies have shown that the illusion of looking at the hand through a mirror reduces the perception and the magnitude of brain responses elicited by nociceptive stimuli delivered onto the hand. However, this effect has not always been



replicated. Understanding the reasons underlying these different effects can be of great value for a deeper knowledge on how visuo-spatial mechanisms influence pain perception and nociception elaboration.

## **Top-down modulations of motor resonance to social stimuli**

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Several previous studies have shown a muscle-specific facilitation of cortico-spinal excitability during observation of others' actions (motor resonance). While motor resonance has been shown to be automatically triggered independently from the observer's effort to simulate the actions, high-level aspects of actions, including the actor's intention and context, can modulate its extent and spatio-temporal selectivity. In a series of studies, we used single-pulse and repetitive TMS and behavioral action prediction tasks to investigate how the observer's motor system maps the kinematics and intention of actions embedded in congruent or incongruent contexts. Participants watched videos showing everyday actions and were asked to predict their final outcome ahead of realization. We manipulated both the context in which the actions were embedded, being congruent, incongruent or ambiguous, as well as the intention of the actor, who could provide either genuine or fooling information to the observers. At different delays from action onset, we recorded Motor Evoked Potentials (MEPs) from arm and forearm muscles to measure motor resonance. We found that both context and intention modulate participants' performance, leading to improved discrimination of actions embedded in congruent context and driven by genuine intention and impaired discrimination of actions embedded in incongruent contexts and driven by deceptive intentions. Crucially, these two high-level aspects modulated motor resonance in a different way. In particular, we found an early facilitation of motor resonance for actions embedded in congruent context and a later inhibition for those embedded in incongruent contexts. Conversely, the reduction of performance in predicting deceptive actions was associated to a muscle-specific facilitation of motor resonance as compared to observing genuine actions. These results suggest that high-level aspects of actions can boost or suppress motor resonance through top-down modulations from high-level systems, including prefrontal and temporo-parietal areas involved in semantic representations and social cognition. To investigate the mechanisms underlying top-down modulations of motor resonance, we used a perturb-and-measure TMS approach, which combines off-line continuous theta burst stimulation of areas within and beyond the action observation network with online spTMS of the primary motor cortex to measure the consequent functional modulation of motor resonance. The results showed that prefrontal and temporo-parietal areas play an important role in modulating the facilitation of cortico-spinal excitability during action observation, suggesting that motor resonance does not emerge from an encapsulated system, but reflects the processing of multiple aspects of actions (e.g. kinematics, intention, context) in different and interconnected networks.

## ORAL AND POSTER PRESENTATIONS ABSTRACTS

### Virtual lesions of pMTG and dlPFC modulate facilitatory and inhibitory (in)congruency effects on motor resonance during the observation of context-embedded actions

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Previous single-pulse Transcranial Magnetic Stimulation (TMS) studies suggest that motor resonance can be modulated by high-level contextual representations. More specifically, in a series of previous experiments, we observed a muscle-specific increase of Corticospinal Excitability (CSE) during the observation of actions embedded in congruent contexts and a decrease when these were embedded in incongruent contexts, as compared to neutral ones. However, direct evidence about the neural areas involved in these modulations is lacking. Here, we used a perturb-and-measure TMS approach, which offers the unique possibility of (i) suppressing neural activity in regions of interest using off-line continuous Theta Burst Stimulation (cTBS), and to (ii) measure the consequent functional modulation of CSE to observed actions via online spTMS of M1. We administered cTBS over the dorsolateral Prefrontal Cortex (dlPFC), the posterior Middle Temporal Gyrus (pMTG), and Vertex was used as a control site. After each “perturb session” participants underwent a “measure session”. During the measure session, Motor Evoked Potentials (MEPs) were recorded from the FDI and FCR muscles while participants watched videos of everyday actions embedded in congruent, incongruent or ambiguous contexts. Video ending was occluded from view and participants were requested to predict action unfolding. We found that, when interfering with dlPFC activity, both effects were abolished. Additionally, when disrupting pMTG activity, we observed a facilitation for actions embedded in either congruent or incongruent contexts as compared to ambiguous contexts, suggesting that motor resonance was not sensitive to the congruency between observed actions and the context in which they were embedded. Importantly, these modulations were observed only for the FDI muscle, which is known to be specifically involved in the execution-observation of reach-to-grasp movements. Overall, these results suggest that (i) the dlPFC might exert a top-down modulation in motor resonance responses by providing contextual information necessary to estimate the probability of a given outcome; and that (ii) the pMTG might be involved in a process of semantic retrieval (encoding of object-related information associated to the action) when processing actions embedded in natural contexts.

### Hungry or stressed? Relationship between stress and attention for food-related words

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Obesity is a major health problem in today's Western society and is caused by different environmental and genetic factors. Among these multiple variables, stress-induced eating is widely thought as a risk factor for obesity. Previous studies found that stress correlates with an increased desire for high-caloric food. An attentional bias for food cues is hypothesized to have a role as cognitive factor in the relationship with pathological overeating. Thus, the aim of this study was to investigate the influence of stress on an attentional bias for high-caloric food-related words on healthy people for the first time. The attentional bias was assessed by an adapted Stroop task, and it was measured by comparing Reaction Times (RTs) for food-related words and non-food related words before and after stress. A within-subjects study was conducted on 41 healthy sophomore psychology students. Their RT was measured while performing a set of paired Stroop tasks (the original version, a neutral words list and a food-related words list) and they filled in the Profile of Mood States (POMS) questionnaire to measure their mood state in the before stress condition (T1). Next, participants were exposed to stress by undergoing the Maastricht Acute Stress Test (MAST), an effective and well-validated laboratory stress test capable of inducing subjective, autonomic and glucocorticoid stress responses at physical, mental and social levels. After twelve minutes of stress test, all participants were tested again with the same RT measurement during the Stroop tasks set and the POMS questionnaire, as an indicator of mood change (T2). Against our expectations, we found that stress had no significant effect on the RT for the food word list compared to the neutral word list. In both conditions, participants turned out to be significantly slower on the food-word list than on the neutral word list. One possible explanation of this effect could be that there is a general attentional bias for food-related cues. Moreover, students were generally faster on both lists after stress: possibly due to learning effect or due to higher level of adrenaline induced by the MAST. An actual increase of the stress among participants due to the MAST was confirmed by a significant increase in negative mood in the POMS score. Overall, our results showed that the attentional bias for high-caloric food is not influenced by stress, perhaps because of the methodology.

## Event-Related Potential and tDCS application in the inhibitory control study

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Inhibitory control is the ability to stop the execution of a planned motor behavior that is considered inappropriate for the situation. Deficit in response inhibition and alcohol-cue reactivity were found to be two main cognitive mechanisms predicting relapse in alcohol detoxified patients. To date, research on neurocognitive interventions to strengthen inhibitory control is still scarce. The objective of our study is to investigate a new neurocognitive method, additional to medications and psychotherapy, aimed at rehabilitating these altered cognitive skills in clinical populations, such as alcoholic patients. A pilot study was conducted using transcranial Direct Current Stimulation (tDCS) to modulate the right Inferior Frontal Cortex (rIFC) four times in a week (20 minutes each session;

2 mA) while participants were performing a cognitive training on inhibition (adapted version of “Flanker Go/No-go task”). Healthy participants ( $n = 59$ ) in age group 18-31 years performed a “Go/No-go task” while an Event-Related Potential (ERPs) recording (T1; 32 channels) was conducted. They were divided in subgroups all randomly assigned to different conditions for four days: Group 1 (G1;  $n = 15$ ) was the control condition; G2 ( $n = 17$ ) was receiving a training on memory (placebo); G3 ( $n = 17$ ) was performing the cognitive training only; G4 ( $n = 10$ ) was receiving the tDCS neuromodulation during the cognitive training. The fourth day (T2), all participants were tested again with the same ERP Go/No-go task; as well after 1-week, considered as follow-up period (T3). To make certain that the cognitive training and the potential tDCS effects were specific to inhibition, ERPs to a face detection task were also recorded at T1, T2 and T3 for every group. An increase in the correct detections and a decrease in the reaction time on the Go/No-go task was registered at T2 for all groups and this effect was maintained at T3. Whereas, the rate of commission errors was similar between T1, T2 and T3 in all groups. At the neurophysiological level instead, there is a significant difference in the latency of the N2d component, reflecting the conflict monitoring. Indeed, N2d was earlier both for G3 and G4 compared to G1 and G2. This was true at T2 compared to T1 and persisted in T3. Moreover, we found a marginal difference in the latency of the P3d component, indexing the inhibition function per se that was reduced at T2 as compared with T1 for all groups. To conclude, our preliminary data suggest that the rIFC neuromodulation with the tDCS and the cognitive training on inhibition specifically impacts neurophysiological processes related to inhibition. Furthermore, the inhibitory skills of healthy people seem to be enhanced by repeated paradigms, such as the Go/No-go task.

## **Hemo-Encephalography training to prevent relapse among elderly sex offenders: a pilot study proposal**

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Sexual delinquency representing a significant societal problem, often evoke fear and other negative reactions increasing public anger and concern, mainly when the victims are vulnerable subjects. The prevention of sexual recidivism is really important, due to the profound impact on victims and the larger community but also from a public policy perspective. Previous studies showed that the main focus is on the issue of assessing the risk of recidivism, while there was a lack of specific literature on the application of neuroscience related to sexual recidivism, in term of treatment and rehabilitation, as well as limited research on elderly sex offenders. Hemo-Encephalography (HEG) is an alternative neurofeedback technique that uses near-infrared technology to measure brain activation, blood flow rather than electrical brain activity, primarily on the pre-frontal cortex, improving the metabolic capacity of this region. Previous studies showed the relevance of frontal executive functions on sex offenders and Frontotemporal Dementia (FTD) patients. To explore these issues, the main aim of this study is to investigate the efficacy of the HEG training to prevent relapse among elderly sex offenders. Another aim of this study is to investigate the cognitive reserve of elderly sex offenders. The last aim of this study is to investigate the similarities of neuropsychological function in term of psycho-

metric results between elderly sex offenders and FTD patients. The sample includes three groups: (1) sex offenders over 50 treated out of prison with HEG training but previously treated in prison with Intensified Treatment Program (ITP) for sex offenders; (2) sex offenders over 50 treated out of prison with HEG training; (3) sex offenders over 50 out of prison not treated. Test including: a neuropsychological test battery, which have been validated in the assessment of FTD; Cognitive Reserve Index questionnaire (CRIq); and about relapse prevention, STATIC 99-R, STABLE 2007, and ACUTE 2007. The design of the study is a pre-test, HEG training (4 months, 35 times, 2 times a week), post-test, and follow-up at 8 months. HEG training to prevent relapse among (elderly) sex offenders have not been previously studied.

## Linking connectivity alterations with cognitive decline in Alzheimer's Disease: the contribution of TMS-EEG coregistration

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Growing evidence suggest that Alzheimer's Disease (AD) may be considered as a “disconnection syndrome”, with a breakdown in the communication between brain regions due to compromised large scale connections which may be the cause of clinical symptoms. The combination of Transcranial Magnetic Stimulation (TMS) with Electroencephalography (EEG) has been proven to be a useful method to test large-scale effective connectivity because the activation induced by the TMS pulse in stimulated area propagates to functionally connected regions. TMS-EEG coregistration allows to measure the reactivity and the efficiency of communication in brain networks analyzing the TMS-induced cortical response in the target area and its propagation to connected regions (i.e. TMS-Evoked Potentials, TEPs). The aim of the present study was to investigate the relationship of global cognitive functioning (as measured with MMSE) with the reactivity and the efficiency of communication of the prefrontal cortex in a sample of AD patients, in order to establish a link between connectivity alterations and clinical symptoms. Twenty-seven mild to moderate AD patients (age: mean = 77.11, SD = 4.21; MMSE score: mean = 20.56, SD = 2.50) participated in the present study. 200 single TMS pulses were delivered, at a random inter-stimulus interval of 0.25-0.5 Hz and with an intensity of 110% of the individual resting motor threshold, over the left dorsolateral Prefrontal Cortex (DLPFC) (F3 electrode position) during EEG recording. Left DLPFC stimulation evoked four main components: P20, P45, N100 and P180. The earlier local response induced by left DLPFC stimulation in the targeted area (P20) was found to correlate with the MMSE: its amplitude increased ( $r = -0.43$ ,  $p < 0.05$ ) and its latency decreased ( $r = 0.44$ ,  $p < 0.05$ ) with more severe cognitive deterioration (lower MMSE score), indicating that DLPFC reactivity increases as AD severity advances. This finding is further substantiate by neuroimaging studies which pointed out the hyper-activation of prefrontal areas in AD. The second TEP component, P45, revealed that the signal spread to connected areas of both hemispheres. Interestingly, the difference in latency between P20 and P45 significantly correlated with MMSE score ( $r = -0.56$ ,  $p < 0.01$ ), so the

lower the score the bigger the difference. Taken together, the presents results show that global cognitive decline in AD correlated with both the local reactivity of the DLPFC and its cortico-cortical connectivity, with more impaired patients having an increased local reactivity but a reduced communication efficiency between connected areas. This study represents the first step to prove TEPs as a potential electrophysiological connectivity-based non-invasive marker of AD, for monitoring the progression of the disease and for evaluating the response to treatments.

## **Functional neuroanatomy of racial bias in visual perception: a meta-analytic study**

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Several psychosocial studies have shown that perception of, and response to, socially salient properties of visual stimuli, such as facial expressions and gaze direction, depend on the interaction between the racial membership of the perceiver and the one displayed in the stimuli. Moreover, in recent years a number of studies have started investigating the neural mechanisms underlying racial bias using functional Magnetic Resonance Imaging (fMRI). Owing to differences in experimental paradigms, stimuli, and analyses, it has proven difficult to disentangle core neural network underpinning racial biases from idiosyncrasies of each study. To overcome these limitations and clarify the differences in brain activity between ingroup and outgroup processing that remain consistent across studies, we performed a quantitative voxel-wise meta-analysis of 53 neuroimaging studies of racial bias. We used an approach based on coordinates, i.e. the Activation Likelihood Estimation (ALE) method, to estimate on each voxel the probability of regional brain activations. Ingroup perception was characterized by significant activity in cingulate and frontal cortices, including left cingulate gyrus, bilateral medial and superior frontal gyrus and left inferior frontal gyrus. There was also enhanced activity in subcortical regions such as the insula, claustrum and putamen, predominantly on the left side. These brain areas seem to be associated with affective and cognitive empathy, self-referential evaluations and mentalizing about similar others. Conversely, perception of social cues in outgroup members was associated with activity in bilateral amygdala and parahippocampal gyrus. These regions seem to encode the emotional component of racial bias, including the ability to respond rapidly to potential social threat, such as those coming from racial outgroup members, or the fear and anxiety of showing prejudice. We also found responses in the right hemisphere, encompassing the insula, claustrum and inferior frontal gyrus. These areas, especially in the right hemisphere, have been previously associated with negative visceral reactions, implicit negative attitudes towards outgroup racial members, and individuals' efforts to inhibit the influence of stereotypes, respectively. Thus the present results suggest that ingroup and outgroup biases are defined by different neural networks that survive to idiosyncrasies proper of each study.

## Neurophysiology of management communication: a pilot hyperscanning study

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Communication is an important factor in understanding intangible organisational assets value, and, together with the construction of robust relationships, is linked to higher performance levels and generating service. Thus, it is important for managers to be able to improve communication within his group. However, conventional modalities focused on management's perspective rather than on the collaborators. Nonetheless, collaborators' primary needs should include complete information and a good communication with his boss, within a circular and constructive perspective. Also, objective psychophysiological data in support of such organizational dynamics are still missing. Thus, the aim of the present pilot study was to explore an organizational interaction between a manager and a collaborator about job performance in a big service's company. The sample consisted in 2 paired manager-collaborator couples. Managers were required to use two different communication styles and were provided a script to play: one was required to adopt a standard approach according to the company's guidelines, while the other adopted a more cooperative approach. Meanwhile, cortical (Electroencephalographic, EEG) and peripheral (Heart Rate: HR; Skin Conductance Level and Response: SCL, SCR) activities were recorded. A first step of analyses permitted to identify 5 main standardized topics during the interviews: collaborator's description of the team work; manager's description of the team work; company's practices; collaborator's personal change; manager's personal change. A second step consisted in the identification of neuro- and psychophysiological markers. Topic, job position (manager vs. collaborator) and manager's style (standard vs. constructive) were considered to interpret data. A first important and general result showed that the interview was more arousing for the collaborator than the manager, with increased SCL irrespective of topic and style. A second result was related to the perceived significance of such topics by the two different job positions: in detail, concerning brain oscillations and their frequency range, greater Delta (0.5-3.5 Hz) and Theta (4-7.5 Hz) bands power emerged over frontal areas while managers talked about company's practices and their own personal change. Since these brain responses are related to salience detection, these specific topics could be the most salient for managers, considering the identification with the company. A third point refers to manager's style: results showed that managers playing a standard script showed increased HR than the cooperative colleague, thus revealing the presence of negative emotions like fear, involved in self-centred dynamics of change. On the other hand, the collaborator of the standard dyad was more activated (increased SCL) when his boss told about his need to change. Contrarily, the collaborator within the constructive dyad was more responsive when the manager talked about his own personal change. These first preliminary results highlight the importance of applying a neuroscientific approach to organizational contexts in a way to explore and



modify important processes related to job position, manager-collaborator dynamics, and communicative style.

## **The cooperative social brain: EEG/fNIRS hyperscanning during a joint performance**

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Understanding the brain dynamics during social interaction has become an important issue for neuroscience research, and brain-to-brain coupling has sought to overcome some limitations of previous approach based on single-person recording. In fact, such studies cannot assess the dynamics of two (or more) brains interacting together, nor reproduce ecological settings. In the present study the neural basis of inter-brain cooperation underlying the execution of joint-actions were explored by using a hyperscanning paradigm involving both Electroencephalographic (EEG: experiment 1) and functional Near-Infrared Spectroscopy (fNIRS: experiment 2) coherence measures. Participants grouped in couples were asked to perform an attentional task in the form of a cooperative game. Synchronicity of the behavioral variables (Response Times, RTs, and Error Rates, ERs) was also considered during some steps of progressive social reinforcing conditions. In fact, during the task, subjects constantly received a feedback manipulated a priori to stress their good synchronizing abilities. Considering both EEG and fNIRS measures, the induced feedback affected both the cognitive performance and brain-to-brain coupling by increasing behavioral and brain synchronization when a positive reinforce was furnished to the participants. For what concerns EEG, high coherence effect was mainly observed when a positive reinforce was produced, but only for low frequency bands within the prefrontal left area, compared to the right one, thus underlining a left lateralization effect. Similarly, an increased brain activity over the prefrontal area was found for fNIRS measures in relation to the positive social feedback. Therefore, it is possible to hypothesize that the role of left PFC is significant induced by the positive reinforce, probably in relation to the perception of social efficacy in cooperative behavior. Finally, the cognitive and cortical coherence measures were shown to be correlated each other. These results underline the importance of simultaneously record brain dynamics in real-time interacting participants for studies on social cognition.

## **Post-anoxic coma outcomes: comparison between two cases**

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The etiology of acute acquired brain injury could be traumatic or non traumatic and can lead to condition of coma with a variable length and resalting motor, sensory, cognitive and/or behavioural impairments and severe disability. The non traumatic causes could be cerebrovascular lesions, cancer, infection of the central nervous system, intoxication, anoxia that can be caused by cardiac or respiratory arrest; these causes had also a worse



prognosis. The lack of oxygen to the brain cells produces reversible lesions that start after 4-6 minutes but these lesions become irreversible in the absence of circulation last more than 10 minutes with more damages to white matter, frontal cortex, parietal occipital junction and more resistant of the brainstem. We evaluated and treated two patients who had an anoxic coma due to cardiac arrest and myocardial infarction. These patients have similar prognostic factors in the acute phase in terms of clinical history, use of adequate and early cardiopulmonary resuscitation, clinical and neurological examination, rating scale, CT scan, EEG and PESS. During rehabilitation both patients showed early recovery of consciousness, recovery of swallow and breath from natural ways but different evolution of the motor and cognitive impairments. One patient has a good outcome with recovery of good motor and personal autonomy, residual cognitive deficit in executive functions, attention and memory; the other patient has important disability despite the absence of motor deficit, dependence in the daily activities, severe cognitive impairment with apathy and constant disorientation. We identified some causes of this different evolution as age, different CT lesions, clinical complications (in particular infectious), pharmacological therapy, different family support, different awareness.

## Smell and 3D haptic shapes

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Some research in recent years has focused on olfactory perception and how it is highly affected by participation of crossmodal and multisensory perception. An important role in crossmodal interaction has the subject bias to naming the odor, or to represent it in an odor mental imagery, even if the task does not require it. However, although the effect of crossmodal interaction in smell is going to be well investigated, little attention has been paid to facilitation expressed by haptic interaction with a manipulation of the odorous object's shape. Aim of this work is to investigate the interaction and haptic facilitation in a smell task. Ten healthy subjects (25 y.o.  $\pm$  5 SD), non-smokers, were trained to haptic manipulation of 3D models and olfactory stimulation in a black case. To avoid effects such as color or different textures of the odorous objects models were 3D printed with a monotone blue with rough texture. The smells were selections from five representative types of categorical spatial dimension on the odors (i.e. Cinnamaldheyde, Citral, Hexanal, Phenethyl Alcohol, Acetophenone, Eucalyptol, Carvone, 1-Octen-3-ol, Isoamyl Acetate). 9 odors were presented in crossmodal haptic mode (OH), and 27 odors were presented in visual condition (OV). Subsequently, an odor-visual recognition task was arranged during an EEG recording, to investigate ERP components. The subject had to press the Left button if his predominant recognition had been codified through OV or Right button if it had been codified as OH. After the EEG recording, the subject had to perform an odor span task and fill a VAS on 3 dimensions: familiar, arousing and pleasantness. The effects of OV and OH condition and lateralization of N200 and P3b were assessed via linear mixed-effects models that allows controlling the variance related to random factors without any data aggregation. Models were estimated with the lme4 package in R whereas F-tests were computed with the Satterthwaite's degrees

of freedom approximation. We found that latencies and amplitudes of N200 increased in the OH condition ( $F = 11.04$ ,  $p < 0.001$ ;  $F = 3.38$ ,  $p < 0.05$ , respectively), with a significant two-way interaction odor  $\times$  left-sided lateralization ( $F = 6.32$ ,  $p < 0.001$ ). Significant effects were particularly observed in left occipital, left parietal, and left temporal areas. Concerning P3b, the omnibus test revealed a significant effect of the lateralization ( $F = 4.11$ ,  $p < 0.05$ ) with amplitudes increasing in left and right occipital and parietal areas as well as in Cpz and Pz. The effects of the OH condition were also confirmed by the behavioral data. Subject's Odor Span was 5, and was linked only to OH condition. The VAS indicated that stimuli assessed in the crossmodal condition were evaluated more pleasant and familiar with respect to the control condition. These results suggest that haptic, comparing visual interaction, can highly affect odor recognition.

## Cognitive profile of childhood idiopathic epilepsy

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Epilepsy is a neurological disorder characterized by repeated seizures, sudden events of varying varied duration, resulting from abnormal neuronal activity. Idiopathic epilepsy is the most common form of childhood epilepsy and is called idiopathic or primary epilepsy when clinical history and diagnostic testing does not reveal causes for repeated seizures. Our main goal is to identify the cognitive areas most frequently affected in children with generalized and focal idiopathic epilepsy. This is essential to complement the diagnostic process, optimize the application of therapeutic strategies available, and hypothesis the prognosis. Therefore, a review of reports concerning the neuropsychological assessment of children aged 4 to 12 years old was evaluated in the neurology department of the children's hospital Vittore Buzzi of Milan during 2007 through 2015. The assessment mainly used BVN neuropsychological battery and the Wechsler children scale (WPPSI / WISC III). Currently the results are still being processed. The studies conducted on patients with idiopathic epilepsy showed a standard IQ, stable in time and with similar scores to those of the control groups with medium-low values, but always within the normality. In the symptomatic form occurs, however, often a more or less serious harm. In other studies we have found that children with epilepsy have a higher incidence of intellectual and educational difficulties; the most relevant neuropsychological disorders include delayed language development, memory disorders, attention deficit disorder, learning disorders, and delayed learning in math, reading, writing, spelling and arithmetic. Several factors are responsible for these outcomes; variables related to the crisis, such as age of onset, seizure type, duration and severity of seizures, drug treatment negatively influence intellectual functioning, behavioral and acquisitions school.

## Getting ready to walk: combining neuromotor control and peripersonal/extraperpersonal space

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The present study aims at understanding the neural correlates of forward and backward oriented stepping using high-resolution Electroencephalography (EEG) to record cortical activities and two force platforms to acquire kinetic parameters. In particular, the purpose is to confirm previous results, showing larger activity of motor-related regions for backward than forward stepping, and to extend the available literature including the study of other brain regions, as prefrontal and posterior parietal areas. 11 healthy volunteers (age:  $22 \pm 3.9$  years) participated in the study. They were instructed to stand barefoot with their arms resting at their sides and their weight equally distributed on their feet. They performed a Forward-oriented Step (FS), from the actual force platform to the second platform juxtaposed to the first one in the anterior-posterior direction. After completing a step forward with both legs on the second platform, they were asked to perform a Step Backward (BS) reassuming the initial upright position with both feet on the first platform. The experiment was divided into 40 runs, each comprising five steps forward and five steps backward. Force platform and EEG recordings were electronically synchronized. The Movement-Related Cortical Potentials (MRCPs) were separately segmented and averaged into 5 s epochs (from -2500 ms to 2500 ms after the step onset; baseline: -2500/-2300 ms; filter: 15 Hz). The MRCPs from FS and BS conditions were processed using repeated measures, two-tailed cluster-based permutation test with a family-wise alpha level of 0.05. Statistical analyses showed significant differences in the interval between -1700 and -500 ms ( $p < 0.003$ ) and from -200 ms to 0 ms ( $p < 0.016$ ). After movement onset, differences between conditions continued to be significantly different up to 1700 ms ( $p < 0.003$ ). The Bereitschafts potential (BP), reflecting motor preparation, was larger for BS (two peaks) than FS (one peak); the prefrontal Negativity (pN), reflecting cognitive control, peaked concomitantly to movement in FS and persisted throughout the steps in BS. In addition, a slow negative activity (posterior BP) was present at parietal sites from -2200 ms, but lasting more in FS than BS. The neural correlates of forward and backward stepping suggest a functional distinction of these actions (e.g. forward stepping allows spatial navigation, backward stepping is often associated with defensive action), which is paralleled by a different cortical organization. During planning and monitoring phases, different areas were involved: FS is mainly based on the control of parietal and frontal areas, BS relies more on frontal and prefrontal brain regions. Nonetheless, the early involvement of parietal areas is shared by the tasks, as well as the activity of the motor-related regions. Therefore, body schema, peripersonal/extrapersonal space and dynamic postural control share the same frontal-parietal circuits and can be empirically combined.

## Beta-band as hallmark of functional architecture correspondence between rest and movie viewing

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Brain hubs act as important points of convergence for the integration of distributed processing across multiple brain regions and systems. Their topological central embedding in anatomical networks supports the idea that hubs play an influential role in multiple aspects of cognition. Despite behavior unfolds not only in space but also in time, temporal dynamics of interaction processing in hub regions remains elusive. To this aim, we explored the spatiotemporal changes of network hubs using Magneto-Encephalography (MEG) by measuring the static and transient networks interaction in  $\alpha$  and  $\beta$  BLP over rest, intact and scrambled-viewing. Both viewing conditions induced decrement of  $\alpha$  but not  $\beta$  BLP within/between-networks correlation with a relative preservation of the within-network topography in both bands. In parallel, the audiovisual stimulation reorganizes the topology observed at rest, especially for the cross-networks interactions, except for the  $\beta$ -band during movie watching where the overall topology remains unchanged. Information integration at rest is marginally affected during movie watching, as we identified a core of network hubs that remain remarkable stable across rest and task states, especially in  $\beta$ . At short time scale, these highly central nodes behave as temporally overlapping transient hubs that together alternate between periods of strong and weak centrality. While in  $\alpha$ -band these joint centrality fluctuations differed across task states, the  $\beta$ -band highlighted a strong correspondence between rest and natural but not scrambled viewing. Overall, our results indicate that in  $\beta$ -band the dynamics of information integration at rest might reflect the slow-varying temporal structure of naturalistic stimulation, presumably representing prior expectations of the environment.

### **Physiological cognitive aging and preventin in life contexts: a project of cognitive enhancement addressed to elderly users of the area 2 territorial social service in Milan**

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This project is part of the broader path of the community service program “Senior Adult: interventions for socializing, support and taking charge”, carried out at the social services. Considering the typical limits and constraints of the context and the users’ socio-demographic and cultural background, I created a short cognitive enhancement program in the field of neuropsychological prevention and, through stimulation and training of memory, attention and executive functions, I set the following specific objectives: to develop a certain level of awareness about cognition’s aspects and, in particular, on patients’ own cognitive functioning; to offer the opportunity to participate in activities with objectives, which are different from recreational ones; to stimulate learning processes related to cognitive flexibility. The project consists of three phases: evaluation, stimulation program and re-evaluation. For the evaluation a mini-battery was created, consisting of tests such as MMSE, MoCA and FAB, characterized by quick and easy administration; while during the week of stimulation sessions, lasting about 45 minutes, “pencil and paper” instruments were used, in particular for three exercises per function. The project was proposed to five users, aged between 64 and 96 years, not suffering from particular diseases, who expressed feelings of anxiety related to the possible consequences of physiological cognitive aging during the monitoring and support meetings. The short

duration of the project did not permit the demonstration of a significant improvement in performance in quantitative terms, although there has been a slight improvement in the test scores. The users, in the closing phase, however, declared to have perceived an improvement in mood and increased motivation to get involved in experiences and activities with specific objectives.

## The Hand Blink Reflex in fighting sports

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The Hand Blink Reflex (HBR) is a subcortical defensive response, elicited by the electrical stimulation of the median nerve at the wrist. In static conditions, this reflex response dramatically increases when the stimulated hand is inside the Defensive Peripersonal-Space (DPPS) of the face. In fighting sports it might be involved in the defense of the body, especially the face, from opponents' blow. Particularly in boxing the defense consists in blocking with arms or covering-up with the gloves, but the boxers learn from the beginning to keep their eyes open when parry a punch, for always being ready to counterattack. This work aimed to investigate whether athletes practicing fighting sports could modulate the HBR. Two populations of subjects were recruited for the study: one was composed of boxers of different level of expertise and the other one was composed of individuals naïve to fighting sports. Electromyographic activity was recorded from the orbicularis oculi while the HBR response was elicited in three static hand positions, depending on the distance of the hand from the face: far, intermediate and near positions. We found that the classical HBR enhancement in the near position was present only in the control group, while no significant difference was found in the three positions in the boxer group. Further, the difference between the nearest and the farthest positions negatively correlates with the years of sport practice, showing that greater expertise in boxing corresponds to higher suppression of the HBR modulation. These findings suggest that experience in fighting sports can modulate the HBR and thus shape the dimension of the DPPS.

## Cerebellum and the defensive peripersonal space

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The cerebellum is involved in a wide number of integrative functions. We evaluated the role of cerebellum in peripersonal defensive behavior, as assessed by the so-called

Hand Blink Reflex (HBR), modulating cerebellar activity with transcranial Direct Current Stimulation (tDCS). Each volunteer underwent to cerebellar (sham, anodal and cathodal) and motor cortex (anodal or cathodal) tDCS (total of five session *per* subject); sessions were separated each other by at least one week to avoid possible confounding after-effects. During each session, we evaluated HBR area at baseline and immediately after cerebellar, or cortical, polarization; electrical stimuli were delivered using a surface bipolar electrode placed on the median nerve at the wrist and EMG activity recorded from the orbicularis oculi muscle bilaterally. Direct current was applied for 20 minutes with an intensity of 1.5 mA. Depending on the hand position respective to the face, we explored four different conditions: “hand far”, “hand near” (eyes open), “side hand” and “hand near” (eyes closed). While sham and cathodal stimulation had no significant effect, anodal tDCS dramatically dampened the magnitude of the HBR, as measured by the area under the curve (AUC), in the hand-patched and side-hand conditions only, for ipsilateral (side-hand:  $F [1, 36] = 23.5, p < 0.0001$ ; hand-patched:  $F [1, 36] = 9.45, p = 0.004$ ) as well as contralateral recordings (side-hand:  $F [1, 36] = 61.2, p < 0.0001$ ; hand-patched:  $F [1, 36] = 13.2, p = 0.0009$ ). Conversely, when tDCS was applied over left M1, no significant modification of HBR area was found, following both anodal and cathodal polarization ( $p > 0.1$ ). These results support a role of the cerebellum in the defensive responses within the peripersonal space, thus selectively modulating defensive behavior when the visual feedback is missing. From a functional point of view, our results could indicate that cerebellum is involved in visual-independent learning of defensive behavior. Cerebellum could not only integrate non-motor functions, but also disentangle different channels carrying multi-sensory information. This selective role could be further confirmed by the results obtained with M1 tDCS.

## The nature of visual experience in blindsight type II: evidence from EEG in a hemianopic patient

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One of the most challenging problems for cognitive neuroscience is the neural correlate of visual awareness. One experimental strategy to cast light on this problem is to study the phenomenon of “blindsight (type I)”, i.e. the presence of unconscious visually guided behaviour in hemianopic patients. Particularly interesting is the case of blindsight type II, that is, the presence of the occurrence of a stimulus in the blind field without visual perception. In this light, the aim of this study was to evaluate, using Event-Related Potentials (ERPs), the neural correlates of visual awareness in a hemianopic patient with large damage to left V1. The EEG-data were collected while the patient performed an orientation discrimination with moving or static square-wave gratings presented in the affected or in the intact hemifield. The behavioural results showed that the patient had a performance above chance for the orientation discrimination with moving but not with static stimuli. Furthermore, she reported a feeling of something appearing in her blind hemifield without perceiving stimulus features. Importantly, we found a reliable ERP response elicited when the stimulus was presented in the blind field. The single-trial ERP analysis showed a significant negative component in the N1 domain for both static and

moving stimuli. This component had a major scalp distribution in the ipsilesional electrodes. The timing of the peak correlated with that of the above form of visual awareness and source analysis showed that the component arose from the parietal lobe, specifically from the left superior parietal lobe. In addition to the presence of N1, it is important to highlight that the early components, C1 and P1, and the later component, P300 were absent. The absence of C1 and P1 fits in well with the impossibility of the patient to perform correctly the orientation discrimination task with stationary stimuli. The absence of P3 could explain the impossibility of our subject to reach a full awareness of the stimuli. In conclusion, following stimulus presentation to the blind field of a hemianopic patient we found a ERP component that might be considered as a neural correlate of blindsight type II. An important point is that the source of this component is outside the occipital cortex in the parietal lobe of the damaged hemisphere. This represents an example of plastic compensation that does not enable full perceptual awareness but a feeling of stimulus occurrence.

## Return to safe driving after severe brain injury: a case study

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The return to driving is a need strongly felt by subjects with severe brain injury outcomes. The autonomy given by the possibility of driving represents an important goal for a full social and work reintegration. In young patients the basic automatized psychomotor skills of the guide can often be preserved after the pathological event, but these are insufficient to ensure safe driving. Indeed, the person qualified to guide should meet the following criteria: a low probability of sudden behavioral dyscontrol; sufficient cognitive, perceptual and motor skills to learn and apply the techniques of driving; adequate judgment and social responsibility. Unfortunately, not all subjects after the traditional rehabilitation have all these prerequisites for safe driving. In this context, some experiences of support to the return to safe driving are born, with structured programs of re-evaluation and training of the preserved abilities. S.P., a 33 year old man with right hemisphere frontal hemorrhage outcomes, occurred in October 2015, has been included in the project about safe driving, undertaken at the Centre for Rehabilitation Cardinal Ferrari (Fontanellato, PR). The multi-professional team involved in the patient pathway is composed of doctors, physiotherapists, psychologists, psychomotor therapists, orthopedic technicians specialized in adaptation of vehicles and driving instructors with specific expertise. The role of neuropsychological investigation is to identify the residual cognitive damage in the areas of attention, learning, memory, visual perception and executive functions. Formal tests (WAIS IV, Trail Making Test A-B, Stroop Test, Phonemic Verbal Fluency, Barrage Test, Corsi Block-Tapping Test, Supraspan Learning Task, Elithorn's Perceptual Maze Test, Wisconsin Card Sorting Test, Raven Standard Progressive Matrices), a specific battery computerized for the evaluation of driving skills (Vienna Test System) and interviews to the patient (SAT-P, BIRT questionnaire) and to the caregiver (BIRT questionnaire) were administered. In summary, the neuropsychological evaluation has documented an impoverishment of the cognitive flexibility



and inefficiencies of working memory, but there aren't severe abnormalities that could interfere with the car's driving. The clinical interviews don't reveal behavioural disorders, with the exception of a slight impulsivity. The SAT-P shows a good satisfaction profile for quality of life. Finally, in relation to the Vienna Test System the performance in attentional tasks is adequate for accuracy but below average for the time. The reaction time and the motor time, in the task with a single stimulus, are placed respectively in and above the average; however in the dual task (visual-acoustic), the reaction time is slightly below. The ability to estimate a moving object is normal and the performance in the assessment of willingness to take a risk in different situations in traffic is higher than normal.

## **Exclude the Emo: how social exclusion modulates social information processing**

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Social exclusion is felt as a threat to the human “need to belong” and activates the brain areas related to physical pain. Social exclusion has been proven to drive aggressive behaviours, to create emotional numbness and it also seems to facilitate implicit processing of positive emotions and enhance re-inclusion finalised behaviours (so-called “tuning to positivity”). These effects appear to be mediated by the individual's empathy. Nevertheless, the effects of social exclusion on emotions and social information processing are unclear. This study aims to test whether exclusion can improve social processing (i.e. emotion recognition and gaze direction discrimination), and whether this can be modulated by empathy. Young adult participants (M = 20; F = 20) were asked to identify either the emotional expression (happy, sad, angry, fearful) or gaze direction (direct vs. averted gaze) of faces after social exclusion (or inclusion) through the Cyberball paradigm. Empathy had previously been estimated through the Empathy Quotient questionnaire. Experimental results on accuracy show that social exclusion makes gaze direction discrimination worse, but not emotion identification. Interestingly, higher empathy was associated with a stronger enhancement of social processing in excluded rather than included participants. Besides, these effects are also modulated by participants' gender: male participants' accuracy is lower when they are socially excluded, while female participants tend to show higher accuracy when excluded. This study brings new evidence indicating that social exclusion has an effect only on one of the two crucial social dimensions (gaze direction discrimination, but not emotion identification). Interestingly, participants' empathy and gender also modulate these effects in different ways. The modulatory effects of participants' empathy suggest that more empathic people are more sensitive to rejection and pay much more attention to social information. The moderation of participants' gender shows that male and female participants show different reactions to social exclusion, in terms of social information processing: male participants seem to show a stronger effect of “emotional numbness”, resulting in a more difficult processing of social information; in contrast, female excluded participants express an enhanced tendency to process potentially re-inclusive stimuli, as faces.



## Mild Cognitive Impairment: a brief review and a clinical analysis

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The aim of the present work is to describe, by analysing literature and clinical cases, clinical characteristics of Mild Cognitive Impairment (MCI). MCI refers to a clinical condition in which alterations of cognitive performances are present primarily in memory functioning but also in cognitive speed, attention, language and executive functions. These alterations, reported by the patients and by caregivers, are objectively measured using neuropsychological instruments. In MCI patient cognitive performances are statistically worse than expected considering age, gender and level of education. However, these performances do not significantly impair patient's usual daily activities or work. Analysing literature, a general agreement emerges on differentiating clinical manifestations of MCI (amnestic/non amnestic; single domain/multiple domain); on the other hand, studies on clinical evolution of MCI (in term of prognosis and probability that MCI converts into dementia) are divergent. Authors converge on the importance of a complete and specific neuropsychological evaluation to completely describe and correctly diagnose MCI. Anyway, as a first step, they still consider all risk factors and the management of medical conditions (including psychopathological symptoms) associated to MCI (that could make worse prognosis). There is agreement among authors on efficacy of cognitive trainings (also using computerized programs) and neuropsychological rehabilitation to treat and manage cognitive alterations of MCI patient. In recent years, many studies have been increasing their attention on potential use of non-invasive brain stimulation techniques, as – for example – Transcranial Magnetic Stimulation (TMS), to improve cognitive performances of MCI patients. By analysing clinical cases, MCI patients are clearly aware of cognitive changes and difficulties in daily life. As a result, they spontaneously use strategies to improve their performances in everyday life. Besides, cognitive symptoms complained by patients are referred to all spectrum of cognitive abilities. However, cognitive deficits, evaluated with neuropsychological instruments, are observed in memory tests: patients show difficulties in long term memory, particularly in delayed recall for verbal items. No deficits are found in attention, language and executive functions. The duration of symptoms is variable among patients (from few months to years). No reductions in social activities and hobbies are observed. In summary, after considering the variability of cognitive symptoms and clinical prognosis of MCI forms, four steps must be followed: (1) to completely diagnose and to investigate cognitive manifestation of symptoms in MCI patients with neuropsychological instruments; (2) to manage and correct risk factors and medical conditions; (3) to use cognitive trainings; (4) to monitor over time the evolution of symptoms.

## Is there a relation between P300 and behavioural scales in the assessment of patients with Disorders of Consciousness?

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After clinical stabilization of vital functions, patients with Disorders of Consciousness (DoC), are usually moved to the rehabilitation intensive unit, where the assessment of self- and environmental-awareness is based on behavioral indexes. Defining a prognosis about consciousness recovery is crucial for patients and their family, and for choosing suited therapeutic approaches. However, clinical scales effectiveness is often restricted by subjective judgement. Electrophysiological examinations brings some advantages for the assessment of patients with DoC due to their objectivity and high temporal resolution. The P300 component of the ERPs is a positive wave generated when patients detect a rare and unexpected stimulus in a regular train of standard stimuli (i.e. oddball paradigm) and might reflect either the recognition of the target's intrinsic meaning or the detection of its acoustic salience. In the present work the P300 was acquired in 12 subjects with DoC at S.D. GCLA of Azienda Ospedaliero-Universitaria Pisana: 4 of them affected with subarachnoid hemorrhage, 4 with traumatic brain injuries and 4 with post-anoxic coma. The oddball paradigm was administered as both passive and active trials. During the active trial patients were instructed regardless of their state of awareness to focus on rare stimuli only. CRS-R was administered weekly in order to assess patients' behavioural responses. All the patients tested showed a transition from an initial Vegetative State (VS) to a Minimally Conscious State (MCS) within 100 days from the admission. In all patients the P300 was absent on admission, but became subsequently evocable. About 10 days before the reappearance of behavioural signs of consciousness of recovery. In conclusion, the P300 wave could be considered as a prognostic marker to be used in evaluating non-responders DoC patients, in order to "estimate" cognitive residual functions and manage early therapeutic and rehabilitating interventions.

## **Inhibition or facilitation? Modulation of corticospinal excitability during Motor Imagery**

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Motor Imagery (MI) is the mental simulation of a given action without any overt movement. Behavioral evidence shows that MI induces Motor Execution (ME) like effects on several tasks and functional evidence shows that brain regions recruited during MI and ME largely overlap. However, techniques examining the effective connectivity between brain areas have shown a neurophysiological dissociation between ME and MI. Indeed, although the Supplementary-Motor Area (SMA) is active during both tasks, the functional connectivity from SMA to primary-motor cortex (M1) shows facilitation during ME and inhibition during MI, depending on whether the overt movement has to be performed or suppressed. A theoretical conflict seems to exist between this inhibitory effect on M1 and a facilitatory effect on corticospinal excitability, reported by several studies employing single-pulse TMS over M1 during MI. The aim of this TMS study is to clarify the role of MI in modulating the corticospinal excitability, by manipulating the instructions given to participants, either stressing or not the necessity to maintain a full muscle relaxation during a MI task. If the facilitatory effects on M1 excitability actually pertain to the MI *per se*, we should expect to replicate it, irrespective of the instructions. Conversely, if the facilitatory

effect depends on the muscle contraction, crucial differences between differently instructed subjects should be expected. Twenty-eight healthy subjects were recruited and divided in two groups, depending on the instructions. Subjects had to perform a kinesthetic MI task with the right hand (i.e. index-thumb opposition task), while single pulse TMS was delivered over left M1. A baseline measure was recorded before and after the task. Motor Evoked Potentials (MEP) were recorded from the right FDI. A  $2 \times 2$  ANOVA on MEP amplitude, with Group (Relaxing; No-Relaxing), as between-subjects factor, and Task (Baseline; MI), as within-subjects factor, showed a significant Group\*Task interaction ( $F [1, 26] = 11.705$ ,  $p = 0.002$ ). By comparing MI to Baseline, an opposite MEP modulation was found between Groups, with a significant increase in No-Relaxing Group ( $p < 0.001$ ) and a significant decrease in Relaxing Group ( $p = 0.02$ ). Furthermore, we recorded the EMG activity 500 ms before the TMS stimulation to ensure that RMS AUC was always lower than  $10 \mu$  Volt/sec. Crucially, in No-Relaxing Group, the pre-stimulus EMG activity significantly predicted the MEP amplitude during the MI task ( $r = 0.655$ ;  $p = 0.011$ ). These preliminary results suggest that the theoretical conflict between inhibitory and facilitatory effect of MI on M1 can be due to methodological factors. When muscle contraction was prevented by a proper instruction, an inhibition of the corticospinal excitability was found during MI. This TMS finding is compatible with other methodological approaches, showing inhibitory functional connectivity from SMA to M1 during MI, when the overt movement has to be suppressed.

## Self-construal predicts the illusory feeling of “owing the other’s face” via other-oriented traits

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Increasing experimental evidence and theoretical models suggest that online integration between interoceptive and exteroceptive bodily signals underlies our sense of self. Simple experimental paradigms used multisensory conflicts, based on the asynchrony between signals coming from different sensory modalities (e.g. visual, tactile, sensorimotor, interoceptive), to alter the feeling of owning a body, a body-part and surprisingly even a face. Experiencing tactile stimuli on the face while seeing the same stimulation delivered synchronously to the face of another individual induces the subjective illusory experience of owning the other’s face and biased self attribution of the other person’s facial features (enfacement). Enfacement depends both on participants’ empathic traits and on how the other person is perceived. Here, we tested the hypothesis that inter-individual differences in self-construal (Self Construal Scale, SCS), that is how individuals define the self in relation to others, determine the extent to which shared synchronous visuo-tactile stimulation makes individuals owning the other’s face. We hypothesized that such self-other merging would be positively predicted by an interdependent self construal characterized by a self fundamentally connected to others, by empathic (Interpersonal Reactivity Index, IRI) and autistic (Autistic Quotient, AQ) traits. To this aim, self-construal, empathic and autistic traits were measured in 83 participants (60 F) before they experienced synchronous and as

a control asynchronous, facial visuo-tactile stimulation with another person. After a Principal Component Analysis (PCA) performed on the IRI and the AQ questionnaires, a factor indexing other-oriented traits was extracted and factor scores were used as mediator in a mediation analysis having SCS as predictor and the illusory feeling of owning the other's face as dependent variable. In line with our hypotheses, we found that interdependent, but not independent, self construal predicts the tendency to own other's face in response to synchronous visuo-tactile stimulation via other-oriented traits. These results suggest that the relation between the plasticity of self-other boundaries, a basic and body-centered aspect of the self and a more high-level self-related trait, namely the way we define the self in relation to others, is mediated by inter-individual differences in empathic and autistic traits.

## The sense of agency affects defensive responses: modulation of the corticospinal excitability during self-generated and other-generated pain

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Converging evidence shows that the intensity of self-generated stimuli is perceived as attenuated respect to the same stimuli generated by someone' else (i.e. sensory attenuation). However, the effect of self-generated pain on the corticospinal excitability has never been investigated and we aimed to investigate it here. We took advantage of the inhibitory modulation of the motor pathway to the muscle of the hand receiving painful stimuli (i.e. freezing-like effect) and we asked whether voluntary self-generated pain might reduce this inhibitory effect on the corticospinal excitability, as consequence of the sensory attenuation process. Motor Evoked Potentials (MEPs) by TMS over left M1 were recorded from the right APB and FDI muscle. During MEPs recording, 21 healthy participants received electrical stimuli on the right digit V in two different conditions: (a) "self-generated pain", when they pressed a button with their left index finger; (b) "other-generated pain", when they watched the experimenter pressing the button. After each stimulus, participants were asked to rate the perceived pain intensity on a 0-7 Likert scale. Before and after each experimental block, to control the effect of movement *per se* on the contralateral M1 excitability, we recorded baseline conditions (without pain), while the subject moved his left index finger to click the button ("self-generated baseline") or observed the experimenter clicking the button ("other-generated baseline"). Separately for each muscle, MEPs amplitude of both self-generated and other-generated pain conditions, expressed as percentage of the relative baseline, were analyzed by means of a paired T-test, two-tailed. If the sense of agency modulates the corticospinal excitability, in self-generated compared to other-generated pain conditions, together with a sensory attenuation in the subjective ratings, we should expect to find a reduced decrease of the MEPs amplitude. Behavioral results showed that participants reported the subjective perception in self-generated pain condition (mean  $\pm$  SE = 4.153  $\pm$  0.258) as attenuated compared to the other-generated pain condition (4.522  $\pm$  0.306;  $p$  = .032). Physiological results showed, in the control FDI muscle, no differences between "self-generated" and

“other-generated” baselines, excluding a possible movement-dependent facilitation effect related to the contraction of the contralateral FDI during button press. More crucially, in the target APB muscle, a significantly reduced decrease of the MEPs amplitude was found in the “self-generated pain” ( $0.190 \pm .020$ ), compared to the “other-generated pain” ( $0.160 \pm 0.018$ ;  $p = .021$ ). Our results show that, when noxious stimuli are self-generated, the conscious experience of the attenuated perceived intensity has a physiological counterpart in the attenuation of the freezing-like effect. Overall, this finding represents the first evidence that the sense of agency affects defensive responses, modulating the corticospinal excitability.

## **Cortical reactivity and cortico-cortical interactions in Persistent Developmental Stuttering investigated by TMS/EEG co-registration** **Busan P.<sup>1</sup> - Del Ben G.<sup>2</sup> - Russo R.<sup>2</sup> - Formaggio E.<sup>1</sup> - Monti F.<sup>3</sup> - Manganotti P.<sup>3</sup> Battaglini P.P.<sup>2</sup>**

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Developmental stuttering is a disturbance in the rhythm of speech. It appears in childhood and may persist in adulthood (Persistent Developmental Stuttering, PDS). Its causes are not understood. PDS is characterized by the presence of abnormal activations of brain regions related to motor and speech function, as well as by weakened/abnormal white matter integrity, especially in motor and speech regions of the left hemisphere. One of the most involved networks is the cortico-basal-thalamo-cortical one, with Supplementary Motor Area (SMA) which plays a crucial role. In the present work, we investigated the effect of Transcranial Magnetic Stimulation (TMS) delivered on bilateral SMA in PDS, while registering evoked responses by Electroencephalogram (EEG). The purpose was to investigate the effect of SMA activation on cortical reactivity and cortico-cortical interactions in stuttering, starting from a “default” condition. A group of 13 participants with PDS was compared with 15 normal speakers (all right-handed males, age range 22-48 years). About 150 trials of single pulse TMS were delivered on SMA (individuated by neuro-navigation on a resonance model), interleaved by sessions of sham stimulation, to control for unspecific TMS activations, such as acoustic stimulation. TMS was delivered at 100% of Resting Motor Threshold (RMT) measured by stimulating the left hemisphere primary motor cortex and registering from the First Dorsal Interosseous (FDI) muscle of the right hand (also RMT of the left FDI, i.e. stimulating right primary motor cortex, was measured). Subjects were asked to stay at rest, with closed eyes, during stimulations. EEG was recorded from 31 electrodes, equally distributed on the scalp, to allow evaluation of TMS-Evoked Potentials (TEPs) and source localization. Resting state EEG, normally recorded before stimulation sessions was also evaluated. RMT values did not differ between groups. Lower patterns of response were bilaterally observed in sensory-motor regions of stutterers with respect to fluent participants. This was partially compensated by qualitatively higher evoked responses in frontal regions, suggesting a different pattern of neural interactions with SMA in the two groups. Resting state EEG, quantified by power spectral density, mainly suggested the presence of lower relative power in the

sensory-motor strip of PDS with respect to normal speakers in beta band, compensated by higher alpha relative power in frontal regions. Findings suggest that an abnormal pattern of interactions is activated in PDS when stimulating SMA complex. SMA plays a role in the successful realization of highly demanding voluntary movements (such as speech execution). Stuttering may result in persistent neural changes such as those highlighted by resting state EEG. Findings may be useful for the implementation of new treatment solutions for PDS, ranging from neuromodulatory interventions to neurofeedback.

## **A rhythmic intervention to improve reading skills in dyslexic adults: evidence from a single case study**

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Rhythmic Reading Training (RRT) is a computerized intervention for Developmental Dyslexia (DD) which combines sublexical reading exercises with rhythm processing training. The efficacy of RRT in improving reading skills of children with DD between the age of 8 and 13 has already been showed to be significant and comparable to other validated treatments. Following these promising results, we are now interested in investigating the effect of the intervention, suitably modified, on dyslexic adults. Here is presented the first administration of RRT to an adult with DD. G.T. is a 20-years-old undergraduate of average intelligence who received the first diagnosis of DD in primary school. G.T. took part in 10 individual sessions of 45 minutes over two weeks in which RRT was implemented by a trainer. The participant's reading skills, verbal working memory, and rapid automatized naming skills were assessed before and after the intervention period. A follow-up assessment took place one month after the end of the intervention. Results showed that RRT enhanced both G.T.'s reading accuracy and reading speed of text, words, and pseudo-words. The highest improvements were recorded in reading speed, namely, the parameter that can usually be hardly modified in subjects with DD. Moreover, improvements in verbal working memory and rapid automatized naming occurred. These gains were maintained for a month after the end of the intervention. This first case study will encourage further research using RRT as an intervention for improving reading skills in dyslexic adults.

## **Assessing and rehabilitating social competence in visually impaired children**

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The development of social cognition is strictly related to the development of spatial cognition: the ability to independently navigate and orient ourselves in the environment facilitates the engagement in social interactions. Since it has been shown that vision guides the maturation of spatial cognition in the brain, we expect to find spatial but

also social deficits in visually impaired individuals: the impossibility to use the visual feedback to calibrate actions in space causes a strong delay in spatial development which in turn determines a difficulty in making social contacts with peers. Indeed it has been demonstrated that early blind children have difficulties in auditory and haptic spatial skills, locomotor and mobility skills, but also in engaging positive social interactions. The aim of our study is to assess and rehabilitate social competence in visually impaired children thanks to a long rehabilitation training using a device that provides an audio-motor feedback of body actions which should resemble the visuo-motor feedback necessary for sighted children to develop spatial cognition. To test the level of social competence in visually impaired children, we used a task assessing the ability of the visually impaired child to initiate and sustain an interaction with the experimenter: the child was asked to understand and imitate a regular arm movement performed online by the experimenter in front of him thanks to a sound source positioned on the dominant arm, while for both subjects kinematic data were registered. The level of social interaction between the two agents has been calculated thanks to a Granger causality analysis applied to their arm movement kinematics. The rehabilitation training followed by the visually impaired children lasted three months and consisted in a series of spatial and social games performed with the use of a sonorous bracelet which provides an auditory feedback of body actions in space. Overall we found that compared to sighted children, visually impaired children present a poorer communication flow with the experimenter indicating a less efficient social interaction. Nonetheless after the rehabilitation training, the amount of communication between the two agents is significantly improved indicating that a specific training based on the substitution of visual with auditory feedback of body actions can enhance the social inclusion for the blind population. We concluded that the spatial and social impairments assessed in the blind population can be avoided or drastically weakened by reinforcing their audio spatial representation of the environment.

## **Neuropsychological assessment and cognitive rehabilitation in patients with cerebral cancer: a case report**

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Cognitive and affective problems in cancer patients resulting from the disease, are often not considered, since the primary objective is to deal with the risk of life. The outcome of surgical interventions or pharmacological treatments, chemotherapy and radiotherapy can have consequences on the cognitive side and impair complex mental functions. Neuropsychological evaluation allows a diagnostic framework that is essential for a possible rehabilitation project in order to having a proper impact on cognitive, behavioral and affective deficit which had been identified in the first instance. The objective of this paper is to describe the whole clinical course of assessment and intervention of a cerebral cancer patient in a private clinical center. In this type of structure the Neuropsychologist figure act a very important role both in cerebral vascular, traumatic or ischemic stroke, and in the cognitive impairment. The case can properly underline the necessity of qualified professionals who are able to operate into the private sector and meanwhile who can manage the multidisciplinary process.



## **Cortical representation of facial and masticatory voluntary movements: a magnetoencephalographic study**

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The cortical representation of orofacial movements in non-human primates is organized in a complex mosaic of different areas beyond the primary motor cortex, including the dorsal and ventral premotor cortices on the lateral aspect of the hemispheres and the supplementary motor area and cingulate cortex on the medial side. In this study we investigated the cortical representation of facial and masticatory movements in humans by means of Magnetoencephalography (MEG) during voluntary smile and voluntary teeth clenching. We asked participants to observe a red dot (4 seconds) turning green (1 second). Participants were instructed to perform, depending on the block, either a voluntary smile or a teeth clenching when the dot turned green, and to completely relax when the dot turned red. Trials have been aligned according to the onset of the electromyographic (EMG) activity on the muscles of interest. We compared activity between -50 and 0 ms (target time-window) before EMG onset with the time-window between -100 and -50 ms (baseline time-window). Event-related activity associated to teeth clenching showed activation outside the Brodmann's area 4, specifically in the anterior mid-cingulate cortex. Interestingly performing voluntary smile relies more on the primary motor cortex bilaterally and right insula. A statistical comparison between the two conditions in the target time-window showed a more prominent activity of the supplementary motor area and cingulate cortex for the teeth clenching action while in the voluntary smile right posterior insula and the primary motor cortex bilaterally were more activated compared to teeth clenching. The present results are in line with the hypothesis that multiple cortical sites are involved in face muscle voluntary activity outside the primary motor cortex. Moreover they also indicate that cortical activity related to masticatory and facial muscles is subtended by partially different networks.

## **Different degrees of sensitivity and specificity to speech comprehension within the language network**

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Neuroimaging findings demonstrated that speech comprehension relies on a vast, left-lateralized cortical network that comprises temporal, parietal and frontal regions. Never-



theless, a meta-analysis on neuropsychological observations confirmed the historical perspective that deficits in speech comprehension are prevalently associated with localized lesions in the left temporal lobe. To close the gap between the *sparsity* of brain activity elicited by language comprehension tasks and the *exactness* of brain lesions producing language impairment, we conducted an fMRI experiment measuring the sensitivity and specificity of brain responses to linguistic stimuli. Twenty right-handed healthy subjects (6 M;  $23.5 \pm 2$  years) were enrolled in the study and asked to alternatively listen to meaningful and unintelligible narratives. By using a multivariate searchlight approach, we identified regions that significantly distinguish between meaningful and unintelligible speech. More importantly, using the same method, we mapped also the sensitivity (i.e. probability that a stimulus is correctly identified as meaningful given the times a narrative is presented) and specificity (i.e. probability that a stimulus is correctly identified as *non-speech* given the number of times an unintelligible narrative is presented) of language comprehension across the whole brain. In accordance with previous studies, we found that activity of frontal (left precentral; left pars orbitalis of the inferior frontal cortex; right inferior frontal), temporal (bilateral anterior temporal; left superior temporal; left inferior temporal) and parietal regions (bilateral intraparietal; bilateral posterior cingulate; left parieto-occipital) distinguished between meaningful vs. unintelligible speech ( $p < 0.05$  FWEc; peak: 79.6%). Nonetheless, most regions of this network demonstrated high levels of sensitivity, but not specificity, for meaningful speech ( $p < 0.05$  FWEc; peak: 96.7%). The only large cluster that showed significant specificity for meaningful narratives was located within the left superior temporal sulcus (left STS;  $p < 0.05$  FWEc; peak: 86.7%). Other regions of the language network, such as the bilateral anterior temporal lobe and the inferior portion of the precentral sulcus, exhibited a patchy organization, in which voxels with high sensitivity laid closely to those with high specificity. Our results demonstrated that left STS (presumably Wernicke's area) is the only large cortical cluster that responds with high specificity to meaningful speech. Other brain regions are recruited during language comprehension, though lack of specificity. This finding could account for the gap between previous fMRI studies and lesion reports. Noteworthy, classification accuracy in multivariate approaches may be biased towards sensitivity and does not necessarily reflect a balance between false positive and false negative rate, which can be critical when inferring the functional role of a brain region.

## Psychophysiological mechanisms guiding recognition of basic and complex emotions without visual cortex

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A longstanding tradition in emotion science concerns the distinction between so-called basic emotions, phylogenetically ancient and biologically rooted, and social emotions, whose meaning depends on the social context and whose recognition emerges later

during development. Prior studies have shown that patients with cortical blindness following destruction of the primary visual cortex (V1) are able to discriminate above chance basic emotions, such as fear or anger, when the stimuli are presented in their blind fields (affective blindsight), owing to the involvement of phylogenetically ancient subcortical structures. However, there is yet no investigation of whether social emotions can be recognized without awareness in patients with affective blindsight, of which psychophysiological changes are associated to this process, and of possible differences with basic emotion. Here we tested in a combined behavioural-psychophysiological study two well-known patients with affective blindsight, GY and DB. In alternating blocks, facial expressions of different basic emotions, anger and sadness, and of social emotions, guilty and arrogance, were singly and randomly presented either to the intact or blind visual fields. The patients were asked to categorize the expression presented in a 2 alternative forced choice task (2AFC) while pupil dilatation was continuously sampled. After this primary 2AFC response, the patients were also required to indicate their confidence on a 4-point scale. Recognition accuracy was comparably high (about 80%) for basic and social emotions in the intact field. Conversely, when stimuli were projected to the blind field, recognition accuracy for basic expressions remained above chance, whereas recognition for social expressions dropped to chance level. Pupil dilation significantly differentiated between angry and sad expressions both in the intact and blind field, whereas there was no significant difference in pupil response to social emotions in either fields. Noteworthy, recognition confidence for unseen basic expressions was positively correlated to the amplitude and time of pupil dilation, but only for correct responses. This suggests that the patients may unwittingly sense psychophysiological changes related to non-conscious processing of basic expressions, and use it as a guide to orient their discrimination without visual awareness. In fact, when these psychophysiological changes are not sufficiently differentiated, as between social expressions, or when behavioural responses are given before they can fully develop, non-conscious recognition of emotions drops at chance.

## Effects of personality traits during the exploration of museum spaces: cerebral (EEG) and autonomic (Biofeedback) responses

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A visit to the museum is a real aesthetic experience where the visitors feel themselves like living a spiritual moment linked to the beauty of the artworks. Aesthetic perception derived by artwork is a complex interplay of cognitive, emotional, behavioural and physiological responses. Previous studies showed that also psychological components could be responsible of aesthetic experience, so the aim of our research is to explore if, in addition to the psychophysiological level, the personality traits could have effects during exploration of different museum spaces. Our sample was composed by 18 participants (M = 23,8; DS = 1,4). They were asked to freely explore for 10 minutes each areas, starting randomly from one of the two spaces: “Leonardo Space”, a traditional museum area which contains models of Leonardo’s inventions and its drawing; “Spatial

Space”, an interactive area which contains multimedia devices and objects about space like shuttles and spacesuits. During the exploration, we measured electrophysiological (by EEG) and autonomic (by Biofeedback) responses; then the participant completed a test of personality, the Big Five Questionnaire 2. After a correlational analysis, we found a significantly negative correlation between the score of Agreeableness of BFQ-2 and alpha band activity in the left frontal cortex during the exploration of the “Leonardo Space”. We suggested that subjects with higher values of Agreeableness paid more attention to Leonardo’s models with an activation of the reward system (left frontal cortex). People tried to understand the mind of the artist. Then we found a significantly negative correlation between the score of Extroversion of BFQ-2 and SCL (Skin Conductance Level), and between the score of Extroversion of BFQ-2 and PULS (heart rate) during the vision of the models of Leonardo da Vinci’s works. Increasing the values of Extroversion, subjects were more concentrated seeing the models of Leonardo’s inventions. Extroverted people, who are dynamic, imaged the movement and the function of Leonardo da Vinci’s creations. Finally, we found a significantly negative correlation between the score of Conscientiousness of BFQ-2 and SCL, and between the score of Conscientiousness of BFQ-2 and PULS during the sight of the less favourite artefact of “Leonardo Space”. Subjects were more concentrated seeing the artefact less favourite of “Leonardo Space”. Conscientious people looked meticulously the artefact less pleasant because they are scrupulous, and they have more rational view.

## **Psychophysiological correlates of complex spherical awe stimuli: a comparison with a conventional induction technique**

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Awe is an intense and complex emotion arising in response to stimuli that are vast and difficult to accommodate. Due to its complex nature, capturing an intense version of awe in a lab remains a challenge. One of the conventional techniques used to induce awe are videos stimuli. Despite their effectiveness, we suggest that 360° videos could be used to elicit a more intense version of awe in the lab, which can be deeply captured by a psychophysiological assessment of this emotion. To test this hypothesis, we recorded psychophysiological activity of 30 participants (15 females and 15 males) watching neutral vs. awe-inspiring videos displayed either on a flat or 360° immersive screen, by two within subject conditions, namely content (awe vs. neutral) × medium (2D vs. 360°). In details, two videos depicted a scene of hens wandering (i.e. neutral content) and were presented either on a flat or 360° immersive screen. Also the other two videos were presented either on a flat or 360° immersive screens but showed a forest of tall trees (i.e. awe content). Order of presentation of each video was counterbalanced for each subject. Blood Volume Pulse (BVP) was recorded using a photoplethysmograph sensor. Skin Conductance (SC) was recorded using two electrodes attached to the dominant hand. Corrugator Supercilii and Zygomatic Major muscles was recorded using facial superficial Electromyography (sEMG). All the signals were recorded during each video session (2 min length) using a ProComp Infinity 8-channel (Thought Technology Ltd, Montreal, Canada). The sam-

pling rate was set at 256 Hz. Heart Rate Variability (HRV) measures were computed by using custom script in Matlab 7.10.0 (R2010a), to analyze the Inter-Beat Interval (IBI) extracted from the BVP sensor, a measure equivalent to the R-R peaks interval extracted from the electrocardiogram. According to the guidelines of Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, typical temporal and spectral HRV measures were extracted to evaluate the response of the autonomic nervous system. In particular, the rhythms were classified as Very Low Frequency (VLF, < 0.04 Hz), Low-Frequency (LF, 0.04 to 0.15 Hz), and High Frequency (HF, 0.15 to 0.4 Hz) oscillations. Temporal domain was investigated by the means of Heart Rate (HR) and its Standard Deviation (SDRR). Our results showed that participants watching an awe both on 360° or 2D video displayed a higher parasympathetic activation as highlighted by higher HF. Moreover, VR stimuli showed a greater sympathetic activation independently from the emotional condition (awe vs. neutral), with higher VLF, LF, HR, SDRR and SC. In line with literature, EMG showed no significant changes. Our results showed that awe leads to a paralyzing “freezing” at autonomic nervous system level.

## Two-Person Neuroscience: multi-brain connectivity during dual exchange

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Recently, a new conceptual and methodological framework has been proposed to investigate the neural basis of human social interaction: the Two-Person Neuroscience (2PN), an approach focusing on the dual exchange rather than the individual behavior, by using simultaneous neuroimaging of two or more subjects (commonly referred to as hyperscanning). The multivariate analysis of data derived from different subjects allows to model a system made of multiple brains interacting and to characterize it in relation with different processes at the basis of social cognition. In this study, we investigate the emotional relationship established between two subjects during the Third Party Punishment (TPP) paradigm using EEG-hyperscanning. The TPP permits an ecological real-time measurement during an empathic experience and the consequent prosocial behavior. In this game, in which the dictator imposes to a receiver the splitting of a sum of money, a third party (the punisher) observes the interaction between the dictator and the receiver and can decide to punish the dictator's behavior. Using a combination of multiple-brain connectivity and specific indices derived from the graph theory, we aimed to (i) analyze the empathy arising between the punisher and the receiver during the observation of fair or unfair behavior; (ii) investigate the relation between emotional reaction and the prosocial behavior consequent to the emotional experience; (iii) explore if the brain-to-brain con-

nectivity patterns arising between the observer and the receiver is modified when the unfair behavior is attributed to a human agent with respect to a PC. 10 participants paired as 5 dyads were recorded with dual-EEG while they were engaged in the TPP game. The setup involved three subjects: player A (the dictator), player B (the receiver), and player C (the observer, that in turn can act as a punisher). The resulting multiple brains connectivity patterns showed stronger inter-brain connections in the social context (human Agent) with respect to the PC condition, as indicated the specific indices derived by denser inter-brain connections and by a significantly reduced divisibility. The comparison between Fair and Unfair/Hyper-Unfair conditions returned significant differences in terms of inter-brain functional causal links which can be attributed to the higher empathy induced by the unfair treatment suffered by the receiver. In particular, the properties of the multiple brains network summarized by the selected brain connectivity indices point toward a greater integration between the two subjects' brain activity in the unfair conditions with respect to the fair condition. The results of this study indicate that EEG hyperscanning can characterize the social and empathic aspects of the interaction between two subjects in terms of the properties of their multiple brains functional model.

## Cognitive and behavioral deficits in Multiple Sclerosis: a case report Cinquegrani R.

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Multiple Sclerosis is a progressively disabling disease characterized by demyelination of the axons of the central nervous system cells. It determines alterations of the sensory-motor performance also compromising the cognitive and behavioral aspects. Mrs Z.G. 59 aa, 8 aa schooling, affected by multiple sclerosis since 1992 and admitted to the Day Hospital of Unit of Rehabilitation and Functional Recovery of the Foundation Don C. Gnocchi Onlus in Milan, was subjected to a cognitive rehabilitation for a cycle of 24 meetings (5 times per week, 45'). The therapeutic procedure also involved neuro-motor rehabilitation, occupational and logopedic therapy. By clinical observation and Nps tests, it highlighted the presence of a clinical picture characterized by multisectoral cognitive impairment of middle-high level. In particular, it pointed out marked distractibility, psychomotor slowing, low awareness of the disease, impulsivity, deficits in retention of memory trace with confabulation moments, deficit in visual-spatial planning, in working memory, tendency towards perseveration, conceptual rigidity, poor ability to self-monitoring and correction of its performance. The objectives of the treatment were the reduction of behavioral disorders and stimulation of attentional and visual-spatial aspects. For this purpose, tests *ad hoc* were used both of "paper and pencil" and computerized kind of software packages currently in use in rehabilitation. After treatment, significant improvement of cognitive and behavioral aspects did not emerged: the patient, significantly anosognosic and egosyntonic with its behaviour, was not able to learn/use/generalize, in everyday contexts, functional compensation strategies showed in the sessions. Therefore, it is necessary the supervision of family members for the conduct of all activities of daily living to avoid risky behaviors.

## **Parsing psychophysiological correlates of mental stress using computational psychometrics**

**Cipresso P.**

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Mental stress can be easily elicited in a laboratory setting using experimental tasks and/or stimuli. The temporary effects have no consequence on the individual's health status. While eliciting stress in a laboratory has no consequences, experiencing repeated stressors in daily life can affect the immune system, the cardiovascular apparatus, and the nervous systems with potential detrimental consequences. A stressor activates an immediate reaction in the sympathetic nervous system due to noradrenaline, which causes an increase in blood pressure and adrenaline, which then causes peripheral vasoconstriction, increased heart beat, and muscular contraction among others. In the short term, a stressor has an effect on cognitive and emotional processes that are used to prepare for an immediate action but chronic stress has a detrimental effect in the long run. In particular our body release glucocorticoid controlled by the hypothalamus (such as the sympathetic nervous system that is activated from the stressors); however, in this case the control is endocrinal. In fact the hypothalamus uses corticotropin-releasing hormone to induce the pituitary gland to release adrenocorticotrophic hormone, which has the adrenal glands as a target. This process, known as Hypothalamic-Pituitary-Adrenal (HPA) axis is a major neuroendocrine system that manages reactions to mental stress and regulates several other body processes, such as digestion, emotions, and sexuality. The most important glucocorticoid is the cortisol, since its release has several effects on the organism, among which an increase of blood sugar with gluconeogenesis and the metabolism of fat. Due to the long-term consequences of stress, it is crucial to understand the processes of mental stress from the short to the long term. In an experimental laboratory setting, we used psychophysiological measures recorded in 30 participants (15 female). In particular cardiovascular, respiratory, and electrodermal physiological signals have been recorded and elaborated with signal processing custom algorithms to extract a total of 40 indexes, among which temporal and spectral indexes of heart rate variability, for the computational analyses based on logistic regression, support vector machines, naïve Bayes, random forest classification, and nearest neighbors. These machine learning algorithms were used to classify different stressors when compared among them and compared to relax stimuli. Our results showed precision levels from 58% to 69.5% and showed an excellent discriminant ability between relax and stress stimuli, ranging from 79.2% to 95%. Our findings have profound implications in computational psychometrics for the assessment of complex stimuli through psychophysiological measures. Moreover, the machine learning algorithms can be implemented in portable applications for ambulatory stress detection and might have a profound impact on a clinical treatment of mental stress.

## **Specific Learning Disabilities: a neuropsychological diagnostic process**

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The assessment request for a suspect Specific Learning Disabilities (SLD) is one of the main troubles exposed by parents to medical center that deals with childhood and ado-

lescence. These disabilities causes problems in learning scholastic skills as reading, writing and/or arithmetical and, actually, SLD it refers to: dyslexia, dyscalculia, dysorthography and dysgraphia. Specific disabilities have an attested neurobiological and constitutional origins, influenced by environmental factors. The aim of this work is to discuss the assessment procedure carried out by a developmental neuropsychologist and his team of work to confirm or reject the suspect of SLD in a seven year and five months girl. The clinic diagnostic procedure includes, as first, an interview held with parents while the anamnestic data are collecting. Additionally, the neuropsychologist evaluates learning disabilities by means of standardized tests. Reading levels has been investigated using MT Reading test of a passage (Cornoldi and Colpo) and with reading lists of words and pseudo-words (DDE-2). Specific spelling disorders are been examined with writing test of a dictated story (BVSCO-2 and Tressoldi test) and words and pseudo-words lists (DDE-2, DDO and Sartori). To evaluate developmental dyscalculia, the clinic uses the battery of tests named AC-MT (Cornoldi, Lucangeli and Bellina). Further neuropsychological details concerned the cognitive function (WISC-IV), visuo-spatial and praxies areas (VMI test), memory area (WISC-IV and VAUMeLF) and attention (Bells test). In addition to this, the girl has been subjected to logopedic evaluation with the aim of learn more about her lexical, morpho-syntactic, phonological abilities and oro-facial praxies. All of the diagnostic procedure has led to a multi-axial diagnosis of: developmental dyslexia (specific reading disorder) with mild/moderate level; dysorthography (specific spelling disorder) and dysgraphia at a severe level and a difficulty in oro-facial praxic level (dyspraxia). At the end of the diagnostic procedure, the clinic suggest to undertake a logopedic rehabilitation treatment that is focused on and intensive in order to improve girl's writing and reading abilities and to allow her to learn useful compensative measures. Essential will be a reevaluation of patient's abilities at the end of the cycle of logopedic rehabilitation. However at the end of coming scholastic year to check the progress of disabilities and to evaluated treatment efficacy.

## **Combining DC stimulation and cognitive training to modulate food-craving and subjective values of unhealthy food: a tDCS/NIRS study**

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Several lines of evidence suggest that in obese individuals eating behaviour may be related to abnormal cognitive control function. Decreased activation of the Dorsolateral Prefrontal Cortex (DLPFC) seems to be related to lower ability to control food intake and with an increased urge to consume palatable foods, namely food-craving. Recently, two approaches have been proposed to counter food-craving: Non Invasive Brain Stimulation (NIBS) and cognitive training. In particular, transcranial Direct Current Stimulation (tDCS) of the DLPFC has been shown to be able to temporarily reduce food craving;



on the other hand, cognitive training with specific stimuli has been proposed as a tool to selectively reduce the value associated with unhealthy foods. However the neural bases of these phenomena are still unknown. The aims of the present study were to evaluate the combined effects of tDCS of the DLPFC and of stimulus-specific cognitive control training in changing food craving and the values of unhealthy food, and to study the neural correlates of these phenomena. We performed a randomized sham-controlled study in which two groups of 20 normal weight healthy volunteers received a 20 minutes-session of active or sham tDCS (2 mA) that was applied bilaterally on the DLPFC, anode right / cathode left (F4/F3). All participants were invited to fast for 3 hours before starting the experimental session. During stimulation participants performed spatial incompatible stimulus-response training with unhealthy foods-pics selected according to individual preferences. Fifty-six food pics (28 healthy / 28 unhealthy) were evaluated in terms of Liking, Wanting and Willingness to Pay (WTP) before and after treatment. Also food-craving was measured two times using 100 mm Visual Analogue Scales (VAS). Changes in oxygenate haemoglobin concentration were measured with functional Near-Infrared Spectroscopy (fNIRS) to monitor changes in the Prefrontal Cortex. The comparison between different scales before and after treatment showed a reduction of Wanting and WTP for trained unhealthy foods-pics compared to non-trained ones, and a reduction of food-craving only in the active-group was also observed. Hemodynamic responses increased after treatment in both groups, however in the sham-group this enhancement was greater specifically for unhealthy stimuli. The results show that combining tDCS over DLPFC and stimulus-specific cognitive training can be effective in reducing food-craving and in modulating subjective values of trained unhealthy foods. fNIRS data highlight that training differently enhances haemodynamic responses in the two groups, suggesting an interaction between the two procedures in modulating brain responses to healthy and unhealthy foods. In conclusion, this study seems to confirm that dysfunctional eating behaviours may be modulated by combining NIBS and cognitive training and highlights the possible utility of these techniques in obesity treatment.

## Links between stimulus-related insular activity and awareness

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Recent Events-Related Potential (ERP) studies revealed that targets in visual decision tasks evoke three prefrontal components within the 400 ms after the stimulus onset. The earlier component is a prefrontal negativity at 110 ms (pN1), while the others two are positive at 170 ms and 350 ms (pP1 and pP2 respectively). The pP2 has been described as the correlate of the *stimulus-response mapping* process emerging only in the context of a discriminative task. At the opposite, the pN1 and pP1 components emerge in both simple and discriminative tasks: based on these observations, we previously suggested that they are associated to the earlier stages of sensory processing. Further, two recent studies revealed that the pN1, pP1 and pP2 components are generated by the bilateral anterior insula (aIns) cortices. To directly assess the role of the pN1 and pP1 components, we enrolled participants in two different experiments. In the first one, subjects

had to perform a simple response task with two different visual conditions: Low vs. High contrast of the stimuli. In the second experiment, subjects had to perform a Passive task and a SRT on the same paradigm (visual contrast was unaltered between conditions). Results of the first experiment showed a significant modulation of the pN1 component (larger in the Low contrast), that presented the opposite trend of the occipital P1 (larger in the High contrast); the pP1 component was similar across conditions. The second experiment did not reveal any modulation of the pN1 component, while the pP1 was larger in the SRT than in the Passive task. Further, electrical neuroimaging analyses confirmed the aIns source of these early prefrontal ERPs. We suggest that the pN1 and pP1 reflect the early insular processing associated, respectively, with the *perceptual awareness* and the *sensory-motor awareness* processes. In other words, these components reflect the multimodal processing of the aIns that allow a stimulus to become available to the motor areas (i.e. they are necessary and enough for a simple response task).

### **The left anterior IntraParietal Sulcus plays a causal role in supporting human-human joint-actions: an rTMS study on freely interacting individuals**

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From birth, we live in a social environment that requires constant motor interactions with others and a fundamental theoretical and methodological challenge for social neuroscience is to create real-life dynamic contexts to study interactive behaviors, preserving the characteristics of well-controlled laboratory settings. The crucial aspect of realistic motor interactions is that individuals mutually adapt to each other on-line, a condition termed “closed-loop” and in contrast with “open-loop” where one of the two participants is non-responsive to the other. To this aim, in recent years, we have developed an experimental set-up where pairs of individuals are asked to interact by performing either imitative or complementary reach-to-grasp movements in synchrony (i.e. “joint-grasping task”). This set-up allowed us describing behavioral and motion kinematics modulations associated with real-time interpersonal coordination. Here, by using inhibitory non-invasive brain stimulation (continuous Theta Burst Stimulation, cTBS), we aimed at investigating whether the left anterior IntraParietal Sulcus (aIPS) plays a causal role in managing the visuo-motor transformations needed to support real-time interpersonal coordination during imitative and complementary interactions. Furthermore, due to the realistic nature of the task, we also tested the hypothesis that changes in the behavior of the interfered participants would be reflected in the behavior of the non-stimulated partners, who try to compensate for the partner’s transient deficit. Pairs of participants (20 pairs, same gender) were asked to synchronize with each other by performing complementary or imitative reach-to-grasp movements. As key behavioural dependent variable we measured partners’ synchrony in grasping the object (while also measuring the arm-hand kinematics). Before performing the joint-grasping task, in different experimental sessions, one

member of each pair received real, off-line, inhibitory cTBS (20 seconds) of either left aIPS or the vertex in counterbalanced order, while the other participant received sham stimulations of the same sites. The behavioural results showed that inhibition of left aIPS selectively impairs synchrony performance during complementary but not imitative interactions as an inverse function of pairs' ability to mutually adjust: the less participants were able to adjust their movements duration to each other at baseline, the more the stimulation impaired the performance. These results suggest that left aIPS causally scaffolds the integration of one's own and others' complementary action goals during joint action. We showed that it is therefore possible to study the contribution of specific brain regions in supporting the ability of individuals to coordinate in "closed-loop" scenarios where they need to adjust to each other, providing the first evidence that aIPS plays a crucial role also in realistic human-human interactions.

## **Modulating the motor system by action observation in right Hemiplegic Cerebral Palsy: an fMRI study**

**Errante A.<sup>1</sup> - Di Cesare G.<sup>2</sup> - Fasano F.<sup>3</sup> - Costi S.<sup>4,5</sup> - Sghedoni S.<sup>6</sup> - Bressi B.<sup>5</sup> Volpe V.<sup>1</sup> - Ferrari A.<sup>4,5</sup> - Fogassi L.<sup>1</sup>**

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Cerebral Palsy (CP) is a major cause of motor disability in children. Among CP children, approximately one third is affected by Hemiplegic Cerebral Palsy (HCP), resulting in abnormal motor function of one body side. In recent years, it has been suggested that the systematic use of observation of goal-directed actions followed by their execution (Action Observation Treatment, AOT) may become a rehabilitative strategy that improves the process of functional recovery in patients with stroke, Parkinson Disease and in orthopedic patients. AOT has been found effective also in HCP children. AOT relies, as neural basis, on the Mirror Neuron System (MNS), first discovered in the monkey premotor and parietal cortex and then found also in humans, in which several studies showed that the passive observation of motor acts performed by another individual determines an increase in activity in a fronto-parietal network. An important assumption for an AOT based rehabilitative approach is the plasticity of the MNS. In this respect, recent studies on adults and children have shown that acquisition of motor expertise affects how actions are perceived and processed in the brain. In fact, stronger activation of the action observation network has been reported during observation of actions well established in the one's motor repertoire. Thus, it is possible to hypothesize that a putative fronto-parietal MNS in HCP children could be more strongly activated by the observation of actions performed by an impaired hand with respect to the observation of those performed by a healthy hand. In this fMRI study we compared the brain activation induced by observation of motor acts performed with different levels of motor impairment. Five children

(aged 9 to 14 years) with right HCP and 5 typically developing children participated in this study. Hand motor impairment was classified according to Ferrari's classification of manipulation patterns in child hemiplegia (only patients with synergic hand were included in the study). Participants observed a simple action performed by a model, consisting in grasping a little object and putting it into a box. Using fMRI block design, we compared brain activation induced by observation of actions performed by an healthy model vs. actions performed by an HCP patient with synergic hand. We found that the MNS was activated in HCP children during action observation, despite the reorganization of the motor circuits. Moreover, the preliminary data showed that the fronto-parietal network was more strongly activated during mere observation of actions performed by the impaired hand, that is with the same observer's level of performance. This suggests that, based on the patient's motor repertoire, the AOT could be adapted in order to make the task more effective in the recovery of upper limb motor functions.

## On the perceptual drift of the fake hand during the Rubber Hand Illusion

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In the Rubber Hand Illusion (RHI), simultaneously brush-stroking a participant's hidden hand and a visible artificial hand induces transient embodiment of the latter. An implicit marker for the illusion is the "proprioceptive drift", a localization bias of the real towards the artificial hand. Recently, Fuchs et al. showed that there is also a drift of the artificial hand towards the real hand, suggesting that visual and proprioceptive information are integrated into an intermediate percept. This notion fits in well with principles of multisensory integration, by which conflicting sensory information are fused into a "compromise", contrasting the idea that with the illusion there is perceptual substitution of the real hand by the fake one. Yet, the actual results of Fuchs et al. do not appear conclusive. Indeed, they failed to demonstrate an actual drift of the fake hand towards the real one, instead showing only a more accurate localization of the fake hand after the stroking. In order to explore this hypothesis in detail, we run two experiments with a new variant of the RHI. The set-up for the two experiments is the same with the exception of the relative position of the fake and real hand. In experiment 1 the fake hand was placed 6 cm to the midline and the real hand was 14 cm apart (laterally to the rubber hand). In experiment 2, the real hand was placed medially to the visible fake one, with constant distances from the midline. In both experiments, there were two conditions relative to the type of brushing (synchronous/asynchronous stroking) and two conditions relative to the target (target real hand and target rubber hand). In the target rubber hand condition, subjects were asked to localize the rubber hand instead of their own hand. Twelve subjects participated in each experiment. The illusion was evaluated with a questionnaire tapping explicit features of the illusion and with the proprioceptive drift. Results showed that the synchronous brushing elicited the illusion in both target conditions and in both experiments. Raw values of the perceptual drifts indicated an actual approach of the two hands towards each other,

in both experiments. No significant differences were observed between target conditions in the questionnaire, with the exception of question 3 (sense of ownership) in experiment 1, where after the asynchronous brushing more disagreement was observed in the target rubber hand condition. In both experiments, question 7 (sense of disownership) differed after the synchronous brushing, with more disagreement in the target rubber hand condition. Our results substantiate the view that an intermediate percept is built as a result of conflicting sensory information. Moreover, our findings might suggest that the sense of ownership for the fake hand does not univocally rely on the disownership of the real hand, the latter being potentially modulated by top-down influences (i.e. the focus on either the rubber or the real hand).

## Improving sustained attention in elderly: a tRNS preliminary study

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Recent studies on cognitive enhancement in the elderly have shown that the cognitive functioning in healthy aging is similar to young adults, however some differences have been found due to sensorial deficits and to a general slowing down of cognitive processing. Training, exercise, and other interventions applied in older age may increase available resources and compensatory potential. Recently, neuromodulation techniques have been successfully applied to enhance cognitive functions in young adults, demonstrating to be potentially promising techniques to maintain and increase brain functions in the elderly. In particular, a direct current stimulation technique (transcranial Random Noise Stimulation, tRNS) has shown to increase visuoperceptual functions. We therefore designed an experiment to measure sustained attention in the elderly at baseline, and subsequently measured subjects' performance on the same task coupled with online cortical stimulation. We used a multiple objects tracking task that consisted of 8 circles, 4 in the left and four in the right visual field. Briefly, a subset of 4 dots (target dots, 2 for each visual field) were highlighted at the beginning of each trial. All the dots then started to move and subjects were asked to "mentally" track the 4 target dots that were highlighted at the beginning of the trial. At the end of the trial one dot turned red (either in the right or in the left visual field, unpredictably on each trial) and the subject indicated whether it was a target or not. We psychophysically measured the speed threshold at which subjects could perform the task at 75% correct in both visual fields. The experiment consisted of three separate sessions: baseline behavioral measurements, and two counterbalanced active and a sham stimulation sessions. All subjects were tested across all three conditions. During the active and sham conditions subjects were stimulated with high frequency tRNS, while they were performing the task (stimulation lasted 20 minutes). The electrodes were placed over the EEG electrodes positions P3 and P4, roughly corresponding to the left and right Intraparietal Sulci (IPS), respectively. We also measured subjects' contrast sensitivity to determine whether changes in sustained attention transferred to low level visual functions. Data were collected from 10 healthy elderly, average age  $66.4 \pm 3.86$ . Preliminary results showed an improvement in visual tracking performance after active stimulation both in the right and

in the left visual hemifield, while contrast sensitivity did not change. These results show that one session of tRNS can modulate visuo-spatial attention in elderly, demonstrating cortical plasticity in old age. This study shows the benefit of cortical stimulation to potentiate sustained attention in the elderly and it might indicate its potential application to the neurological population affected by acquired or degenerative diseases.

## Effects of Neuromuscular Electrical Stimulation on the excitability of the Corticospinal System

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Neuromuscular Electrical Stimulation (NMES) represents a valid tool to regain, maintain or increase muscular strength and function. For these reasons, NMES is extensively used in the field of physical therapy to activate specific muscles, especially in the absence of volitional control. Though the peripheral effects of this non-invasive stimulation technique are well-established, relatively little is known on whether NMES affects the excitability of the Corticospinal System (CSS). By directly activating skeletal muscles, NMES bypasses the volitional drive and elicits ascending volleys from the target district to the cerebral cortex. The aim of the present study was to investigate whether the afferent inputs induced by peripheral neuromuscular stimulation promote neuroplasticity in the CSS. To this end, 18 right-handed healthy subjects (mean age: 20.7 years) received a 15-min NMES protocol on extensor muscles of the right forearm (30 stimulation cycles, each one of 28 s at 2 Hz + 2 s of 50 Hz tetanic contraction, which evoked wrist and finger extension). By applying Transcranial Magnetic Stimulation (TMS) on the contralateral motor cortex, Motor Evoked Potentials (MEPs) were recorded from 3 relaxed muscles of the stimulated upper-limb (First Dorsal Interosseus, FDI; Extensor Carpi Radialis, ECR; Extensor Digitorum, ED). The TMS protocol consisted in sequences of 12 pulses (120% of the resting FDI motor threshold; inter-pulse interval, 5 s). Two sequences were applied before the NMES protocol (baseline stimuli) and 4 sequences followed it (test stimuli). The inter-sequence interval was 3 minutes. Data showed that NMES conditioning was followed by long-lasting changes in upper-limb CSS excitability. Specifically, mean MEP amplitude elicited by the test stimuli in the muscles controlling hand fingers (ED and FDI) was higher than baseline values. By contrast, no MEP modulation occurred in ECR muscle, which is involved in the control of wrist movements. The facilitation of cortically evoked MEPs in finger muscles demonstrates that the neuromuscular stimulation of the forearm elicits long-lasting plastic changes in the excitability of the upper-limb CSS in a highly specific manner. This finding suggests that NMES is not only an effective technique to induce neurofacilitation at the peripheral level, but it can also have relevant implications in the context of physical therapy. Indeed, modern rehabilitation techniques are primarily intended to recover close-to-normal motor schemas, by limiting the occurrence of alternative compensatory strategies. In this vein, therefore, neuromuscular stimulation may play a role in shaping functional reorganization at cortical level following brain injury, for example after stroke.

## Assessment of behavioral disorders through BIRT test

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Non-cognitive neurobehavioral sequelae are common after severe acquired brain injury. These difficulties can undermine the capacity for independent social behavior. Nevertheless the assessment of behavioral disorders has received poor attention from researcher; in fact there are few reliable tools for these kinds of changes. The behavioral disorders cause the failure of rehabilitation treatment because anosognosia and the lack of cooperation may prevent the patient's participation in a project of neuropsychology rehabilitation. The purpose of this study was to understand how some questionnaires utilized to evaluate behavioral disturbances, are able to assess disorders. In order to explore it, BIRT personality questionnaires was administered to a sample of six patients with severe acquired brain injury. The sample included 6 male patients with the following characteristics: 19-54 years old, 8 to 13 years of school attendance, onset 1 to 6 years, GCS 3 to 5, period of unresponsiveness 6 to 30 days, and severe traumatic brain injury / intraparenchymal hemorrhage / subarachnoid hemorrhage / ischemic stroke / anoxia as etiology. The BIRT PQ battery consists of five questionnaires to assess the personality dimensions that are more frequently altered after acquired brain injury: apathy, impulsivity, disinhibition, emotional regulation. There are two different versions of each questionnaire. The first version has to be administered to the patient who has to provide a description of his behavior, and the second one to their families; we have administered both versions. Participants evaluated on a four point rating scale the frequency with which a behavior occurs during everyday life. There are five independent questionnaires measuring motivation (BMQ), impulsivity (BIQ), disinhibition (BDQ), social cognition (BSCQ) and emotional regulation (BREQ). The use of two different points of view (self and relative) for the same problem, make possible having an indirect measure of the awareness level of patients. The answers of patients were compared with those of the family members to evaluate if patients were aware of their disorders. The results revealed a discrepancy between the answers given by family members and those given by the patients. This inconsistency confirms the fact that patients are not aware of their behavioral disorders. Patients underestimate their problems, while the family highlights a strong pain in everyday life. We underline that a scale administered only to patients is not reliable. Therefore it is important for the evaluation of behavioral disorders to use tests which provide for the contributions of the family. In fact the family of patient is the one that observes him in his everyday life and realizes problems cannot be observed through neuropsychological assessment. We believe that a good assessment of behavioral disorders is critical to the patient's recovery.

## The effect of intensity in visual cortex neuromodulation: a tDCS study

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Recent studies have demonstrated that the choice of the transcranial Direct Current Stimulation (tDCS) parameters is a crucial aspect in determining its outcome at behavioral level. Some of these studies, in the motor and visual domain, demonstrate that the intensity of stimulation is one of the key factors in determining the final effects of tDCS. In a previous work, we demonstrated that cathodal tDCS is able to induce a facilitatory effect in a perceptual learning task. This effect was present only if the stimulation was delivered at a specific intensity. In this work, we aim to test the effect of two commonly used intensities of anodal tDCS (a-tDCS), in a contrast perception task. a-tDCS at low or high intensity (namely 1 and 2 mA) was applied in 27 young healthy subjects during the execution of a contrast sensitivity task. Subjects were stimulated on the primary visual cortex with the return electrode positioned on the right arm. Participants were asked to perform 8 blocks of a visual discrimination task, of which the first two were baseline blocks. Then the tDCS was delivered for 13 minutes during which participants performed 4 task blocks. After the end of stimulation, 2 additional blocks were performed in order to investigate any possible after-effect of stimulation on performance. The analysis revealed a crucial role of the intensity in shaping the effect of a-tDCS. A repeated-measures ANOVA highlighted a statistically significant interaction between “stimulation condition” and “time point” ( $F[6, 63] = 2.629; p = 0.02$ ). *Post hoc* comparison revealed that only in the 1 mA condition the first time point (baseline) was different from all the others (all  $p$ 's < .05). In the 2 mA and sham conditions there were no differences between the time points. Therefore, the so-called a-tDCS “facilitatory” effect was found only in the low intensity condition. Our results highlight the non-linearity of the stimulation intensity in shaping the final behavioral outcome, and contribute to confirm that the simple stimulation dependent framework (i.e. anodal facilitatory / cathodal inhibitory) fort DCS is now overtaken.

## Relative contribution of Mirror-Neuron and Mentalizing System areas to motor mapping of deceptive actions

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Understanding others' intention by observing their movements is crucial in social interaction. Recent studies demonstrated that the observation of actions driven by deceptive intention increases Corticospinal Excitability (CSE) more than seeing actions driven by genuine intention even when they require kinematic adaptations. Indirect evidence suggested that the CSE facilitation effect might be mediated by the activity of the Mirror Neuron System (MNS). However, the relative role of the MNS versus the Mentalizing System (MS) in intention comprehension is still under debate. Using a perturb and- measure Transcranial Magnetic Stimulation (TMS) approach we assessed how disrupting the activity of regions within the MNS (i.e. the ventral Premotor Cortex, vPMC) or the MS (i.e. the Temporo-Parietal Junction, TPJ) affects motor facilitation to deceptive intention during Action Observation (AO). Sixteen participants received

continuous Theta Burst Stimulation (cTBS) over the left vPMc, left TPJ and vertex (as control site), and soon after we used online single pulse TMS to record Motor Evoked Potentials (MEPs) from hand and forearm muscles as measure of CSE during AO. In the AO session, participants were asked to perform a weight discrimination task, namely predicting the weight of cubes lifted by actors who were asked to provide either truthful (truthful actions) or deceptive (deceptive actions) cues to the observers after receiving either truthful or fooling information (deceived actions) about the object weight. This way, we assessed the involvement of the target areas in modulating the activity of the motor system in response to deceptive intention, independently from the processing of the kinematic adaptations required to attain deceptive actions. Results showed that, in keeping with previous studies, after vertex cTBS we obtained an increase of CSE during the observation of deceptive actions as compared to the observation of actions driven by genuine intentions. Importantly, the pattern of CSE changed after interfering with the activity of the two target sites. Indeed, as compared with the vertex condition, vPMc cTBS canceled out the facilitation in response to deceptive intentions, while TPJ cTBS led to a general decrease of CSE in all AO conditions. In keeping with a different role of the two areas in processing deceptive intentions, the behavioral results showed that, after stimulation of vPMc, participants were more sensitive to deceptive intention (i.e. less susceptible to fooling information) than after TPJ and vertex cTBS. Thus, interference with the activity of vPMc reduced motor resonance to deceptive intentions and decreased the observers' susceptibility to fooling behavior. Conversely, the general decrease of motor resonance after TPJ cTBS was not associated to any behavioral change. This suggests that the frontal node of the MNS has a causal role in mediating the intentional modulation of motor resonance during action understanding.

## **The nocebo effect in motor performance: the role of treatment perception and personality traits**

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Believing in the detrimental effects of a treatment can lead to negative outcomes, even if the treatment is actually inert. This phenomenon is called “nocebo effect” and represents the negative counterpart of the well-known placebo effect. Nocebo effects have been more extensively described in pain (as hyperalgesia), but evidence suggests that they are present also in the motor domain (as reduction of force or increase of fatigue), although knowledge is less advance in the latter case. Experimental studies of the nocebo effect commonly deploy a conditioning procedure in order to expose participants for a short period to the real (or fake) effect of a treatment, thus inducing belief in its detrimental effects. Afterwards, the nocebo response is measured in a final test session, in which the treatment is applied without any effect. No study until now examined whether participants continue perceiving the treatment as effective when passing from the conditioning (in which its effect is present) to the test session (in which its effect is removed) and whether this perception could modulate the nocebo effect itself. In the current study,

we directly measured the persistence of belief in treatment effectiveness as a modulator of the placebo response in motor performance and related this cognitive function to dispositional factors. Forty-one healthy volunteers were recruited and asked to perform a motor task by pressing a piston, as strongly as possible, with abduction movements of the right index finger. A visual feedback on the computer monitor signalled the level of force. All the participants underwent the same placebo procedure, in which an inert treatment (TENS) was applied to the right hand together with verbal instructions about its negative effects on force production. In a conditioning session, subjects were exposed to the (fake) effects of TENS, by surreptitiously reducing the visual feedback on the level of force. In the test session, TENS was applied again and the motor task was performed with the real visual feedback. Subjects' perception of TENS effectiveness was measured after task execution in the conditioning and test sessions. We also measured the level of force, sense of effort and weakness, and personality traits through an extensive battery of questionnaires. Results showed that 56.1% of participants, who perceived the treatment as more effective in the test than in the conditioning session, also had a more pronounced reduction of force, felt more effort and sense of weakness and were characterized by lower levels of optimism and higher anxiety traits compared to the other 43.9% of participants, who conversely perceived the treatment as less effective in the test session than in the conditioning. These findings highlight for the first time a link between changes in perception of treatment effectiveness, personality traits and the magnitude of the placebo response in motor performance.

## **Effectiveness of physical exercise on balance and falls in people with Mild Cognitive Impairment and Alzheimer's Disease**

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Emerging evidence underlined the importance of physical activity on frailty, independence, gait ability, depression, cognition, and quality of life in patients with cognitive decline. However, it has been recognized that the effects of standard physical activity programs is very limited in patients with Mild Cognitive Impairment (MCI) and Alzheimer's Disease (AD). Therefore the aim of this study was to investigate the effect of physical exercise on balance and falls in people with MCI and mild to moderate AD. Nine patients were randomly assigned to a specific Exercise-Training program (ET). Other fourteen patients were assigned to a standard Cognitive-Training (CT) program. Each session of ET program consisted of 10 min (for each) of bike, walk, and an exercise on ergometer arms. Then, the patients performed on isotonic ergometers for a number of 10 reps and 3 sets, at 75% of the maximum strength. Finally, exercises for the abdominal muscles and stretching were performed. CT program is a multimodal stimulation to reinforce the cognitive abilities. The ET group and CT group underwent 72 treat-

ment group sessions, 90-minute/session, and 3 days/week for 6 consecutively months. At baseline (T0) and after 72 treatment's sessions (T1) patients were assessed by mean of stabilometric balance test and Conley Scale. Non parametric analyses were utilized to verify significant difference between the treatments and time. All patients completed the training sessions and demonstrated a good adherence to both treatments. Between the two groups no differences were noted. In the ET group, a significant improvement in the path of the center of pressure and the area sway were noted. In the CT no significant changes were observed. This preliminary promising result showed that an ET program may have positive effects on balance ability in patients with MCI and AD. This improvement can be important to prevent the risk of falls of these patients. Further studies on larger patients samples are warranted in order to verify such hypothesis.

### **Effects of physical activity on cognitive performance in Mild Cognitive Impairment and mild to moderate Alzheimer's Disease patients**

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Cognitive Training (CT) is today considered one of the most effective non-pharmacological methods in dementia. Recent studies demonstrated that also Physical Activity (PA) could decrease the progressive cognitive impairment in patients with dementia, but the effects are not fully elucidated, due to excessive difference in the type, duration and frequency of the programs proposed in the literature. The aim of this study is to evaluate the effects of PA and CT on neurocognitive function and independence in patients with Mild Cognitive Impairment (MCI) mild and moderate Alzheimer's Disease (AD). Thirty-five patients (F/M = 21/14) with MCI and AD have been recruited, and randomly assigned to a PA or CT group. PA group performed a program consisting of 15 min of warm-up, 60 min of aerobic and resistance training, and 15 min of cool-down. Patients assigned to the CT group were treated with multimodal stimulations. Both PA and CT groups performed 72/90 minute treatment sessions (3 per week). At baseline (T0), after 72 treatment's sessions (T1), and at a follow-up of 3 months after the training (T2) Mini Mental State Examination (MMSE), Frontal Assessment Battery (FAB) and a specific cognitive battery were assessed. MCI patients underwent to the Rivermead Behavioral Memory Test (RBMT), Trail Making Test (TMT), Dual Task (DTask) and Tower of London (ToL); AD patients performed the Alzheimer's Disease Assessment Scale (ADAS-Cog) and Attentional Matrices (AM). Furthermore all patients carried out the Instrumental Activities of Daily Living (IADL). Non parametric analysis were utilized to verify significant difference between the treatments and time. All patients completed the training sessions and demonstrated a good adherence to both treatments. No significant differences were observed between PA and CT. In MCI patients, within

group comparisons showed in PA no differences between T0-T1 and T2 and in CT a significant improvement in the immediate recall of the route and of the story (RBMT). Between groups comparison showed a significant difference between PA and CT in IADL at T1 and in the delayed recall of appointment, route and message (RBMT) at T2. In AD patients, within group comparisons showed in PA a difference between T0 and T2 in AM and IADL, in CT a significant change in the word recall task (ADAS-Cog) between T0 and T1 and in constructional praxis (ADAS-Cog) between T0 and T2. Between groups comparison showed a significant difference between groups in word recall task (ADAS-Cog) at T1 and in the comprehension (ADAS-Cog) at T2. From the results obtained following the two treatments, it is possible to conclude that both PA and CT are effective in slowing down the progressive cognitive impairment in patients with AD and there is no superiority of one another, but that each acts on different spheres of cognition.

## **Quantification of MEG power changes after M1-tDCS stimulation in a patient with Hereditary Spastic Paraplegia**

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Transcranial Direct Current Stimulation (tDCS) is a non-invasive brain stimulation technique for modulating excitability of targeted cerebral areas. It is currently unknown whether tDCS may be considered a valid option for modulating motor function and spasticity in Hereditary Spastic Paraplegia (HSP). The mechanisms occurring at cortical level after spinal long tract degeneration have been poorly investigated in HSP. The aim of this study is to evaluate the topographical distribution of Event-Related Synchronization/Desynchronization (ERS/ERD) during a single-joint cyclic ankle foot movement in a patient with HSP, who underwent a specific rehabilitation program (tDCS) to improve ambulation and to reduce spasticity. Magnetoencephalography (MEG) data were acquired at a rate of 600 Hz, using a 275-channel MEG system (CTF Systems Inc., Vancouver, Canada), with a block protocol. ERS/ERD values were calculated in alpha (8-12 Hz), and beta (13-30 Hz) frequency ranges. A one sample z-test was applied to compare the map of the patient to the grand average of the controls. Thus, the statistical map defines the sensors in which ERD from an individual patient differs statistically from that of a reference population. The patient was evaluated before and after a tDCS treatment (cathodal M1-tDCS, 2 mA - 20 minutes/day for 10 days, during walking). tDCS was well tolerated and no side effects were reported. MEG analysis assessed before tDCS showed significant widespread ERD over contralateral motor area, central motor and parietal areas compared to controls. After tDCS these desynchronizations were significantly reduced, localizing in the sensors over foot area. A clinical reduction of spasticity and an improvement of tiptoe gait with no deterioration of other motor performances was observed. This preliminary study evidenced an altered neurophysiological pattern in a subject with HSP. This study describes a preliminary approach to evaluate the effects of specific rehabilitation by means of quantitative MEG analysis during motor performance. The results of this pilot study could be relevant in the evaluation of the brain activity of these patients and in the neurological rehabilitation.

## Visuomotor Prismatic Adaptation modulates tactile perception in healthy subjects

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Prismatic Adaptation (PA) is induced through a visuo-motor pointing task performed with the dominant arm while wearing prismatic goggles shifting the visual field laterally. Prismatic deviation initially biases pointing movements in the direction of the optical shift, progressively decreasing up to correct pointing (adaptation). Following PA, participants experience again pointing errors, but contralateral to the original optical deviation (aftereffects). In brain-damaged patients with neglect, rightward-deviating prismatic goggles are effective in reorienting attention to the left (neglected) side not only in the visual domain, but also in the somatosensory domain, improving tactile perception in the neglected field. Furthermore, in healthy subjects leftward-deviating prismatic goggles induce a neglect-like behavior in a number of visuo-motor tasks. However, there is contrasting experimental evidence on the strength of attention modulation effects in normal individuals. Here, we aimed at investigating whether, in healthy subjects, leftward-deviating prismatic goggles induce a neglect-like attentional bias in the somatosensory domain, worsening tactile detection ipsilaterally to prismatic deviation (i.e. leftward). We delivered tactile stimuli to the left digit V by means of a constant current electrical stimulator at the individual sensory threshold level in 10 healthy subjects. Participants' task consisted in reporting tactile stimulus detection in two different conditions: (a) following visuo-motor prismatic training with prismatic goggles shifting the visual field 11° to the left (VPT); (b) after a visuo-motor training without prismatic goggles (SHAM). Experimental conditions were counterbalanced across subjects. If leftward-deviating prismatic goggles induce a rightward crossmodal attentional shift, to the detriment of the left side, we expect to observe a reduction in the detection rate of tactile stimuli delivered at threshold level to the left "neglected" side. A paired T-test (2 tails) comparing the effects of VPT and SHAM conditions on tactile detection, revealed a highly significant difference between VPT and SHAM conditions (mean  $\pm$  SD: SHAM =  $9 \pm 6.7$ ; VPT =  $6 \pm 4.81$ ;  $T = 5.4$ ;  $p = .0004$ ), showing a dramatic reduction of the detection rate of tactile stimuli delivered to the left hand in the VPT as compared to the SHAM condition. Our results suggest that, in healthy subjects, perceptual threshold paradigms are effective in highlighting PA attentional effects in the somatosensory domain. Leftward VPT significantly modulated the tactile perceptual threshold, worsening the detection rate of tactile stimuli delivered ipsilaterally to prismatic deviation, thus mirroring leftward tactile detection impairments showed by neglect patients. This preliminary finding demonstrates the effectiveness of PA in inducing attentional modulation of tactile perception in healthy subjects, thus improving our understanding of crossmodal neurocognitive mechanisms.

## Visual perspective changes subjective and psychophysiological reactivity to the virtual pain and pleasure on self and others

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Vicarious sharing of others' states may rely on implicit, largely automatic (e.g. mirroring, affective resonance or emotional contagion) as well as on explicit higher-order processes (e.g. emotion labelling, mentalizing, perspective taking, appraisal of the situation). While several empathy studies have focused on the empathic reaction to other's pain, much less attention has been paid to the study of empathy for positive states (e.g. the conditions in which imagining, recalling and observing joy in others trigger positive states in the empathizer). In particular, it seems that information about how taking a physical perspective may influence reactivity to pain and pleasure is extremely limited. To explore this issue we devised a novel paradigm that capitalizes on the potentiality of Immersive Virtual Reality (IVR) to induce feelings of ownership over virtual body parts, particularly when the virtual character is seen from a first-person perspective. In this study 24 healthy participants were immersed in a virtual reality scenario where they observed virtual stimuli penetrating (a needle, Pain condition), caressing (the hand of another avatar, Pleasure condition) or touching (a ball, Neutral condition) the hand of an avatar seen from a first- (1PP) or a third-person (3PP) perspective. Subjective ratings about the illusory feeling of ownership, the (un)pleasantness and the intensity of the stimuli were collected after each trial using Visual Analogue Scales (VAS). Moreover, physiological responses (Skin Conductance Responses, SCR, and Heart Rate, HR) were recorded through each trial. All participants reported strong feelings of ownership of the virtual hand only in 1PP. Subjective measures also showed that Pain and Pleasure were experienced as more salient than Neutral. SCRs analysis demonstrated higher reactivity in 1PP than in 3PP. Importantly, vicarious pain induced stronger responses with respect to the other conditions in both perspectives. HR analysis revealed equally lower activity during Pain and Pleasure with respect to Neutral. These physiological findings could suggest that SCR may reflect egocentric perspective while HR may merely index general arousal. Crucially, behavioural and physiological indices of reactivity to seeing others' pain and pleasure were qualitatively similar (but quantitatively different) in 1PP and 3PP. None of these effects correlated with ratings of ownership suggesting that they cannot be explained by mere embodiment. To the best of our knowledge our experimental paradigm is the first IVR attempt to compare behavioural and physiological reactivity to stimuli that participants can perceive as delivered on their own or an avatar's body, depending on the perspective. This paradigm may open new avenues for exploring vicarious sharing of pain and pleasure without actually delivering any stimuli and for assessing whether taking a different physical perspective influences basic reactivity to pain and pleasure.



## Mood fluctuations in Parkinson Disease: the effect of dopamine replacement therapy

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Long term treatment of Parkinson Disease (PD) is associated to motor and non-motor fluctuations (anxiety, depression, behavioral disorders etc.). While the former are well characterized and easier to recognize, psychological non motor fluctuations are less familiar to clinicians and underestimated by patients. To analyze changes in affective dimensions before (OFF condition) and after (ON condition) the take of a standard daily dose of dopamine replacement therapy in non-demented patients with PD undergoing stable dopaminergic therapy. We assessed general cognitive status by means of MMSE and CDT. In OFF and ON we evaluated: mood state using Profile of Mood States Scale (POMS). We calculated the percentage of change, before and after drugs administration, in POMS. This scale has been developed in order to be sensible to mood changes and can be used in short term test-retest settings (i.e. before and after cocaine intake) and is composed by 6 factors: tension, anger, depression, fatigue, vigor, confusion. The maximum is 100 and the highest is the score, the worst is patient's status except for factor V where 100 means complete well-being. General cognitive level assessed by the MMSE and CDT guidance tools showed a normal cognitive status. The 75% of patients had an improvement in POMS subscales factor tension, factor depression, factor anger, factor fatigue, factor confusion, factor vigor. About 50% showed a decrease in one subscale (factor V). This study showed an improvement in the non-motor symptoms as revealed by POMS scale after intake of dopaminergic therapy. POMS is sensitive to changes in affect states induced by dopamine replacement therapy administration. These changes are not completely explained by motor improvement induced by therapy as demonstrated by a previous study. Mood fluctuations can present in patients's everyday life since they can be related to therapy intake.

## Combined use of transcranial Direct Current Stimulation and psycho-sensory stimulation in a patient with severe disorder of consciousness

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The main aim of this work was to evaluate the effectiveness of the transcranial Direct Current Stimulation (tDCS) on alertness improvement in a patient in a Minimally Conscious State (MCS) by means of DOCS scale combined with a structured psycho-sensory protocol and specific individualized checklists. A further purpose was to estimate the effects of tDCS on muscle hypertonus through the Ashworth scale. Transcranial Direct Current Stimulation (tDCS) (1.5 mA, 10-second ramp, 20 minutes a day, 3 days a

week, for 3 months) was performed through a two-channel intra-cephalic stimulator. Two stimulating electrodes (anodes) were applied on the left Prefrontal Cortex (PFC) and the cerebellar cortex, respectively. The cathode was positioned on the right primary motor cortex (M1). This protocol aims at activating the fronto-parietal mesocircuit. After stimulation, the patient followed a cognitive behavioural psycho-sensory stimulation training associated with physiotherapy and speech therapy sessions. The results, obtained through the systematic observation of the patient during the treatment, showed an improvement in the level of alertness, as well as an increase in the quality of the rehabilitation intervention, highlighted both by a higher DOCS score and by *ad hoc* scales set up specifically for the patient. Although these data refer to a single subject, they seem to demonstrate the usefulness of the non-invasive brain stimulation techniques combined with rehabilitation treatment. The importance of this combination was already proposed by other authors, who reported an improvement in the sensory abilities and in the level of consciousness in a group of individuals with a diagnosis of Vegetative State (VS) or Wakefulness Unresponsive State (UWS) by stimulating the left primary sensorimotor cortex and inhibiting the right orbito-frontal one. Furthermore, this study highlights some fundamental aspects which could be useful for the implementation of an intervention protocol addressed to patients suffering from a disorder of consciousness, by building a personalized treatment, based on patient's specific clinical features and not only on standardized measures. In conclusion, the outcomes of this research highlight the key role of transcranial electrical stimulation in producing improvements in patients with disorders of consciousness, especially when applied in combination with individualized and *ad hoc* protocols built on patient's clinical features.

## The functional role of ventral Premotor Cortex in motor monitoring of voluntary actions: an fMRI study during mechanic limb immobilization

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Anatomo-clinical evidence from brain-damaged patients with motor awareness disorder (anosognosia for hemiplegia) suggests that the Premotor Cortex (PMC) is involved in motor monitoring of voluntary actions. A PMC lesion is supposed to prevent patients from detecting the mismatch between the intended, but not executed, movement with the paralyzed limb. In the present fMRI study on healthy subjects, we sought for evidence of a comparison between motor planning and sensory feedbacks in PMC. To this aim, we contrasted conditions in which subjects were free to move the hand with conditions in which movement execution was prevented by a cast. We predicted that the PMC activity could be modulated by the presence of the cast and the duration of the immobilization. Twenty healthy subjects underwent four fMRI scanning session using

a 3-Tesla MR scanner. The first day, participants performed a hand motor task (open/close right or left hand alternately) in free condition (T1); at the end of the scan, participants' left hand was immobilized with a cast and they performed the same task with the left hand blocked and the right hand free (T2). The second day, after one week of immobilization, the task was performed as in T2 (T3); at the end of the scan, the cast was removed and the task was performed as in T1 (T4). A meta-analytic approach was used to identify ROI commonly implicated in the hand movements. ROI beta values were analyzed with a  $2 \times 2 \times 2$  ANOVA with "Side" (Left and Right hand, including the contralateral hemisphere activity), "Time" (Day1; Day2) and "Cast" (Free; Blocked). Furthermore, Psycho-Physiological Interaction (PPI) was used to estimate the functional connectivity between right vPMC and the rest of the brain. Left hand data were analyzed with a  $2 \times 2$  ANOVA with "Time" and "Cast". The ROI analysis results showed that the right vPMC activity was significantly modulated by the presence of the cast on the left hand (Side\*Cast Interaction:  $p < 0.01$ ). In particular, when efferent and afferent signals are incongruent, as during immobilization, a greater activity of the vPMC was found, suggesting vPMC involvement in detecting the mismatch between motor planning and sensory feedbacks. Interestingly, the increased right vPMC activity was present only on Day1, as soon as the left hand was immobilized (Side\*Cast\*Time Interaction:  $p < 0.001$ ). After one week, when the motor system likely learns that no movement can be executed with the immobilized hand and changes its prediction about the sensory consequences of the movement, the vPMC comparator system no more detected the incongruence. The PPI results showed a main effect of Cast ( $p < 0.05$ ), suggesting that, when the left hand was immobilized, the right vPMC activity was coupled with an increased activity in right S1, from which it receives (incongruent) sensory feedbacks for the comparison with motor planning. These findings provide compelling evidence for the proposed role of PMC as a comparator system.

## Sex differences in cooperation: an hyperscanning study

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When we talk about cooperation we refer to a group of voluntary behaviors adopted by two or more individuals or groups with the aim of promoting the collective well-being. Cooperation, defined as a set of interactions with others that increase shared performance, is one of the most important human social behaviors. Men and women exhibit differences related to social behaviors: sex, as a biological variable, significantly influences social behaviors and cortical activations. Several studies have pointed out that there are differences related to social phenomena between men and women dyads. Thus, many researchers have tried to understand how sex affects human social behavior. In the same way cooperation can be influenced by personality traits. Several theorists have argued that two general motivational systems underlie behavior. A Behavioral Approach System (BAS) is believed to regulate appetitive motives and a Behavioral Avoidance (or Inhibition) System (BIS) is said to regulate aversive motives. This study aims to investigate the neural correlates of sex differences in conjunction with personality components (Behav-

ioral Activation System, BAS, and Behavioral Inhibition System, BIS) during a cooperative joint task. To do this an hyperscanning paradigm has been used which consists in the simultaneous recording of the cerebral activity of two or more subjects involved in interactive tasks. The task performed by the subjects, seated side by side, consisted in an exercise of selective attention. Thus, 18 participants paired as 9 dyads (same sex dyads) were recorded with dual-EEG, dual-fNIRS and dual-biofeedback setups while they were engaged in a task finalized to engage cooperation. The task was sub-divided in 8 blocks with a pause halfway assessing the goodness of the cooperation scores. The feedback was defined a priori in order to provide a social manipulation about the performance and modify their responses. The feedback was negative most of the times in order to frustrate the subjects and induce them to improve the performance in the next step. Results showed that male-male dyads reported a higher beta and theta oscillatory activity. In the frontal region beta waves are associated with active wakefulness and most challenging mental activity. Furthermore, the increase of theta waves (in male dyads), is compatible with the use of spatial working memory requested to the subjects during the task. In general, the synchronization in the areas involved in the task increases. The results also showed that higher BIS indices determined a decrease in alpha activity: high BIS subjects, before receiving the feedback on their performance, showed increased brain activity compatible to the process of negative emotions. After the feedback, instead, alpha activity decreased within the right hemisphere (lower brain activity) since they received a gratification.

## Rehabilitation of Global Amnesia: study case

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Memory is the ability to store, consolidate and remember information. Amnesia is a deficit of memory caused by brain damage, disease or psychological trauma. There are two main types of amnesia in Global Amnesia: retrograde amnesia and anterograde amnesia. Retrograde amnesia is the ability to retrieve information that was acquired before the date of the event. In some cases the memory loss can extend back decades. Anterograde amnesia is the inability to transfer new information from the short-term store into the long-term store. We describe the case of N.B., female, 57 years old, married since 1997 with two children that in October 2015 entered in ER after an aneurysmal subarachnoid hemorrhage of the cerebral anterior artery. The TC revealed bilateral stroke lesions in fronto-basal lobe and left damage in the fronto-temporal lobe. We have done the first Neuropsychological assessment in December 2015 and the behavioral observation revealed a severe Global Amnesia, with confabulation, complete anosognosia and disorientation. She has forgotten 12 years of life. The formal assessment with attention and memory tests was altered. In collaboration with the occupational therapist we organized a rehabilitation program, one hour each day of neuropsychological treatment, physiotherapy treatment and occupational treatment. We used non-specific methods, such as the personal exercise book for the autobiographical memory, timer and calendars. We use also behavioral methods for examples checklists and procedural sequences and Tangram, for procedural memory. During treatments she has never recognized the different therapists and us. At the neu-

ropsychological assessment in March 2016, we observed a reduction of confabulation and an improvement of attention abilities. Memory abilities weren't changed. Sometimes the patient was aware of memory deficits and, with the collaboration and the help of her family, she learnt to use memory instruments such as: calendars and checklists.

## **Artistic creativity in Parkinson Disease: a single case follow-up study**

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Creativity is the ability to generate ideas that are both novel and useful. Creative drive is a more easily manageable phenomenon that can be evaluated by behavioral tests. Creative drive was observed in some neurological disease such as Frontotemporal Lobar Degeneration (FTLD), Alzheimer Disease (AD) and in Parkinson Disease (PD). Researchers have found examples of artistic creativity in stroke. In PD, dopaminergic therapy seems to play an important role, because it was observed that those patients who had the creative drive, started some form of art after the beginning of dopaminergic treatment. However it is not clear if this artistic production is a form of Impulsive Control Disorder (ICDs), that can develop compulsive tendencies with art, or a form of innate skills, triggered by dopaminergic drugs. The present study describes a patient, O.C., with Parkinson Disease from 2002, makeup artist for profession. She had a moderate ICD in the form of compulsive shopping; (UPDRS III score = 8). The patient was in treatment with LDopa (300 mg/die), dopamine agonists (2.11 mg/die) and antidepressant drugs. At T0 we evaluated the patient using a complete neuropsychological battery, Abbreviated Torrance Test for Adult (ATTA) to evaluate creative drive and Minnesota Impulsive Disorder Interview (MIDI). At T1, five years later, we repeated the same evaluation (UPDRS score = 11). The total score of ATTA at T1 (92) was found to be lower than in T0 (102) in the verbal section (T0 = 31, T1 = 12), in figurative section (T0 = 74, T1 = 80) we observe a reduction of the number of details in the drawings. Other scores were found to be similar to T0. The MIDI score was higher than in T0 with two forms of ICDs (T0 = compulsive shopping, T1 = compulsive shopping and binge eating). This single case suggests that creative drive is not associated with ICDs because we observe a reduction of creative drive and an increase of ICDs.

## **Body and mind in driving abilities: how electrodermal correlates can explain the improvement of hazard perception in a virtual training**

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Hazard perception is a high cognitive ability, crucial to predict the potential occurrence of dangerous events in order to prevent them and their outcomes. Research in road safety showed that driving experience modulates hazard perception, leading to the paradoxical consequence that novice drivers have to experience on-road risks to improve their hazard perception. The aim of the present study is to investigate the psychophysiological mechanisms through which learning in hazard perception develops, using virtual reality tech-

nology in order to guarantee a safe context. The study is based on the recent evidence that inexperienced drivers show a greater percentage of Skin Conductance Responses (SCRs) while driving in a virtual environment, than during the passive viewing of risky scenarios. Sixteen undergraduates, with a mean age of 20 years old, participated in the study. All the participants were novice drivers/riders (less than 2, 5 years of driving license). We used a moped-riding simulator (the Honda Riding Trainer, HRT, specifically developed for hazard perception training) and an acquisition system to record electrodermal activity during the HRT training. The experiment consisted in riding the HRT during two sessions scheduled a week apart. All the participants were administered the same 5 courses per session according to the degree of difficulty (from the easiest to the most difficult), representing peripheral road at the HRT, with an initial familiarization course. In each session, the same 39 potentially hazardous scenes were shown and we recorded changes in electrodermal activity (SCRs) in proximity of hazardous events. In the second session, we expected to observe an overall improvement of riding performance, together with earlier SCRs onset associated with the detection of hazard. The design was a 2 Sessions  $\times$  5 Courses repeated-measure design. The dependent variables were the percentages of accidents and SCRs over the total of the scenes, and the mean onset anticipation of SCRs. We found a reduction in the number of accidents as the training develops, both within and between sessions. The percentage of SCRs decreased along the courses: such reduction might be interpreted as a consequence of an improved ability to behave in such a way that the hazard does not occur at all. This is confirmed by the results of the analysis on the SCRs onset, which is significantly anticipated in the second session, indicating an earlier implicit response to hazards that might enhance the likelihood ability to avoid them. These results represent a further contribution to the comprehension of implicit mechanisms underlying hazard perception and its development, that might become a turning point both for road education and road safety.

### Effects of music reading on motor cortex excitability

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Neurophysiological studies suggest that reading sheet music facilitates sensorimotor cortex in musicians. Reading the notes of a musical score activates specific expectations about the type of sound to be produced by an audio-visual integration processes. Moreover, reading a music note is also linked to a specific action that depends on the instrument used to produce the sound. The aim of the present study was twofold: to evaluate (1) whether in piano players, reading notes in the bass clef (usually played with the left hand) and in the treble clef (usually played with the right hand) selectively enhances right and left M1 excitability, respectively (inter-hemispheric effect); and (2) whether reading notes played with the thumb or with the little finger selectively modulate the excitability of the Abductor Pollicis Brevis (APB) and Abductor Digitorum Minimi (ADM) muscles,

respectively (intra-hemispheric effect). Fourteen musicians (7 pianists and 7 non-pianists) participated to the study. Single pulse TMS was applied to either M1 while subjects alternatively read the bass or the treble clef of five sheets music without any movements. As a baseline condition TMS was delivered during the observation of a blank pentagram. When piano players read the treble clef, the excitability of the left M1 was significantly higher compared to that recorded in the right M1. No significant differences emerged during reading of the bass clef. Moreover, motor-evoked potentials were higher in the ADM muscle regardless the note in both treble and bass clef conditions. In contrast no significant MEP modulation was observed in non-pianists. These preliminary data support the view that music reading may induce some specific inter-hemispheric modulation of the motor cortex excitability, particularly during reading of treble clef notes.

### **A pilot study of neurofeedback intervention modulates cortical activity during emotional experience in schizophrenic patients: fNIRS and EEG data**

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Reviews and recent evidence have demonstrated the frequency, type, and clinical significance of brain dysfunction in Schizophrenia (S). Neuroimaging measures and electroencephalographic (EEG) data, in fact, suggest anomalies in brain responsiveness in S patients. Moreover, empirical evidence suggests that the disturbances in emotional functioning are a major cause of persistent functional disability in S. However, no integration of these methods is usually applied to test and to clarify what specific aspects of emotional functioning are impaired in S. In this current pilot study the aim was to investigate the behavioral and neural correlates of emotional attribution in patients with S and to train these patients to restore the “unbalance cortical activity” through Electroencephalography (EEG-based) Neurofeedback (NF) technique in response to emotional cues. These evaluation procedures were conducted through a “multimethod” approach with functional Near-Infrared Spectroscopy (fNIRS) and EEG in three times: (a) the initial (T0) assessment of prefrontal activity while viewing standardized visual stimuli (positive, negative and neutral) selected from the International Affective Picture System (IAPS). After the emotional picture task, the patients was asked to rate the pictures on the Self-Assessment Manikin (SAM) dimensions of valence and arousal; (b) the NF application during a training protocol of five weeks (T1); (c) the assessment of NF efficacy that revealed a balanced cortical activity after the treatment (T2). 8 patients have been randomly assigned to either control (3 patients, C), or neurofeedback group (5 patients, N). Results showed that in T0 an unbalanced prefrontal activity was present within the left/right hemisphere (higher delta). Nonetheless, no anomalous behavior was observed in S about the explicit evaluation about stimuli emotional valence (SAM ratings). Moreover, the NF treatment effect in T2 was observed for N group in comparison with C group: indeed in T2 the anomalous responsiveness to emotional cues was modulated as shown by both EEG and



fNIRS measures. These results suggest that the integration of fNIRS and the EEG measures may be considered a valid method to be used to test the efficacy of clinical treatment (NF) by contemporarily elucidating the cortical oscillation and the hemodynamic effects obtained within the PFC. Finally, these findings underline the potential relevance of NF assisted EEG band modulation to a wide scope of optimal performance applications within and beyond the clinical realm.

## **Cognitive deficits in Amyotrophic Lateral Sclerosis: is there a worsening in cognitive status? A brief review and a illustrative case**

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The original description of Amyotrophic Lateral Sclerosis (ALS) underestimated the presence of cognitive dysfunction and focused on motor manifestations. Up to half of ALS patients displays a degree of cognitive and behavioral impairment at diagnosis, while the estimate of the prevalence of overt Frontotemporal Dementia (FTD) is about 15%. The current evidence is that cognitive and behavioral deficits in ALS range from an overt FTD to milder forms, including ALS with behavioral impairment (ALS-bi), ALS with executive cognitive impairment (ALS-ci), ALS displaying deficits in other cognitive domains (memory, language, social cognition). Some studies have suggested that language and social cognition deficits might be as prevalent as executive dysfunction or as a primary linguistic disorder and that memory deficits can also occur. These findings support the overlap between ALS and FTD, as studies in FTD have shown extensive impairment of social cognition correlated to cortical atrophy of the right orbitofrontal, superior temporal, occipital and posterior cingulate regions. The evidence that cognitive impairment in ALS does not occur only in the executive domain suggests that additional cognitive phenotypes might exist. Recent studies indicated a third dimension of cognitive impairment: language, social cognition and episodic memory, as a distinct pattern of non-motor manifestations in ALS patient (in addition to ALS-ci and ALS-bi). A recent study reported that patients with ALS displaying normal cognition at diagnosis tend to remain cognitively intact over time; executive dysfunction may arise in very late stages and patients with early executive or non-executive cognitive changes may show a cognitive impairment over time. About this last hypothesis I'll present a report of a case. The project developed over two phases, with an evaluation of the patient using the same neuropsychological battery at diagnosis and after 6 months. Neuropsychological assessment included: MMSE, Verbal Fluency, Trail Making A and B, Digit Span Forward and Backward, Corsi Test, CPM, 15 Word of Rey, Rey Osterrieth Figure Complex, Clock Drawing Test, Frontal Assessment Battery (FAB), Wisconsin Card Sorting Test Nelson Version (MCST), HADS for Anxiety and Depression and FrSbe Family Form for behavioral alteration. At the first evaluation all tests were significantly over the normative cut off in all domains; only MCST was borderline. FrSbe Family showed a behavioral impairment, including disinhibition, low attention and emotional alteration. After six months the patient had a significant worsening in all scores tests (under cut off in FAB and in MCST). His scores in the HADS and FrSbe tests were similar in the two evaluations.

## Olfactive Event Related Potentials and Volatile Organic Compound: from physiological response to olfactory perception

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Several studies, analyzing the sensory components of olfactory stimuli, highlight laboriousness to estimate a precise stimulation interfaced in EEG and the consequent psychophysiological stimulus effect. Olfactory perception, starting with a breath, could elicit neuronal and cortical responses which could be investigated through Olfactory Event Related Potentials (OERPs). Nowadays no correlation has been examined between brain cortical response and physiological activation through respiratory markers. The purpose of this work is to investigate OERPs linked to breath physiology by using a new technological device dedicated to olfactory stimulation in EEG and a novel sensor able to detect biomarkers through the Volatile Organic Compound (VOCs). In order to record OERPs correlated to physiological effect on VOCs emission, we interfaced VOS EEG (MI2014A001344), a patent olfactometer connected to an electroencephalogram and an electronic sensor (e-noseiAQ-2000, Applied Sensor) for VOCs parallel recording. This condition allowed us to control olfactory stimulations and to relate them to psychophysiological responses. Consequently, we detected the olfactory response to record, for each given single step of stimulation, the EEG, the OERPs components and VOCs responses. The experimental settings allowed us to investigate, through OERPs and VOCs, the olfactory response to a neutral stimulus (Vaseline Oil C<sub>n</sub>H [2n + 2]), and to a natural stimulus of rose characteristic odor (PEA, 2-phenyl ethanol C<sub>2</sub>H<sub>4</sub>O<sub>2</sub>). We recruited 15 safe adults (mean age 25 ± 5 SD) non-smokers. Subjects performed a passive olfactory behavioral task during the experiment. Afterwards, the subjects filled the VAS on familiar and arousing stimuli dimensions. A general linear model repeated measure was performed on OERPs. Statistical analysis shows main OERPs results on slow potential components, in particular for P3b on frontal right lobe (PEA  $p = .003$ ) (PEA\*arousing  $p = .023$ ) in direction of a greater amplitude vs. control; N4 on right frontoparietal (PEA  $p = .037$ ); and on right frontotemporal ( $p = .025$ ) positions; N6 on right frontoparietal position (PEA  $p = .038$ ) (PEA\*arousing  $p = .009$ ) both in direction of greater amplitude in PEA condition. The control exhaled VOCs frequencies are fitted by a normal distribution (single peak fit  $R^2 = .8$ ), PEA administration exhaled VOCs frequencies are fitted by a bimodal distribution (double peak fit  $R^2 = .9$ ). Exhaled VOCs are significantly different, according to the results of different cortical activation induced by olfactory stimulation. Our study suggests that in smell perception (both in odorous and neutral) we can observe the involvement of slow components, related to the breath of the subject, according to the time of perceptual processing. Furthermore, we connected in real time a given stimulus to olfactory cortical activation, analyzed through OERPs, and breath exhalation, as VOCs (physiological response), innovative connection never yet investigate.

## Neuropsychological intervention and recovery of a higher level of consciousness after 5 years: a single-case report

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Severe acquired brain injury is a clinical condition where, following head trauma or other events (i.e. cerebral haemorrhage or anoxia), the damage to cerebral tissues leads to a state of coma characterized by variable length and initial Glasgow Coma Scale (GCS) score equal or lower than 8. Following a period of coma, the patient may enter a Vegetative State. Chances of recovering minimal levels of consciousness progressively decrease with the duration of the VS and become minimal after 1 year when the etiology was traumatic and after 6 months in other cases. Cases of late recovery of consciousness have been reported, but authors usually describe outcomes and interventions focusing on sensation/ motor skills while neglecting cognitive aspects. Contrarily, we report a single case where the patient showed late recovery of consciousness, has been assessed to define residual neuropsychological deficits, and then involved in a specific rehabilitation intervention that lead to documented late recovery of cognitive functions. G.G. is a young male adult (27 y.o.) who suffered from severe brain injury following a car accident (event: May 2010; GCS = 3). Structural imaging (CT) highlighted multiple bi-frontal, temporal, and cerebellar lesions, and cerebral oedema. After a period of coma, during which G.G. underwent various medical operations, he entered VS, namely alternating wake and sleep periods with no sign of intentional motor, affective, or cognitive responses to different stimuli. No primary improvement of his ability to interact with the context was subsequently recorded during various follow-up evaluations in two different rehabilitation centres. In 2011, we performed a further assessment noting the stability of the VS. In March 2015, 5 years after the clinical event, GG began to produce brief linguistic sequences. We have then been able to perform a neuropsychological assessment using both standard tests and tools created *ad hoc* taking into account his limited range of residual responses. A specific neuropsychological rehabilitation program has then been devised and planned to work on observed deficits. Subsequent neuropsychological assessment sessions highlighted and confirmed patient's improvements. The present case of late recovery underlines how, by devising specific individualized rehabilitation programs and by using intervention tools that allow for calibrating the complexity and effort requested by the exercises on the basis of actual patients' resources and ability to respond, it might be possible to obtain relevant improvements even in the cognitive domain. It seems then desirable that rehabilitation of VS patients also includes neuropsychological interventions, aiming at improving quality of patients' and caregivers' lives. Indeed, empowering cognitive functions also increases the ability to get involved in motor rehabilitation and in social interactions with family and friends.

## Effects of neuropsychological rehabilitation with holistic approach on a patient with severe acquired brain injury: a case report

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Neuropsychological rehabilitation fitted on a subject with severe acquired brain injury aims to achieve the maximum and possible autonomy with the recovery or compensation of cognitive and behavioral compromised skills, improving the overall level of functioning and quality of life of the person and his family. In the last few years, many scientific contributions and investigations have been proposed regarding rehabilitation programs for this kind of patients, paying particular attention to the approach to use. The study of the following clinical case report has proposed the objective to investigate how the level of cognitive and relational skills of a 52-year-old female patient with severe acquired brain injury, institutionalized in a rehabilitation centre, could change by effect of the neuropsychological rehabilitation with holistic approach. The patient was tested with Esame Neuropsicologico Breve-II (ENB-II) to get an assessment of her cognitive profile and it emerged that almost all of the scores were below the norm. Later, the patient underwent neuropsychological rehabilitation, characterized by group work of cognitive stimulation to improve cognitive functions and of music therapy to enhance her communication and relational skills and to decrease depression. Both activities included a frequency of one hour once a week each. During this period the patient, with a history of anxiety-depressive syndrome, expressed feelings of very hopelessness (as highlighted by her depressed profile in Rorschach Test and individual psychological interview) because of her pain and her troubled relationship with her son. In order to assess the effects of neuropsychological rehabilitation about the development of cognitive-relational condition of the patient, monitoring is required in the course of time retesting ENB-II and through clinical observation, with particular attention to the influence that could have depression as it regards both cognitive performance and level collaboration.

## Biological cosmetic products: difference between consumers' thoughts and perceptions about biological world

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Biological products often represent the cutting edge of medical science and research. These products replicate natural substances such as enzymes, antibodies, or hormones. Nowadays, the biological products are used in different ways, for example for making cosmetics. The difference of biological cosmetic products compared to traditional cosmetics is the use of natural components to take care of ourselves. The present research aimed at detecting the consumers' engagement during the test of different cosmetic products, biologicals and traditional (chemicals) ones. The main purpose was to explore the consumers' cognitive and emotive responses to understand the efficacy of biological products. Implicit (brain oscillations and hemispheric lateralization effect) and explicit (preference consumers) measures were considered in order to define the cortical network related to the reward mechanisms

that were supposed to be frontally left-lateralized. Also, we have compared the consumers' emotive responses to smelling and tasting of two different products. Brain oscillations (delta, theta, alpha, beta) and lateralization effect (Log-Transformed-Asymmetry, LTA) were monitored within the prefrontal area when 16 women participated to the study: at first they were asked to smell two skin creams, biological and traditional, without showing the product packages; then, they tasted the same creams by spreading the products blindly on the palm of their hands (one cream for each palm in randomized order). Right frontal theta band power revealed a significant increase (cortical activity) in all consumers during the biological product smelling and testing, despite it was itself evaluated as more preferred to take care of themselves compared to traditional chemical products. The perception of biological product was negative in the cases where participants were not aware of the tested product types: the subjects did not like the smell and the biological cream resulted hard to spread. In different ways, participants talked about cosmetic products and recognized their special properties for body. Therefore, in this research an incongruity between the consumer thought (explicit level) and her perception (implicit level) of biological cosmetic world was present.

## Would you like to pay? Taxpayers' physiological and behavioral responses

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Paying taxes is no fun, yet it is necessary to finance public goods. For this reasons, tax compliance is a key and ambivalent topic, and taxpayer behavior can range from deliberate tax evasion to voluntary cooperation. The present research aimed at detecting the physiological and behavioral responses on a tax compliance experiment. We evaluated participants' intentions to pay the taxes in two different phases: individual phase, where the participant was the only one taxpayer to decide unconditionally whether paying taxes on his incomes; social phase, where the participant paid taxes together with four other taxpayers with the aim of ensuring public welfare. Each phases consisted of twenty rounds where thirty participants had to decide whether paying taxes. During the whole experiment, autonomic responses (skin conductance and heart rate) were measured by biofeedback. At the end of the experiment the participants completed a questionnaire, the Italian version of the tax compliance inventory TAX-I. TAX-I assesses tax compliance and distinguishes between two forms of compliance and non-compliance: voluntary compliance (spontaneous willingness to cooperate, emanating from taxpayers' moral obligation to contribute to the public welfare) and enforced compliance (tax payments according to the law arise from taxpayers' concern of being audited and fined). The behavioral results show a greater propensity to evade taxes for participants with a higher level of enforced tax compliance compared to those who had a higher level of voluntary tax compliance, in particular in individual phase. In the same way, the physiological results show greater SCR (Skin Conductance Response) for the participants with a higher level of enforced tax compliance during decision-making in individual phase. In general, the participants with higher levels of enforced tax compliance evaded in particular during individual phase. Probably, they feel the responsibility for making wrong decisions that could harm public welfare during social phase.

## Non motor aspects in early Parkinson's Disease: neurophysiological assessment of the interaction between dopamine and serotonergic tone

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In the last decades neurobiological correlates of non motor aspects in Parkinson's Disease (PD) have been an increasing research subject. Particularly, clinically significant nondopaminergic symptoms, as cognitive, mood and sleep disturbances, could be explained by neurodegenerative involvement in brain serotonin neurons. Moreover, neural mechanisms that underlie motor complications as levodopa-induced dyskinesia in PD have been recently correlated to a maladaptive plasticity of the striatal serotonergic system. Indeed, direct synaptic contacts between 5-HT terminals and DA cells in the midbrain have been showed and a variety of 5-HT receptors in the striatum has been demonstrated. Neuropathological evidence of striatal serotonin deficiency in caudate and relative preservation in putamen could account for the different clinical aspects of the question. Serotonergic involvement in PD is still an open debate. In this context, our aim was to define an in vivo evaluation of serotonergic tone in *de novo*, drug-naïve PD patients and to investigate the interaction between dopamine and serotonergic activity by means of recording Intensity Dependence of Auditory-evoked Potentials (IDAP), widely considered a reliable non invasive neurophysiological indicator of central serotonergic function in human. A strong dependence of the amplitude of auditory-evoked N1/P2 component of AEPs from stimulus intensity has been associated with low levels of serotonergic neurotransmission in humans and negatively correlated with serotonin serum levels in depressive patients. Twenty-eight drug-naïve patients with a first clinical diagnosis of PD, according to the UK Brain Bank and 30 age and gender-matched controls performed a clinical, cognitive and psycho-behavioral assessment. Neurophysiological evaluation by means of IDAP recording was performed in PD patients in three times: basal condition and, in that same first session, 90 minutes after acute levodopa oral challenge. After four months of chronic dopaminergic therapy, the same complete clinical and electrophysiological study protocol was performed during the third observation. The AEPs were recorded during the presentation of 4 series of 250 stimuli of 1000-Hz binaural tones of increasing intensity (60, 70, 80, 90 dB). A steeper IDAP slope, reflecting a large increase in N1/P2 amplitude related to loudness of stimuli, was evident in PD patients compared to healthy subjects, suggesting dysfunctional central serotonergic activity, yet in early disease. Moreover, levodopa assumption clearly improved serotonin neurotransmission, especially after acute challenge, as showed by a dramatic decrease in the IDAP slope. Our study provides neurophysiological evidence that serotonergic neurotransmission is precociously involved in PD; this condition could be modulated by changes in dopaminergic tone. Furthermore, this observation confirms that IDAP, widely considered a marker of central serotonin function, could also be influenced by other neurotransmitter monoaminergic systems. This methodological approach could support the comprehension of physiopathology of non motor symptoms in PD.

## **I wanna hold your hand: other-touch induces sensory attenuation as in self-touch**

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According to the gate control theory of pain, non-painful concurrent stimuli close the “gates” to painful input, inducing an analgesic effect due to the overlapping receptive fields. Recently, an additional analgesic effect resulting from self-touch has been described during the Thermal Grill Illusion (TGI). An Electroencephalography (EEG) study, exploring the neural bases of self-touch analgesia, highlighted the correlation between P100 amplitude and self-touch, with larger amplitudes matched with joined own hands condition. However, outside the context of TGI, no significant analgesic effect on pain ratings has been observed in self-touch. In the present study, we focused on this controversial result, exploring whether a more sensitive parameter, such as subjective perceptual threshold, can be modulated by the self-touch, altering the Detection Rate (DT) of tactile stimuli. In our paradigm, we delivered electrical stimuli, at the individual perceptual threshold level, to the right digit V of 15 healthy participants, by means of a constant current electrical stimulator. Participants’ DT was recorded in four different conditions, depending on the kind of contact with the stimulated hand: no-touch, self-touch (joined own hands), other-touch (contact with other’s hand) and object-touch. Experimental conditions were counterbalanced across subjects. If physical contact between the own hands affects the tactile perceptual threshold, we should observe a DT modulation during self-touch condition, compared to all the other conditions. Note that, according to previous TGI and EEG studies of self-touch analgesia in threatening context, the other-touch condition was designed as a control condition. The one-way ANOVA on the mean DT, with Condition as within-subjects four-level factor, revealed a main effect ( $F_{3, 42} = 12.04$ ;  $p < 0.001$ ) with a significant DT reduction (i.e. increased perceptual threshold) during self-touch, compared to both no-touch and object-touch ( $p < 0.001$ ). No significant difference in DT was found between object-touch and no-touch, thus confirming that sensory attenuation is specific for physical contact. Surprisingly, in other-touch we observed a similar DT modulation as in self-touch, with significantly reduced DT compared to both no-touch and object-touch ( $p < 0.001$ ). Coherently, no difference between self-touch and other-touch was found. This is the first evidence that physical contact between two hands (own or other’s) lowers the detection of external stimuli, modulating the tactile perceptual threshold. Further investigations are needed to interpret the unexpected result in other-touch condition. However, we can speculate that, in our non-threatening context (tactile stimuli), discriminating between self and other is less relevant than in threatening context (painful stimuli). Thus, when self/other discrimination mechanisms are weakened, an implicit form of embodiment can induce sensory attenuation also when we hold someone else’s hand.



## Neuromodulation of the perception of an illusion of length

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The Müller-Lyer figure is a visual illusion in which two identical horizontal lines are perceived as different in their physical length because of the presence of fins (inducers) at the line ends. The Brentano illusion combines the two configurations of the Müller-Lyer illusion in one figure on the horizontal planum. In healthy subjects this configuration generates a displacement of the subjective midpoint of the horizontal line. In brain-damaged patients, with Unilateral Spatial Neglect (USN+) without Hemianopia (H-), the Brentano illusion is preserved, with illusory effects even enlarged in the contralesional hemisphere. This finding suggests an inhibitory modulation of the top-down mechanisms on the bottom-up processing at the basis of such illusory phenomenon, likely mediated by the right Posterior Parietal Cortex (PPC), which represents the main neural substrate of neglect. In order to verify the hypothesis that the attentional system can modulate the Brentano illusion and that this modulation is lateralized, a group of healthy subjects was tested with the Brentano Hemianopia Test (BHT) while receiving cathodal or sham transcranial Direct Current Stimulation (tDCS) to the right or left PPC. The results show an increase of the illusory effect after cathodal tDCS of the right PPC and a decrease after the stimulation of the left PPC. This evidence uphold the involvement of attention and its hemispheric asymmetry in modulating the perceptual processing underlying the Brentano illusion of length.

## tDCS to induce long-lasting positive effects on episodic memory in physiological aging

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Episodic memory displays the largest degree of age-related decline. A noninvasive brain stimulation technique that can be used to modulate memory in physiological aging is transcranial Direct Current Stimulation (tDCS). However, an aspect that has not been adequately investigated in previous studies is the optimal timing of stimulation to induce long-lasting positive effects on episodic memory function. Our previous studies showed episodic memory enhancement in older adults when anodal tDCS was applied over the left lateral prefrontal cortex during encoding or after memory consolidation with or without a contextual reminder. Here we directly compared the two studies to explore which of the tDCS protocols would induce longer-lasting positive effects on episodic memory function in older adults. In addition, we aimed to determine whether subjective memory

complaints would be related to the changes in memory performance (forgetting) induced by tDCS, a relevant issue in aging research since individuals with subject memory complaints seem to be at higher risk of later memory decline. The results showed that anodal tDCS applied after consolidation with a contextual reminder induced longer-lasting positive effects on episodic memory, conceivably through reconsolidation, than anodal tDCS during encoding. Furthermore, we reported, providing new data, a moderate negative correlation between subjective memory complaints and forgetting when anodal tDCS was applied after consolidation with a contextual reminder. This study sheds light on the best-suited timing of stimulation to induce long-lasting positive effects on memory function and might help the clinicians to select the most effective tDCS protocol to prevent memory decline.

## Attentional impairment in chronic tinnitus: evidence from a P300 study

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Tinnitus is an auditory phantom sensation experienced in the absence of sound source. The prevailing opinion is that chronic tinnitus is a consequence of a maladaptive cortical plasticity into auditory and non-auditory cortical associative structure following damage to the peripheral auditory structures. Cognitive dysfunctions are frequently reported, especially in working memory and attention. The aim of this study was to investigate the attentional functioning of a group of subjects with chronic tinnitus using ERPs, in particular P300 components. We studied 20 patients with chronic tinnitus and 20 healthy subjects that underwent a P300 Novelty task. Latencies and amplitudes of N1, P3a and P3b components were acquired. All subjects underwent the Mini Mental State Examination (MMSE) and self-administered questionnaires (Beck Depression Inventory, BDI; State-Trait Anxiety Inventory 1 e 2, STAY1 and STAY2). The Tinnitus Handicap Inventory (THI) scale was used to grade tinnitus severity in all the patients. P3a amplitude was significantly lower in tinnitus subjects than controls ( $p < 0.001$ ), while P3a latency was comparable between patients and controls ( $p = 0.81$ ). P3b parameters were similar in the two groups (amplitude:  $p = 0.78$ ; latency:  $p = 0.80$ ). Moreover, N1 latency for all the stimuli was longer in tinnitus subjects than controls ( $p < 0.001$ ). These results point to a general slowing in the early perception of the stimulus in tinnitus. Moreover, a specific difficulty emerged in the attentional switching to unexpected events as suggested by P3a component, probably owing to a dysfunction in the ventral attention network. We retain that this attentional dysfunction emerged because attention is directed to the “phantom symptom” and this depletes cognitive resources. It is thought, in fact, that tinnitus, like chronic pain, is a competing stimulus that attracts attention, and that cognitive performance is impaired when other demanding tasks involving attentional switching processes are required.

## Investigating the effects of an edutainment Virtual Reality experience using biophysical data

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Investigating biophysical responses using biosensors is becoming increasingly relevant in the field of Human Computer Interaction for recognising emotions and eliciting arousal levels during an experience. This enable us to better understand the effect of technology on consumer behaviour and eventually design more engaging digital content. This study, to the best of our knowledge, is one of the first proposing an approach for assessing users' reactions during a Virtual Reality (VR) edutainment setting with the use of biophysical data. We collected biophysical responses, such as Electrodermal Activity (EDA), and Heart Rate Variability (HRV), from 46 adult visitors of the Genova Aquarium, a popular tourism attraction in Genova (Italy), where a VR edutainment experience – developed by ETT – was first introduced to the public. VR applications are generally experienced using head-mounted devices that tend to reduce the effect of external stimuli (e.g. external visual stimuli or sounds in the case earplugs are used). Thus, any detected effects on collected EDA and HRV data during a VR experience can be increasingly attributed to the VR content displayed. Our study took place in August 2016. Each participant was recruited voluntarily, and the study was conducted in a room dedicated to the VR experience, equipped with eight Samsung Gear headsets, displaying a three-minutes experience about the “Deep Sea” topic. After obtaining participants' consent, each participant wore a headset and an Empatica E4 wristband, a multisensory device for real-time biophysical data collection, enabling us to track participants' biophysical responses corresponding to the VR content viewed. In addition, a pre-post questionnaire was completed, inquiring into the following aspects: appreciation, knowledge, and ability to recall the VR contents viewed. A content analysis of the elements displayed during the VR experience was combined with the biophysical data generated by the wristband, and with the most memorable contents reported by participants. Our analyses will determine if there is a correlation among the main biophysical reactions (e.g. an increase in HRV) and the display of surprising or unusual content, such as a virtual encounter of a deep sea monster. We hypothesize that detected HRV peaks will correspond to VR graphic design elements that tend to change the usual perspective of users, forcing them to focus on a re-adaptation of their view to a new scene. Moreover, our preliminary results show that those who participate in a VR experience for the first time, tend to remember and report more the feeling of immersion, instead of what it was actually displayed. We believe this is due to a novelty effect that a first VR experience imposes. To the best of our knowledge, this study is one of the first that proposes the use of biophysical data for investigating media effects of a virtual reality edutainment experience, and discusses the use of “neuromarketing” techniques for media effects studies in virtual reality settings.

## **Sense of Agency and Sense of Body ownership in Functional Movement Disorders**

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Functional Movement Disorders (FMD) are characterized by motor symptoms that, although physiologically similar to voluntary movements, are experienced as out of control by patients. This gap might be related to abnormalities in two fundamental components of self-consciousness: the Sense of Agency (SoA) and the Sense of Body ownership (SoBo). The SoA is the feeling of control over own actions, while the SoBo is the experience of the body as part of the self. We used the moving Rubber Hand Illusion (mRHI) to investigate SoA, SoBo and the relationship between them in FMD. 21 FMD patients and 21 healthy volunteers underwent the mRHI. In the mRHI, participants can control the movement of the index finger of a visible rubber hand by moving their hidden index finger. We systematically changed the temporal congruency of fingers movements (synchronous, asynchronous), the type of movement (active, passive) and the position of the rubber hand (anatomically plausible, anatomically implausible). Agency and ownership were assessed by means of a questionnaire. Synchronous movements enhanced both agency and ownership that were instead abolished by asynchronous movements. Furthermore, passive movements suppressed agency but not ownership, whereas the anatomically implausible position of rubber hand eliminated ownership but not agency. This pattern of response was similar in both groups. Previous studies found altered implicit measure of agency (e.g. action-effect binding) for normal voluntary movements (e.g. button press) in FMD. Conversely, we found unaltered explicit feeling of agency in FMD. These contrasting evidences could hint at a dissociation between explicit and implicit SoA for normal voluntary movements in FMD, with the former being preserved and the latter impaired. Regarding the SoBo, our results are in line with previous RHI study finding spared SoBo in FMD.

## **Hypnotic trance and state of flow compared: a pilot neuropsychological and psychophysiological study**

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Hypnosis and flow are among the most studied states of consciousness. However, scientific investigations in which these states and their psychophysiological signatures are compared are still lacking. Hence, following a preliminary theoretical comparison of the two states of consciousness, in which we pointed out several similarities (i.e. concerning the basic terminology and core constituent concepts of the constructs, the way they arise and develop, involved physiological processes, and even the potential difficulties in modulating such states), we formulated an hypothesis on their relationship and tested experimentally whether and how they were similar. Therefore, we devised a pilot study

aiming at investigating – from both a physiological (thanks to EEG recordings) and classical psychological (thanks to a qualitative and quantitative *ad hoc* self-report battery: FQ, FSS, 5D-ASC) points of view – psychophysiological correlates of the two experimental conditions and at exploring potential common features. We then induced and compared the two altered states of consciousness, namely a hypnotic state induced via a double indirect induction procedure, and a state of flow induced via a PC videogame (fLOW). To increase the chances of actually making participants experience those states in the laboratory setting, we focused on a sample that already proved to be able to enter both the states we were interested in. We then opted for a group of clinical psychologists who were specializing as ericksonian psychotherapists ( $n = 7$ ). There have been two data collection phases. In the first phase, we collected subjective data regarding previous experiences of hypnosis and flow proposed by the subjects, to be used as a reference. In the second phase, in the laboratory, each subject underwent both experimental conditions, and we collected both physiological and self-report subjective data regarding those experiences. Physiological data showed significant variations in the power of delta, alpha and gamma frequency bands, but only in the condition of hypnosis. The state of flow was associated to a qualitative modulation of theta power over prefrontal areas. Subjective data demonstrated that participants qualitatively recognized to be in a flow state during the relative induction condition, with the exception of only one of them. Self-report quantitative data showed that the experimental condition of hypnosis presented similar features with respect to the reference state of flow. To sum up, our main hypothesis was partially verified: while physiological data during the flow condition were less consistent, hypnosis was overall associated to the slowing of cortical rhythms, and first evidences suggested that hypnosis and flow states may be similar at least for subjective experience.

## **tDCS effects on implicit association tests in Eating Disorder patients**

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Transcranial Direct Current Stimulation (tDCS) has been increasingly used in experimental and clinical studies on food-related pathological behaviours and attitudes. However, neural mechanisms underlying eating disorders are still partially unknown and controversial results have been reported concerning tDCS effects on eating behaviours. This study aims at assessing whether tDCS applied to two cortical regions involved in food and body representation, namely the medial Prefrontal Cortex (mPFC) and Extrastriate Body Area (EBA), affects implicit attitudes towards food and body images in female healthy con-

trols and female patients with Eating Disorder (ED). Implicit association tests (IATs) on tasty and high calories food versus tasteless and low calories food (food-IAT), overweight versus underweight body images (body-IAT), flowers versus insects (control-IAT), were administered to 10 patients with anorexia or bulimia nervosa and thirty-four healthy volunteers. In three separate sessions anodal tDCS was applied on mPFC, right EBA or in sham mode immediately before the IATs. Results showed that control participants evaluated tasty food as more positive both in explicit ratings and in food-IAT. Reaction times of the food-IAT generally increased when tDCS was applied over mPFC. Moreover, ED patients performed the three IATs overall slower than controls and their reaction times increased in mPFC- and EBA-tDCS conditions both in body-IAT and control-IAT. These results demonstrate that tDCS differently affected cognitive tasks in healthy and clinical populations. Indeed, only in the ED participants tDCS increased reaction times in the three IATs. However, this effect could be related to a general interference with the cognitive mechanism involved in stimuli categorization, since it was unspecific for the cortical site of stimulation and IAT material. This study confirms a tDCS effect in modulating cognitive tasks in ED patients, but it also shows that research is still needed to clarify the role of different target areas, which could be selected for clinical trials.

## **Motion or e-motion? Representation of observed Emotional Bodily Expressions in the anterior Intraparietal Cortex and superior Temporal Sulcus: a TMS state-dependent study**

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The human being is an extremely social animal. Detecting prey or predators, identifying pleasant or dangerous situations, learning new skills and inferring social norms are just some examples that clearly illustrate the fundamental importance of comprehending our conspecifics' movements. In the visual domain, the encoding of whole body gestures has traditionally been studied with the so called Point-Light Display (PLD) paradigm. In the human brain, a widespread network of areas is activated by the sight of body movements, but their role in comprehending the emotional content of bodily expression is still unclear. The goal of the present experiment was to investigate the existence of a neural system involved in the processing of Emotional Bodily Expressions (EBE). In an initial behavioural study, 26 participants were adapted with PLDs depicting fearful, happy or neutral actions and were subsequently asked to recognize happy or fearful PLDs. Adaptation is a phenomenon in which changes in neural tuning and excitability, induced by prolonged exposure to sensory stimulation, can bias the perception of subsequently presented stimuli. We found an adaptation after effect for the emotional – but not neutral – stimuli, with faster RTs for incongruent conditions. This adaptation effect demonstrates the existence of a neural mechanism specific for EBE perception. We then examined the cortical locus of this mechanism with the use of TMS-adaptation paradigm ( $n = 17$ ). We targeted two areas of the action representation system: the anterior Intraparietal Sulcus

(aIPS) and the posterior part of Superior Temporal Sulcus (pSTS). Our hypothesis was that if the stimulated brain regions contain neurons coding for EBE, then the application of TMS should interact with the adaptation aftereffect. We found that the adaptation aftereffect was still present following TMS stimulation over the control site and pSTS. Importantly, TMS over aIPS abolished the adaptation effect; in other words, it reduced the RTs difference between congruent (same emotion) and incongruent (different emotion) conditions. Our findings demonstrate the existence of a mechanism in the human brain selective for the emotional content of body movements, and locate it within the anterior part of the intraparietal sulcus.

## **The relationship between emotional components and the embodiment effect during the Rubber Hand Illusion: an EEG-fNIRS study**

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Repeatedly stimulating the hand of a person and a dummy hand in front of him it is possible to induce the inclusion of the object in the body schema (Rubber Hand Illusion, RHI). One of the key strengths of the RHI is the incongruence between what a person feels via the somatosensory pathways and what he sees. When the illusion has been induced, participants tend to provide irrational and supernatural explanations for sensory phenomena that do not fit. In view of this fact, stimuli presented on or near to the artificial hand generally elicit behavioural and neural responses that would normally occur if they had been disclosed on the participant's own hand. However, previous investigations focused mainly on primary variables such as physical features of RHI. In order to investigate the contribution of some affective processes in the definition of the phenomenon, in the present research the classic paradigm was amended to include a phase of stimulation with emotional value, by using an emotional threatening condition. The illusion was induced in 16 participants, stimulating synchronously the dominant and the artificial hand for three minutes with two brushes. The study included three induction sessions, followed by the emotional stimulation or by a control condition. The emotional condition included the presence of a direct aversive stimulus toward the artificial limb. Simultaneously, cortical responses of the participants were measured using Electroencephalography (EEG) and functional Near-Infrared Spectroscopy (fNIRS). The analysis focused on data related to the subjective experience, the cortical hemodynamic responses and the modulation of the frequency bands components of EEG. All participants reported having experienced the illusion, with different reactions to emotional stimulation. fNIRS data suggested the contribution of the frontal and parietal regions to support this illusion, with oscillatory responses partially different as a function of the emotional stimulation condition. Therefore, where as previous study have shown some crucial factors for the onset of the RHI, such as spatial coherence between the position of the artificial hand and the coordinates of the body schema, the present results showed that even the emotional processes are able to modulate the appearance of the illusion and the related embodiment effect.



## **Autistic traits influence interpersonal motor coordination in a joint-action task**

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Deficits in social communication and interaction are at the core of Autism Spectrum Conditions (ASC). Surprisingly however, information on how ASC individuals behave in an on-line, cooperative, joint action task is lacking. In our study we aimed to assess whether autistic traits impact on participants' ability to ease motor cooperation and facilitate on-line interpersonal coordination by predicting and adapting to one's partner's movements and by adjusting motor behaviour depending on the role taken during the interaction. Sixteen pairs of adult participants (one ASC and one control, both with no cognitive disability) played an interactive game in which they had to synchronize their reach-to-grasp movements. In the game, one participant knew what action to perform (i.e. power/precision grasp of a bottle's bottom/top), while the other had to infer it from his/her partner's action, which could be either opposite or similar. Participants also played a non-social control game in which they had to synchronize with a non-biological stimulus. We analyzed indexes of individual and pair performance including accuracy, reaction time, movement duration and grasping asynchrony via repeated measures ANOVAs, with the number of autistic traits as moderator, and via correlational analyses. Results show that the higher the autistic traits the less participants were able to modulate their joint action according to their interactive role in the social interactive task. In particular, participants with high autistic traits, in trials in which they needed to adapt to their partner's movement, did not wait for their partner and showed longer movement duration both for same and opposite actions. No such effect was found in the conditions that did not require adaptation to the partner's movements. Autistic traits did not predict differences in movement preparation and planning in the non-social task, thus ruling out that the results at the social interactive task were due to basic motor or executive function difficulties. Instead, when participants played the non-social game, the higher the autistic traits the more they were interfered (higher asynchrony and longer movement duration) by the non-biological stimulus. Overall, reduced use of communicative and adaptive strategies to facilitate coordination during joint action seems to suggest a difficulty of participants with high autistic traits to on-line update individual action plans according to the constraints of the interactive task. Such reduced interpersonal coordination strategies during on-line motor cooperation may shed light on ASC basic and early difficulties in social interaction.

## **Executive functions assessment in addiction: a four-cases study on addicted teenagers during abstinence from drugs**

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In the present work four clinical cases of young men with a history of drug abuse will be analyzed, ranging from 16 to 21 in age, a period that is considered critical for the development of frontal lobes. All four patients had a history of cannabis, cocaine, and even heroin abuse. They were recruited at Casa del Giovane Community of Pavia and differed from each other in the period of placement within the community and, therefore, in the time of abstinence from drugs. A neuropsychological assessment was conducted to assess their executive functioning through different standardized tests, with the aim to provide a snapshot of the current state of their cognitive abilities, among which planning, categorization, attention, shift abilities, and mental flexibility. After administering specific tests such as the Tower of London, the Wisconsin Card Sorting Test, the Trail Making Test, the PASAT and the Iowa Gambling Task, very different neuropsychological profiles emerged, which could be ascribed to the period of abstinence from drugs. In fact, subjects with a long period of abstinence obtained higher and pathological scores, together with impaired performance from a qualitative point of view, comprising little execution tightness, frustration in response to errors, and the prevalence of inappropriate language. To conclude, this study highlights the importance to consider the period of abstinence when assessing cognitive impairment in drug users.

## EEG Gamma band and empathy for pain in healthy subjects

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This study wishes to evaluate the empathic pain by means of the Gamma band oscillation induced by laser stimulation in a healthy population. Empathy is defined as the ability to have a direct and experiential understanding of the mental states of the others, especially in pain. It depends on a mirror mechanism that encodes the sensory experience directly in emotional terms. Electroencephalographic Gamma Band Oscillations (GBOs) have been hypothesized to reflect cortical processing involved directly in pain perception, because their magnitude correlates with pain intensity. We evaluated 13 female subjects. All the subjects were submitted to 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 the stimulation of the dorsum of the right and left hand in two conditions: (a) CLOSE by the interposition of a panel between the subjects, in order to prevent them to see each other; (b) HAND SIDE BY SIDE 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. We observed an increased cortical response of GBO occurred in both protocol stimulation CLOSE and HAND SIDE BY SIDE; the subjects with higher EPS score and lower TAS-20 score have a bigger representation of GBOs during the stimulation HAND SIDE BY SIDE. These results provide evidence for a close relationship between GBOs oscillation and both subjective and empathic pain perception; in fact the amplitude of GBOs oscillation increased even during the stimulation HAND SIDE BY SIDE.

## **A case of pure prosopagnosia after right brain lesion: new insights for face perception**

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Faces are social stimuli, which convey several information about others such as identity, mood, gender, age and attractiveness, contributing in this way to social interactions. Individuals with Acquired Prosopagnosia (AP) lose the essential ability to recognize familiar faces and to encode new faces after brain lesions encompassing areas of the face-selective network widely distributed over occipito-temporal regions. Since several cases of AP present concomitant difficulties in object recognition, clinical cases of pure AP are rarely described. Here we present the case of ST, a 48 y.o. woman who showed pure AP after right occipital hemorrhage. The patient did not exhibit any other perceptual and cognitive deficit except for left homonymous hemianopia and prosopometamorphopsia. We investigated her holistic processing abilities by means of composite face paradigms (with regard of both identity and emotional expressions). Furthermore, the ability to discriminate and categorize Thatcherized and typical faces were investigated. Findings from the face recognition assessment revealed severe impairment in recognizing familiar faces, together with deficit in unfamiliar face matching and difficulties in face memory. However, face categorization appeared spared. Results from the holistic processing assessment showed lack of composite face effect for both identities and emotions, suggesting holistic processing impairment, and consequently a face recognition based on weak feature-processing strategies. This pattern was confirmed in a follow-up examination one-year later. Our results, together with the presence of a composite effect for facial expressions in healthy subjects, contribute to the debate about the dissociation of identity/emotion processing, giving support to the hypothesis of shared cognitive mechanisms, at least at an early stage of analysis, for unfamiliar faces. This impairment was further studied by means of an experimental paradigm involving the analysis of unusual configural relationships among face parts (i.e. Thatcher effect). According to part of the theories on this topic, we hypothesized an absence on this effect due to the proved impairment in face processing. Surprisingly, the patient did not show any differences compared to the results obtained by the healthy subject (i.e. a different effect on the performance in the detection of the local changes between upright and inverted Thatcherized faces). Such findings lead us to suppose that the adoption of a feature-by-feature strategy is sufficient to immediately detect the illusion when the Thatcherized face has an upright orientation, but this is not for the inverted condition. In conclusion, we think that this clinical case provides new insights in the field of AP and, more in general, in face processing. Actually, on one hand we found common cognitive mechanisms for emotions and identity in a pure prosopagnosic patient and, on the other hand, our results seem in line with the hypothesis of a feature-by-feature analysis of faces with unusual configurations.

## **Time-frequency EEG correlates of body parts visual perception**

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Research on visual processing of human bodies is steadily increasing in cognitive neuroscience. Based on EEG recordings, the vision of faceless full bodies and single body parts (e.g. hands) generates a modulation in the amplitude of a bilateral negative Event Related Potential (ERP) at a latency of 190 ms (i.e. N190) over parieto-occipital electrodes. This component is likely generated by the activity of the Extrastriate Body Area (EBA), a brain region that responds differently to the sight of single body parts, compared to full bodies, and that may contribute to a local (part-based) visual processing of the body. Even though this body-specific ERP modulation has been well described in the time domain, little is known about its counterpart in the time-frequency domain. Describing the frequency-specific responses to the sight of body parts is fundamental in order to understand the neural communication mechanisms underpinning our ability to transform these images in meaningful stimuli for our social behavior. In order to explore any body-related band-specific modulation of Event Related Synchronization/Desynchronization (ERS/ERD) and Inter-Trial Coherence (ITPC) we recorded EEG in participants who observed four different kind of body stimuli (fingers, hands, arms and faceless bodies) and four hierarchically comparable plant stimuli (leaves, clusters of leaves, branches and trees). We identified topographical body-specific frequency modulation by creating three different (bilateral) clusters of electrodes (occipital, EBA, parietal). Over the electrodes that correspond to EBA and where the N190 amplitude was maximal, we found that observation of body vs. plant stimuli brought about greater Theta (4-8 Hz) ERS in the 150-200 ms time window as well as a significantly higher ITPC within the same band. Thus, beside the ERP modulation, body stimuli seem to induce frequency, and time, specific modulation over the EBA together with a greater Theta phase ITPC. In summary, our results pave the way to the comprehension of the functional mechanisms underlying body processing.

## Social support modulates the neural correlates underlying social exclusion

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Human beings have a fundamental need to interact with each other. Ostracism (social exclusion) impairs this need and has various effects on cognition, affect, and behavior. It is often associated with experiences of pain, often called social pain, defined as the distressing experience arising from the perception of actual or potential psychological distance from close others or a social group. Several neuroimaging studies showed that this experience activates brain regions similar to the ones recruited during physical pain – such as the dorsal Anterior Cingulate Cortex (ACC) and the Anterior Insula (AI). On the other hand, experiences of social support such as the perception of help received from others

can act as a psychological resource used to cope with stress. The present study thus aimed to investigate the role of social support in modulating the neural correlates involved in experience of social exclusion, elicited via the well-known cyberball task. We focused on two different forms of support: physical and cognitive. By *physical support* we refer to physical contact through the touch of the participant's hand provided by a real friend; by *cognitive support* we refer to the verbal communication of useful information about the social exclusion experience, e.g. "I think these players are friends", also provided by a real friend. 61 women divided in three groups – cognitive support ( $n = 19$ ), physical support ( $n = 20$ ) and control group ( $n = 22$ ) – participated in the study. The experimental fMRI session was divided into 3 phases. (A) *Social exclusion I*: each group was scanned while playing the virtual cyberball game. During the game two (virtual) persons played with a ball, and excluded the experimental subject from the game. (B) *Social support*: the different experimental groups received physical or cognitive support, while the control group did not receive any kind of support. (C) *Social exclusion II*: each group was scanned for the second time during the exclusion experience elicited by the cyberball game. We then compared physical and cognitive groups to control group using the contrast *social exclusion I vs. social exclusion II*. fMRI results show that during social exclusion II, physical support decreases the activation of AI, usually associated with visceral pain and negative affective experiences, and that cognitive support decreases the activation of both AI and Temporal Parietal Junction (TPJ), an area involved in the representation of mental states of other individuals. Our study suggests that after the experience of social exclusion, physical support reduces social pain mirrored by a reduced activation of AI. Similarly, social exclusion after cognitive support is associated with reduced activation of AI and TPJ, possibly due to an additional lower engagement of theory of mind.

## **Brain Injury: diagnosis, rehabilitation, and single-case study**

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The present work will highlight the most distinctive features of a common and resource-consuming health issue, that is Brain Injury (BI). It has been calculated that BI occurs every 15 seconds, and that it is accompanied by a fatal outcome every 12 minutes. For what concerns the Italian scenario, it has been estimated that between 100 and 250 per 100.000 inhabitants, every year, suffer from BI. Mortality is typically high, occurring up to 50% of cases. Considering these data, it is important to recognize the role of health care associations in supporting the management of this phenomenon. Among these, the role of the neuropsychologist will be highlighted, as well as of his important contribution in the diagnosis and rehabilitation of BI patients. In the first part of this work diagnostic and rehabilitation issues concerning BI will be framed, as well as the most important neuropsychological deficits that characterize the symptomatology. Specific interest will be devoted to the neuropsychological tools that are available, at present, for the assessment and differential diagnosis. Then, a single-case for car accident will be described in the attempt to better elucidate the clinical steps and the role of the specialists. Finally, some important proposals of rehabilitation strategies will be defined in order to highlight some issues about the reintroduction of these patients to every-day life.

## **Emotional and practical implications for caregivers of patients with behavioral disorders following severe brain injury**

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Behavioral disorders are very common in severe brain injured patients and, besides the cognitive impairment, produce a significant pain in their relatives and caregivers. This burden needs to be intercepted to give them help and relief. Personality changes are the most difficult to deal with and are a significant source of long-term stress. This is an important factor to consider: a cooperating and organized family, less emotionally tried, is determining in a successful long-term rehabilitation. The aim of this study is to assess burden and needs in caregivers of brain-injured patients. Multidimensional instrument utilized is the CBI scale (Caregiver Burden Scale), that measures the impact of burden on caregivers. Questions research factors as: Time-Dependence Burden (due to restrictions on the caregiver's time); Developmental Burden (caregiver's feelings of being "off-time" in their development with respect to their peers); Physical Burden (caregiver's feeling of chronic fatigue and damage to physical health); Social Burden (caregiver's feelings of role conflict); Emotional Burden (caregiver's negative feelings toward the care receivers and their bizarre or unpredictable). Other questionnaires were administered to caregiver with the purpose to achieve his/her evaluation of patient behavioral disorders: FBI (Frontal Behavioral Inventory) and the BIRT PQ (Brain Injury Rehabilitation Trust Personality Questionnaire). Caregivers were interviewed in hospital with a questionnaire with fixed-choice questions. The study included 1 man and 5 women 28-70 years old, with 8-18 years of school attendance. They were caregivers of 6 brain-injured patients with the following characteristics: onset 1 to 6 years, GCS 3 to 5 and period of unresponsiveness 6 to 30 days and severe traumatic brain injury / subarachnoid and intraparenchymal hemorrhage / ischemic stroke / anoxia as etiology. Family had to evaluate on a four point rating scale with which frequency each behavior occurs during their relative everyday life. Results from this study confirm the existence of behavioral disorders that weighs caregivers and the lacking reliability of behavioral disorders tests if administered only to patients and not compared with families and caregivers. Specifically, CBI shows the considerable burden in caregivers and support the requirement of any help for them, especially referring to most critical group of items: Time-Dependence Burden, Developmental Burden and Physical Burden. In conclusion, the study shows how behavioral disorders produce significant outcomes in relatives and caregivers. Furthermore, that these symptoms need of tests with family versions to be actually assessed.

## **Response-inhibition and Dyskinesias-Reduced-Self-Awareness in Parkinson's Disease: a piloting fMRI study**

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PD patients may be partially or even completely unaware of the presence of involuntary movements in terms of Dyskinesias-Reduced-Self-Awareness (DRSA). This phenomenon was previously related to executive-metacognitive deficits due to dopaminergic overstimulation of mesocorticolimbic circuits. Interestingly, response-inhibition dysfunction is often assessed in PD. Besides being involved in response-inhibition tasks, the Anterior Cingulate Cortex (ACC) is part of a functional system based on self-awareness that is engaged across cognitive, affective, and behavioral contexts. The primary endpoint of our piloting study was to approach the relationship between response-inhibition disabilities, ACC functionality, and DRSA using fMRI and an event-related specific executive task. Two cognitively non-impaired PD patients receiving levodopa treatment, and presenting motor fluctuations were enrolled. A good clinical response to levodopa with the presence of wearing off or on-off phenomena and peak-of-dose dyskinesias was the required selection criteria. PD patients were compared on two different scales to measure awareness of movement disorders: (1) Global Awareness of Movement Disorders and (2) Dyskinesia Rating Scale. The latter was used to classify patients into aware and unaware. The neurological and neuropsychological assessment were based on the Italian Health System - National Guideline System for Parkinson Disease (2013). Cingulate functionality was assessed with fMRI, while they performed an ACC sensitive go/no-go task. Neuroimaging data acquisition was performed on a 3T Philips Ingenia scanner. Subjects had to respond to “go” stimuli inhibiting the response to infrequent “no-go” stimuli. Image preprocessing was performed using SPM8. All functional images were spatially realigned to the first volume and anatomical images were coregistered to the mean of them. The functional images were normalized to the MNI space and smoothed. After preprocessing, we applied a General Linear Model to convolve the “no-go” and “go” stimuli with canonical hemodynamic response function. A difference between the unaware and aware subject was performed to compare functional activations. Results were expressed for the ACC ROI corrected for the coordinates MNI  $x = 4$ ,  $y = 21$ ,  $z = 38$ . The neuropsychological assessment appeared to be normal. The unaware PD patient showed worse response-inhibition as measured by the go/no-go task. Moreover fMRI acquisition revealed significant different brain activations in ACC for the contrast “no-go” vs. “go” between patients. These preliminary findings may have implications in considering executive functions and the related ACC functionality as a clinically important imaging biomarker for DRSA. Our piloting study suggests that functional abnormalities of the cingulated frontal-subcortical neuronal network are detectable in patients with PD as a clinical feature of impairment of higher level cognitive functions. Theoretical models of DRSA will be more effective if they integrate fMRI and neuropsychological data, given the relevance of detecting possible neuropsychological biomarkers of this phenomenon in PD patients. Future studies with a greater sample size must confirm the results.

### **tES effects in a short-term memory task depend on participants' age**

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Arousal reflects a state of generalized physiological and psychological activation and has a key role in cognition. We have previously showed that it is possible to modulate arousal in healthy young subjects through bursts of transcranial Electrical Stimulation (tES) in a sustained attention task. The objective of this study was to investigate whether the same tES protocol may be used to exogenously increase the participants' level of arousal during a Visual Short-Term Memory (VSTM) task to improve behavioural performance in young and healthy elderly subjects. 20 healthy young (mean age = 24 years; SD = 2.8) and 20 healthy elderly subjects (mean age = 68 years; SD = 3.6) participated in the experiment. After a brief presentation of a circular array of 8 letters (3 black high-salience and 5 grey low-salience letters) subjects were required to report as many stimuli as they remembered. All participants completed two experimental sessions during which they performed the same behavioral task combined with real or sham tES (within-subject design). Real tES consisted in bursts of high frequency random noise stimulation (100-640 Hz), delivered from 600 ms before the onset of the array of letters, until 200 ms after its offset. Pupil size and skin conductance responses were recorded during the task execution as physiological measures of arousal. In line with previous evidence, statistical analyses revealed that both young and elderly participants reported overall a higher proportion of high-salience stimuli in comparison to low-salience stimuli. In young participants, however, the factor "tES condition" did not show any significant effect, meaning that both behavioural and physiological responses were not modulated by tES application. In elderly participants, instead, real tES significantly decreased the proportion of high salient stimuli, compared to the sham condition, suggesting a reduction of the memory span. The physiological indexes resulted unreliable in elderly participants and thus they could not be used to draw firm conclusions on the tES modulations of the level of arousal. The different effects induced by tES in the age groups may be ascribed to the different levels of endogenous activation showed by young and elderly subjects during the task. Alternatively, tES may differently act according to the physiological changes that normally accompany aging, such as neurobiological alterations of the sensory pathways (e.g. retinal degeneration; reduced visual contrast perception) or functional reorganization of the brain activity during cognitive task performance (e.g. increased frontal recruitment). Overall, these results showed that bursts of tES, applied during a VSTM task, differently modulated behavioural performance in young and elderly participants.

## Scene segmentation of natural stimuli in human early visual cortex

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Scene segmentation is one of the most challenging topics in visual neuroscience and is classically considered as an initial, pivotal step of content recognition. From a psychophysiological perspective, the ability to isolate image regions corresponding to the different scene elements is considered to be a non-linear process that relies on feed-forward computations in cortical modules from V1 to V4. Although described in the early visual cortex of primates, visual segmentation has never been investigated in ecological con-

ditions (i.e. natural scenes) and its role in content recognition has been challenged by several appearance-based computational models, able to perform content recognition without the aid of scene segmentation. Equally, behavioral studies demonstrated that visual content recognition might, in turn, affect segmentation. In order to investigate the occurrence of foreground-selective computations during perception of natural scenes in human early visual areas, we performed a representational similarity analysis and a selectivity analysis on fMRI data, recorded while two participants viewed a large collection of images. Data have been obtained by a public repository (<http://crcns.org/data-sets/vcl/vim-1>; Kay et al., *Nature*, 2008; Naselaris et al., *Neuron*, 2009). Particularly, we focused on seven visual regions of interest: V1, V2, V3, V3A, V3B, V4 and Lateral Occipital Cortex (LOC). Two appearance-based descriptions of the stimuli were created: the first description was based on the unaltered, original version of the stimuli (i.e. intact description), while a behaviorally-based foreground segmentation was applied for the second one (i.e. segmented appearance). According to the scene segmentation hypothesis, foreground-related information becomes more relevant to visual processing: the segmented-appearance model showed a linear increase of explained variance through the stream of visual information processing, culminating in V4 and LOC. On the other hand, a similar linear trend is not observed for the intact description. The selectivity analysis clarified that the linear trend observed for the segmented-appearance model neither is accounted by differences in the receptive fields of the investigated regions, nor by a bias in the retinotopic distribution of foreground pixels. These findings endorse the hypothesis that foreground-background segmentation of natural scenes is achieved in the retinotopic areas of the human early visual cortex, and are coherent also with several investigations on shape features selectivity in V4, LOC and their analogous in monkey: the activity of cortical modules known to be selective for shape properties, is, as expected, selective and thus significantly explained by a behavioral assessment of foreground segmentation. Even if the theoretical and computational challenge to characterize scene segmentation is far from its conclusion, here we proved that the sensitivity of fMRI pattern analysis and the richness of natural stimuli are adequate tools to test how different descriptions of visual scenes are represented throughout the human visual pathway.

## **Should I stay or should I go? Involvement of the human left dorsal premotor cortex and pre-supplementary motor area in response inhibition: a stop-signal paradigm**

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Stopping promptly an initiated action, a triggered movement, or a response, etc. requires a fast control mechanism that is capable to prevent the execution of the motor response when appropriate. The humans' neural substrates of monitoring and stopping are still a matter of debate and most of the data come from disease and lesions studies. The purpose of the current study is to take advantage of the Transcranial Magnetic Stimulation (TMS), to assess whether and to what extent specific cortical regions are involved in monitoring and adjusting performance. TMS allows high focal on line modulation of selected areas

in healthy subjects while they are performing the target behaviour, e.g. stopping a fast response only when required. The stop-signal paradigm is a popular tool for the study of this behaviour in an experimental setting. In the present version of this paradigm, subjects perform a go task (i.e. moving an item with the mouth as fast as possible from a starting point to a final position). In half of the trials, the go stimulus is followed by a stop signal, which instructs the subjects to withhold the response and not complete the movement, going back to the starting point. A single-pulse TMS is delivered during different percentages of the subjects ( $n = 16$ ) individual reaction times (response phase) over the two putative regions involved in this behaviour (i) left dorsal Premotor Cortex (PMCd) and (ii) pre-Supplementary Motor Area (pre-SMA). Real stimulation error rates are compared with sham stimulation error rates. Results show that the subjects' performance is clearly affected by real stimulation at early times during the response phase in both areas. In details, real stimulation of PMCd produces a significant and highly replicable increase in error rates in the stop-trials only, while this is not the case for pre-SMA stimulation, in which this selectivity is not displayed, since the stimulation of pre-SMA affects the go-trials as well. In literature, pre-SMA is associated with monitoring or resolving the conflict between the opposing task demands typical of the stop-signal paradigm and our results, although they are just a first hint, could be in line with this feature. Data from PMCd are more intriguing, since PMCd classically seems not to be engaged in response inhibition. However, in our precedent work, that specific portion of left PMCd was shown to be responsive for withholding a forthcoming action to be released only when appropriate. The hypothesis of an involvement of the PMCd in a specific feature of the control of behaviour, i.e. when a fast-single-choice (starting and complete the movement vs. withholding or stopping it) strategy is required, could be a first step in accounting for the current data.

## **The influence of Non-Verbal Communication and interaction frame on cognitive-affective functioning: a pilot psychophysiological study**

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Communication is an intentional, complex, and multi-faceted process qualifying human interactions. It is a widely-accepted and well-supported notion that Non-Verbal Communication (NVC, understood as the ensemble of communication channels that do not primarily rely on linguistic contents and transmission modalities) actually conveys a large portion of exchanged information and play a critical role in defining both an intended message and hidden meanings and attitudes with regard to the interlocutor. Apart from exchanging pieces of information, by communicating we shape our identity and our social image and we create a shared vision of ourselves and other social agents, and NVC is particularly important in those processes. The influence of NVC on actual cognitive-affective functioning of interlocutors in an interaction situation is however still a matter of debate. We then devised a pilot study to test whether a positive vs. negative non-verbal communication frame might up- vs. down-regulate cognitive performance and emotion appraisal in a group of 20 participants (10 females, 10 males). In particular, we decided to focus on a simulated job interview and assessment procedure so to enact an asymmetric interac-

tion schema stressing the role of performance. Further, the positive vs. negative frame was defined by manipulating also haptics (i.e. NVC behaviours concerning touch) and proxemics (i.e. inter-agents distance and relative position in the space). Participants were asked to undergo the simulated standardized job interview, a focused attention test (computerized Stroop task), and an emotion appraisal test based on IAPS stimuli. As for the experimental interaction, the positive and negative frame groups showed, as expected, increased arousal but only partially different autonomic profiles. Groups qualitatively differed also in electrophysiological responses (N100 event-related potential) at the computerized Stroop test, with the positive group presenting ampler deflections. During the emotion appraisal task groups do not significantly differed in terms of cortical oscillatory and autonomic profiles, while participants in the negative frame group reported qualitatively higher arousal ratings in response to IAPS stimuli and rated negative stimuli as less unpleasant. Present first evidences suggest that a connoted NVC frame may partly influence cognitive-affective functioning; further research is however needed to confirm and strengthen those qualitative findings. In particular, the mediation role of personality traits may plausibly account for partially inconsistent results and is worth specific future investigations.

## Sound into action translation in healthy and Spinal Cord Injured people: a Mismatch Negativity study

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Embodied cognition theories postulate that perceiving and understanding the actions performed by other individuals is a process underpinned by neural structures largely overlapping with those activated during execution of the same actions. Using the Mismatch Negativity (MMN), a component of the Event-Related Potentials (ERPs), we explored whether the perception of human action related sounds may also be altered in Spinal Cord Injured (SCI) patients whose brain cannot receive somatic information from and send motor commands to the body parts represented below the lesion level. We recorded MMN generated in response to multi-deviant stimuli consisting of three human action-related sounds (Tongue click, Hand clapping and Footsteps) and a non-human action-related sound (Water drop). Participants were divided in three groups of nine subjects (healthy, paraplegic and tetraplegic). During EEG recording, participants were instructed to concentrate on watching a silent movie and listen to original sound-stimuli (Deviant) and sounds obtained by altering acoustic parameters of the original ones (Standards). Repeated Measures ANOVAs of VAS ratings about stimulus identification revealed that only the original sounds were well recognizable in comparison to all the other sounds presented to the participants. ANOVA performed on the MMN mean amplitudes revealed a significant Sound  $\times$  Group interaction ( $F[6, 72] = 12.2, p < .001$ ). *Post hoc* test showed that the tongue click original sound elicited a clear MMN in all groups. It is worth noting that in the tetraplegic group the MMN was significantly bigger than in the paraplegic and healthy group (all  $p < .007$ ). Furthermore, the healthy and paraplegic groups showed higher MMNs for the hand clapping sound with respect to the

tetraplegic group (both  $p < .001$ ). The footstep sound elicited higher MMN amplitude in the healthy than in the paraplegic and tetraplegic groups (both  $p < .011$ ), which in turn did not differ from one another ( $p = .90$ ). Finally, no significant across-groups MMN amplitude differences were elicited when listening to the water drop sound (all  $p > .92$ ). Overall, these data suggest that massive somatosensory and motor disconnection between the body and the brain may induce functional cortical and subcortical changes, particularly in the regions involved in somatosensory and motor processing.

## Abdominal Acupuncture reduces pain at spinal level

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Acupuncture is known to reduce pain, although the exact mechanism is unknown. Abdominal Acupuncture (AA) reduces Laser-Evoked Potentials (LEP) amplitude and laser pain perception in healthy subjects. The aim of the current study was to investigate the site of AA analgesic effect. We recorded LEPs in 15 healthy volunteers by using the 32 EEG scalp electrodes. The experimental protocol included 3 times: (1) baseline, in which LEPs to stimulation of the bilateral dorsal wrist and right foot were recorded before acupuncture; (2) acupuncture, in which LEPs were recorded during AA performed in the abdominal area corresponding to right wrist; (3) rest, in which LEPs were recorded 15 minutes after the needle removal. The N2/P2 LEP amplitude to stimulation of both wrists was reduced in the acupuncture and rest times as compared to baseline, while LEP amplitude to foot stimulation was not modified. There are experimental evidences that acupuncture acts also at the spinal level and the used study design, as previously applied, suggests a segmental mechanism of action. The results of our study suggest that the AA analgesic effect occurs at spinal level.

## CO<sub>2</sub> versus Nd:YAP laser: it's really the same? Preliminar results of a Laser Evoked Potential study

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Aim of the study is to compare the amplitudes and latencies of Laser Evoked Potentials (LEPs) delivered by CO<sub>2</sub> and Nd:YAP laser stimuli. 6 healthy subjects (4 men

and 2 women, mean age  $27,5 \pm 1,9$ ) were studied. A-delta LEPs were acquired using a 32 channel system. Laser pulses were delivered on the dorsum of both hands and feet, in two separate sessions using a CO<sub>2</sub> and a Nd:YAP laser. Latency and amplitude of N1-LEP was not significantly affected by the type of laser. On the contrary, the type of laser significantly affected the N2 latency after stimulation of both hands and feet, which was shorter in CO<sub>2</sub> LEPs than in Nd:YAP LEPs. The type of laser influences also the amplitude of N2, which was significantly enhanced in YAP-LEPs compared to the CO<sub>2</sub>-LEPs in most of the derivations analyzed. P2 latency was affected by the type of laser only after foot stimulation (being significantly shorter with CO<sub>2</sub> than Nd:YAP) and not after hand stimulation. The type of laser influences also the amplitude of P2, which was significantly enhanced in YAP-LEPs compared to the CO<sub>2</sub>-LEPs in some of the derivations analyzed. Our data shows earlier latencies when using CO<sub>2</sub> laser and larger amplitudes when using Nd:YAP laser. This data is in contrast with previous data reported in literature, where earlier latencies were recorded using Nd:YAP pulses. Further studies are needed to determine whether CO<sub>2</sub> and YAP laser determine a comparable nociceptor activation.

## Physiological interpretative model of Computerized Tomography signals

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Human brain instrumental diagnostics experiences great progress in various areas, be it by exploring anatomo-functional areas with RMN, be it by controlling the electrical field with EEG, be it by observing the metabolic field with NIRS. These instruments are being used also combined (NIRS and RMN or EEG-NIRS) in order to find a univocal and artefact free signal, able to allow a clearer evaluation. This study wants to demonstrate that the CT signal is not only of an anatomo-pathological type, but also of an anatomo-functional one. This aspect was present in the first studies which brought the English engineer Godfrey Hounsfield and the southafrican physicist Allan Cormack to the Nobel Prize for medicine back in 1979 for “the development of computer assisted tomography”. Their intention was to capture the signal and their first aim the exploration of the brain’s functions. Signals, however, need to be interpreted. As CT is the most widely used diagnostic instrument, both for its easy functionality and its diffusion in every hospital it is very likely to meet MDs who notice chromatic anomalies in CT scans. During the last 10 years many MDs did not consider enough to read the radiological report, but started to observe CT scans attentively. They noticed anomalies in the brain images, to which the radiologist did not give attention at all, nor any pathological evaluation. These anomalies are generally considered artifacts, but producers deny that they might occur. These anomalies base on the principle of chromatism (the 16 degrees of grey scale) thanks to which CT analyzes the anatomical structure of the brain. The study originated from the previous observation of brain CT scans of patients who underwent it for other reasons. So we asked for the opinion of the ethical committee and explained to a new group of patients the aim of the scanning, bringing them to the subscription of an informed consent. So this study could start. 65 patients had a CT scan. They all had endocrine metabolic diseases. 38 had thyroid pathologies, 27 had diabetes type 1 and all

had a small control of glycemia values. The aim of the study was to detect areas which had to be considered anatomo-functional signs and not anatomo-pathological ones. We can affirm that when patients suffer from thyroid problems and diabetes type 1 there are always typical signs in specific areas, which cannot be considered neither artifacts nor anatomopathological signs, in their brain scan.

## **The symptomatology of the sympathetic and vagal system as monitoring model of the therapeutic act (Neurotest)**

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Normotony schedules the physiological hormone release during the day. The accentuation of sympathetic and vagal aspects gives elements for disease monitoring and for the choice of the most appropriate therapeutic act. In all types of disease we observed a quite rigid sequence of alternations of sympathetic and vagal symptoms. In the first sympathetic, symptoms characterized by constriction prevail. In the following vagotonic phase, symptoms are characterized by expansion. This neuroendocrine biphasic model is not the dominant one in physiology, although it adheres totally to its principles, thus becoming an optimal study topic. 102 patients were involved over a period of 5 years. They suffered from different pathologies, diagnosed by lab tests and instrumental exams. Patients were followed for six weeks and they were asked to take the test every day between 9 and 10 a.m. when values are more stable. During the week preceding the start of the study patients were instructed and trained to awareness and comprehension of the single symptoms, in order to avoid bias due to patients confusion of symptoms. In the test each sympathetic and parasympathetic symptom has an evaluation scale, considering frequency and repeatability. Evaluation, originating from our clinical practice, is still under study in order to become always more precise. Results are interesting and require further speculation. The method is quite simple and allows to keep the sympathetic and vagal system under control and to verify how normotony changes every time pharmacological or rehabilitative therapy changes.

## **Signals from an hidden island: novel ERP components from the anterior Insula and their involvement in visual recognition and in action-related evidence accumulation**

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Neuroimaging studies suggested that the anterior Insula (aIns) might contribute to perceptual decision-making. A recent study suggested that the aIns is the neural source of a complex of prefrontal post-stimulus ERPs in the visuo-motor tasks: the pN1 (at 115 ms),



the pP1 (at 170 ms), and the pP2 component (at 300 ms). In the present study, we employed two independent neural source analysis techniques (BESA and sLORETA) to confirm the insular origin of these ERP components in a large sample of subjects. Results confirmed the aIns source of the pN1, pP1, and pP2 components: this latter was the main focus of the present investigation. The pP2 has been associated to the stimulus-response mapping process because its amplitude is larger in the target than non-target trials. In the present study, we found different aIns activity profiles in the two hemispheres. The left aIns showed a peak of activity at 420 ms (i.e. 30 ms before the response time) for targets and non-targets, that is independently from the ultimate choice (motor response or inhibition depending on the stimulus category). On the other hand, the right aIns showed an activation starting at about 250 ms and progressively increasing well after the motor response; it was larger in case of target than non-target stimulus. In other words, left and right aIns presented activation profiles consistent with different functions: the left linked to the timing of decision process, the right to the categorization and performance monitoring processes. A control experiment not requiring discrimination between stimuli, but motor response to all stimuli, revealed that the pP2 component and the aIns activation were nearly absent after the 250 ms: this result confirmed that the aIns activation in that stage is related to the need of a categorization process, and not to the motor behavior *per se*. While the specific functions of the pN1 and pP1 components need to be assessed in future studies, the present investigation shed new lights on the pP2 and on the insular contribution to the perceptual decision, revealing inter-hemispheric differences in the process of mapping a stimulus with the relative choice. Finally, the present investigation opens to the possibility of assessing the aIns activity via ERP analysis.

## The role of sleep disorders in neurodegenerative diseases: review of the scientific literature and description of a screening questionnaire

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Diagnosis of neurodegenerative diseases is known to be complex and challenging because of the richness of factors involved in the onset and development of pathology. A wide number of scientific contributions explored the co-occurrence of sleep disorders in neurodegeneration processes. Indeed, a review of the literature shows strong data concerning the relations between specific sleep disorders and types of dementia. For example, REM sleep behavior disorder and excessive daytime sleepiness seem to be strictly connected to the diagnosis and progression of Lewy Body Dementia (LBD) and Parkinson's Disease (PD) Dementia. On the other hand, Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI) are frequently associated with more general sleep alterations, while Sleep-Disordered Breathing is commonly observed in patients with vascular dementia. Specifically, the role of REM sleep behavior disorder seems to be crucial in LBD. This disorder is described as a parasomnia characterized by loss of REM sleep atonia and persons affected tend to "act out" dreams at night. It is proven that these manifestations can begin years before LBD is diagnosed and they are considered as a prodrome of  $\alpha$ -synucleinopathy degeneration. Besides, poor performances in cognitive tasks, such

as visuo-spatial deficits, are observed in persons with idiopathic REM sleep behavior disorder. Actually such cognitive difficulties generally reflect an early stage of neurodegeneration. Concerning parkinsonism and dementia, literature provides data on the risk of developing pathology in association with REM sleep disorder with a probability stated from 18% to 65% of the examined cases. An instrument that allows a rapid clinical screening of sleep disorders in patients with suspect neurodegenerative pathology, even including MCI, may hence be useful. We focus on a tool known as the Mayo Sleep Questionnaire (MSQ), a 16-item questionnaire that targets various sleep disorders (REM alterations, periodic limb movements during sleep, restless legs syndrome, sleepwalking, obstructive sleep apnea, sleep related leg cramps), and can be easily administered to the person who sleeps in the same room with the patient. It was validated by Mayo Clinic as a tool for the identification of REM sleep behavior disorder in normally-aging, MCI and dementia patients. Strong results on sensitivity and specificity were found: a “yes” response to the first question – dream enactment behavior – shows a 98% sensitivity and a 74% specificity for the diagnosis of REM sleep behavior disorder, as confirmed by polysomnography. Thus, this questionnaire appears appropriate for identifying probable sleep disturbances in a population affected by suspect neurodegenerative disease. We claim and discuss how the implementation of the MSQ in clinical neuropsychological examination may be recommendable to provide further details that could be helpful in the diagnosis process of neurodegenerative diseases.

### **Neural correlates of enhanced empathy in X-linked Spinal and Bulbar Muscular Atrophy: a neuropsychological and EEG study** Pick E.<sup>1</sup> - Capizzi M.<sup>2</sup> - Kleinbub J.R.<sup>1</sup> - Marcato S.<sup>2</sup> - Meconi F.<sup>3</sup> - Palmieri A.<sup>1</sup> Querin G.<sup>2</sup> - Sessa P.<sup>3</sup> - Vallesi A.<sup>2</sup> - Sorarù G.<sup>2</sup>

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X-linked Spinal and Bulbar Muscular Atrophy (X-SBMA), also known as Kennedy's disease, is a rare adult-onset motor neuron disorder caused by an elongated CAG repeat in the Androgen Receptor (AR) gene, affecting only males. The function of the AR is therefore deficient and patients can present motor involvement, dysarthria, gynecomastia and hypogonadism. ARs are present in the brain as well, and research highlights the role of testosterone (T) in shaping brain and behavior. The literature is extremely scarce and controversial on cognitive peculiarities of such patients. Our recent findings showed lower performance on cognitive mentalization, but a preserved affective dimension of mentalization compared to control subjects. Thus, the pathological imbalance of T might impair the first, while protecting the latter. The aim of the present pilot study was to further investigate the empathic abilities of patients with X-SBMA also at the neural level. We compared 14 patients to 12 matched controls on tests focusing on neuropsychological general main functions, empathy (*inter alia*, Interpersonal Reactivity Index, IRI), and a computer-delivered task empathy-related while their EEG was recorded. This recently-developed paradigm by Sessa and colleagues permits to distinguish neural activity underlying two main facets of empathic response: cognitive, through the modulation of P3

(400-800 ms) elicited by a painful vs. neutral sentence; and affective, through the modulation of P2 and N2-N3 (120-320 ms) elicited by a painful vs. neutral facial expression. Interestingly, in the neuropsychological screening patients showed increased memory for a story with emotional content, and lower scores in tests focusing on cognitive empathy. Moreover, our results showed a significantly larger positive shift in P2 and N2-N3 in patients compared to controls. In spite of lower performance at IRI (*fantasy* subscale) in patients compared to controls, no difference in P3 across the two groups was found. Such increased P2 and N2-N3 components in patients, for painful facial cues, and the better memory for emotional content, can be interpreted as a point towards a paradoxical improving factor for affective empathy. Overall, such intriguing data are in line with other research showing that the level of testosterone is inversely proportional to scores in affective empathy, and that cognitive deficits might be found only when fine-grained abilities, such as mentalizing, are tested. To the best of our knowledge, this work represents the first use of an EEG setup to measure the different components of empathy in a motor neuron disease, showing that neurological/metabolic changes can also have paradoxical functional facilitations of some cognitive functions.

## Aesthetic foster our perception of every-day objects: an ERP study

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Over the last few years several theories hypothesize a main role of aesthetic in driving our adaptive interaction with the environment. However despite the broad interest in the exploring the cortical distribution of aesthetically-related brain areas, little is known about the temporal dynamics of the underlying neural processes. Since only few studies have investigated the temporal processes mainly involved in the dynamics of the aesthetic evaluation thus, what remain surely unexplored is to understand which processes are affected by attractiveness. In light of this, our main goal was to investigate the time course of the interaction between the aesthetic experience and the emotional and cognitive processes. As experimental stimuli three couples of everyday objects previously selected by a rating procedure were employed. Each couple of items contained a high and a low rated object (of the same category) regarding perceived aesthetic. Twelve healthy Italian students (7 females, mean age of 24.66, SD = 3.82) were tested using an oddball paradigm where the couples of pictures representing objects of the same category were presented. Each object was used both as standard and target stimuli in two different procedures. EEG was recorded during the all experiment through 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 aesthetic perception (high or low aesthetic) and the category of the stimulus (target or standard stimulus). Cognitive and attentional effects were observed on ERP components (P100, P250, P200, N200, P300 and LPP) by suggesting that aesthetically pleasant and unpleasant tools may elicit distinct pattern of neural activity. Positive aesthetic feelings may prompt cognitive information processes from early visual feature extraction/integration, motor response selection to categorization and decisional processes. Differently, negative aesthetic feelings would not

influence cognitive processing but could activate a negative emotional bias toward task-relevant stimuli. Concluding, our findings suggest that aesthetic experience concurs to shape cognitive and emotional processes as well as the underlying neural activity.

## How is the brain going to respond? The importance of prestimulus functional connectivity

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An increasing amount of evidence underscores that information exchange between distant areas regulated through synchronization of oscillatory activity plays a crucial role in the brain functional efficiency. Nevertheless, there is still little knowledge on how brain connectivity pattern at the time of an external event can predict how the event will be processed. The present Transcranial Magnetic Stimulation and Electroencephalography (TMS-EEG) co-registration study aimed at investigating the link between prestimulus network organization and TMS-induced response in the brain by means of a graph theory approach. 15 healthy young participants received single TMS pulses delivered over left primary motor cortex at random intervals at 110% of the resting motor threshold during EEG recording. Pre and post TMS activities were analyzed separately. Pre-stimulus source functional connectivity was calculated in the 1 s preceding the TMS pulse through the cross-spectrum and the weighted phase lag index for each pair of ROIs selected from the cortical sources of EEG, and for each of the following frequency bands: theta, alpha, beta, and gamma. Several graph measures were computed to reveal the global organization of the graphs for each frequency band. Considering the post-stimulus activity, we individuated and localized five secondary responses, i.e. TMS-Evoked Potential (TEPs) components that followed the activation of primary motor cortex (M1): N15, P30, P60, N100 and P180. Crucially we investigated the relationship between the pattern of M1 connectivity before TMS, and the diffusion of secondary responses. We found two important results: First, TMS activated a group of areas that highly overlapped with the network in which the stimulated area was embedded before the TMS. Second, the strength of the early TEP within this network was correlated with the strength of prestimulus connectivity in specific frequency bands. Therefore, two crucial aspects of stimulus processing, i.e. which areas will be activated and how strongly they will be activated, were conditioned by the state of connections at the time of stimulation. Importantly, these data support the role of phase synchrony and prestimulus network organization in the regulation of cortico-cortical communication.

## Cognitive rehabilitation with tDCS and depression in Alzheimer's Disease

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Alzheimer's Disease (AD) is a progressive pathology where symptoms gradually progress over a number of years with memory loss and decline of intellectual abilities being serious enough to interfere with daily life. Cognitive impairment is distressing and may lead to psychosocial consequences, and depression is consistently associated with decreased Quality of Life (QOL). It has been proven that applying transcranial Direct Current Stimulation (tDCS), a non-invasive technique for focal modulation of brain functions, to patients with AD, could improve memory and it has been proposed as a possible adjuvant therapy in AD. The aim of the present work is to investigate the effects of tDCS applied over the Dorsolateral Prefrontal Cortex (DLPFC), combined with cognitive training on depression and apathy, as well as on cognitive functions, in patients with AD. In fact, the DLPFC is connected with the temporal lobes, which are important areas for memory functions, and the network between these two areas is thought to be involved in various and important cognitive activities. Participants were patients affected by AD, diagnosed according to the criteria of Dubois (women and men; age  $60 \pm 75$  years). Exclusion criteria were the presence of other neurological disorders and a scoring at the Mini Mental State Examination (MMSE) lower than 23/30. Executive and memory functions (working memory in particular), depression and apathy, Autonomy in Daily Life (ADL) and QOL have been evaluated before and after the cognitive rehabilitation. Follow-up have been conducted after one, three and six months. Patients have been divided into four groups according to different procedures: tDCS + cognitive training; tDCS alone; cognitive training alone; sham controlled + cognitive training. The treatment comprised 10 sessions (5 sessions/week for 2 weeks). An improvement of cognitive performance and an increase of ADL and QOL were expected. Also, the relation between such improvement and the presence of apathetic and depressive symptoms have been explored.

### **Direct evidence of tDCS effect on cortical excitability and task performance: a TMS-EEG study on verbal fluency**

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The application of anodal transcranial Direct Current Stimulation (a-tDCS) can enhance cognitive performance in healthy and clinical population. It has been suggested that such cognitive facilitation occurs through the induction of plastic changes at specific cortical sites. However, direct electrophysiological evidence for this causal relationship is still missing. In this study we explored how and if cognitive enhancement induced by a-tDCS is followed by increased cortical excitability of task-related cortical networks. Several studies report an improvement in language production after a-tDCS applied over the Left Inferior Frontal Gyrus (LIFG). We chose thus to investigate the neurophysiological underpinnings of this effect by means of TMS-EEG, applied before and after a-tDCS, coupled with a verbal-fluency task. The experiment was run in 3 sessions, performed on separate days. Two TMS-EEG recordings for session were acquired before and after tDCS. In all sessions the anode was applied over F5 (20 minutes, 0.75 mA, 16 cm<sup>2</sup>), with standard cephalic reference, and phonemic and semantic verbal fluencies were administered during the last 5 minutes the stimulation. In the main experimental sessions TMS was delivered over left

BA6, an area involved in the behavioral task. In a control session, the same paradigm was used but sham tDCS was delivered. A further control session was performed, applying a-tDCS, but targeting with TMS the left BA7, i.e. an area not involved in the task. Local Mean Field Power (LMFP) of TMS-Evoked Potential (TEPs), a measure of cortical excitability, was computed for six different anatomically defined electrodes clusters. Moreover, cortical sources were computed by performing a source modeling on TEPs data. Results confirmed an enhanced verbal fluency after real tDCS. Moreover, after real but not sham tDCS, LMFP increased in the TMS site and in the anatomically connected areas, in a late time-window, reflecting a functional network excitability enhancement, but only when cortical activity was elicited by stimulating BA6, which was active during the task, while no change was detectable when the TMS target was BA7. Conversely, in the tDCS target site LMFP increased in an early time-window, indicating an increment of local cortical excitability. tDCS-driven enhancement of cortical excitability, thus, was confined within the task-related functional network, confirming animal *in vitro* models suggesting that only firing neurons could be modulated by electrical stimulation. Interestingly, the increment in semantic verbal fluency significantly correlated with increase in LMFP over F5, thus directly linking the behavioral results with tDCS neuro-physiological effects. The present results add new knowledge on how tDCS impact cortical excitability, suggesting that biophysical current spread modelling analysis should be implemented with state dependent information of the targeted areas.

## The topographic brain in identity and diversity selection functions

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This paper deals with one of the Cognitive Science paradoxes: although nowadays extremely sophisticated mental processes can be easily simulated, mental constructs of the lowest logical complexity – such as identity, inequality and denial – seem to elude modeling at neural level. The paper aims to concretely test the recent hypothesis according to which general mental relations of the aforementioned kind lay upon topographical connections, i.e. sets of systematic axonal connections from a neural region to another that preserve (or reverse) the spatial relationship between neurons. Topographic maps are present throughout the nervous system, and appear to extend well beyond the transmission of sensory information. This suggests that they may be critical even in different types of complex mental tasks, including analogical making. Indeed, they might play an important role in representing various aspects of “non-topographical” stimuli – which depend on the more abstract perceptual aspects – such as in the organization of the conceptual similarity. This process can be computationally conceived of through Universally Quantified One-To-One Mappings (UQOTOMs). At a cognitive level, the importance of the organization seems indisputable in recent studies: the human beings’ response appears to reflect a preference for one-to-one mapping in identity and diversity selection functions. And from this point of view, unlike other neural models, topographic organization allows to naturally characterize UQOTOMs. In our suggestion, the Topographica simulator – designed to simulate the topographic maps in any cortical or subcortical two-dimensional region – permits to



clarify the mechanisms of perceptual selection on diversity and equality relations, by integrating the low-level simulators and the abstract ones, and by focusing on biologically realistic networks of tens or hundreds of thousands of neurons that topographically maps tens or hundreds of millions of connections. Our model provides a simplified portion of the visual system, in which the area V1 is sampled twice with respect to two objects – no matter whether different or equal. The two samples are evaluated in a topographic way from top area, generically represented as part of the prefrontal cortex, within which is then identified a distribution of neurons in learning the “identity” relation. In the currently conducted simulation, there have been used four simple and common objects, presented in a random way in portions of the retina, and in any possible combination. PFC shows the gradual change of the plastic connections: in every cortical area, neurons receive either inhibitory or excitatory external afferents and intracortical lateral connection. The data obtained show a good ability to compare perceptual configurations of the four elements proposed, based on autonomous identification of abstract type of relations – identity and diversity. This result may offer a new conceptualization of how the brain accesses complex cognitive problems.

## To trust or not to trust: a Thermal Imaging study on the effects of social exclusion

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While emotion regulation seems to be well understood in the individual domain, information about the inherent link between emotion regulation and social contexts is lacking. In this study, we investigated the behavioral and physiological consequences of social exclusion in control participants ( $n = 16$ ) and in patients ( $n = 16$ ) with psoriasis, a skin disease known to be often accompanied with emotion regulation deficits. Firstly, participants faced the social induction phase by playing the Cyberball Game in which they were excluded or included by other players. Then participants played the Trust Game (TG) in the role of investor. All participants took part in both exclusion and inclusion social inductions and played the TG twice. In the TG, the investor has to decide how much of € 10 to invest on familiar and unfamiliar players. The familiar (bad vs. good) players were the same players previously encountered in the Cyberball Game. Participants' face temperature (peri-orbital region) during the task was measured by means of functional Infrared Thermal Imaging (fITI). Face temperature in this area is known to reflect the activation of the sympathetic system. We tested whether the social inclusion vs. exclusion affected participants' trust toward other players by entering mean investments into a Repeated Measures 2 (social induction: exclusion, inclusion)  $\times$  2 (player: familiar, unfamiliar) ANOVA. We found a statistically significant social induction  $\times$  player interaction ( $F [1, 31] = 4.78, p < .04$ ). A *post hoc* LSD test showed that unfamiliar players were trusted significantly more after the social exclusion phase respect to the inclusion one



( $p < .02$ ); in fact, after social inclusion, participants tended to trust more familiar participants respect to the unfamiliar ones ( $p < .09$ ). A linear regression was calculated to predict a behavioral index (i.e. the differential investment on familiar minus unfamiliar players) based on mean peri-orbital temperature during social exclusion induction. A significant regression equation was found ( $F [1, 31] = 7.16, p < .012, R^2 = .20$ ), suggesting that the higher the activation of the sympathetic system during social exclusion, the more participants tended to trust the unfamiliar with respect to the familiar players who previously excluded them. Interestingly, a correlation analysis showed that the behavioral adjustments triggered by peri-orbital temperature increase during social exclusion were present only in the control group ( $r = .535, p < .05$ ), while patients' decisions were not influenced by temperature change ( $r = .29, p = .27$ ). This result suggests that sympathetic activation during painful social interactions is pivotal in order to learn whether to trust others and to adjust future behavior consequently. This mechanism is probably deficient in patients with emotion regulation deficits.

## Interpersonal Multisensory Stimulation enhances emotional contagion

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Recent studies based on simple Interpersonal Multisensory Stimulation (IMS) paradigms have challenged the idea of a rigid bodily self and highlighted the importance of integrating multisensory bodily signals to build a coherent sense of self. Psychophysical studies indicate that the sensation of being touched on the face while observing synchronous touches on the face of another individual, blurs self-other distinction and induces the illusory experience of owning the observed face (enfacement). While previous studies showed that IMS may increase visual perceived similarity with another person, there is no evidence that IMS can even blur self-other emotions. We aimed to test if synchronous visuo-tactile IMS can increase Facial Mimicry (FM) and therefore emotional contagion, an automatic and developmentally early empathic response to another person's emotions. Forty-two adult participants (22 F; mean age  $24.2 \pm 4.7$ ) received either synchronous, asynchronous or no visuo-tactile IMS on their face while observing videos of same sex actors with a neutral facial expression. After each IMS condition we recorded electromyographic activity from four face muscles while participants observed videos in which the actors displayed FACS-coded happy/sad facial expressions. Results from separate one-way ANOVAs for each muscle confirmed that video stimuli evoked FM responses in 3 out of 4 muscles. Interestingly, multiple regression analysis showed that FM responses were positively predicted by Empathic Concern (EC) ( $R^2 = .30, p = .004; b = .62, p = .001$ ), a subscale of the Interpersonal Reactivity Index, an empathy trait questionnaire. Moreover, ANCOVA on FM with IMS (synchronous vs. asynchronous) as within-subject factor and Baseline FM (recorded after no-IMS), as continuous predictor, revealed a significant  $IMS \times Baseline FM$  interaction ( $F [1, 40] = 8.06; p = .01$ ). We further investigated it via correlational analysis showing that the higher the Baseline FM, the higher the FM after synchronous IMS ( $r = .34, p = .03$ ). Tellingly, no significant correlation was found for FM after asynchronous IMS ( $r = -.22, p = .17$ ). Finally, and most importantly, we found a sig-

nificant moderated mediation (Index of Moderated Mediation = .0014; 95% confidence interval: .0001 - .0045) with EC as independent variable, participants' ratings of videos' realism as moderator, Baseline FM as mediator and increase of FM after synchronous (vs. asynchronous) IMS as dependent variable. Simple slope analysis, for different levels of the realism moderator, showed that the increase in FM after synchronous IMS was positively predicted by EC via Baseline FM, just for those participants who considered the videos realistic. Our results show that simply sharing synchronous visuo-tactile IMS with another person can boost emotional contagion especially in individuals with high empathy and therefore stronger baseline tendency to resonate with others' emotions.

## Hypnotizability-related activity of $\mu 1$ opioid receptors

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In the general population, expectation-induced (placebo) analgesia is sustained by endogenous opioid mechanisms, whereas the analgesia produced by explicit suggestions in highly hypnotizable individuals (highs) is not associated with release of endogenous opiates. Nonetheless, the possible co-operation between explicit suggestions and placebo mechanisms in the highs' analgesia has not been clarified; thus, the study investigates the genetic bases of hypnotizability-related activity of the  $\mu 1$  opioid receptor. The OPRM1 gene encodes the  $\mu 1$  opioid receptor, which is the primary site of action for endogenous and administered opioids. OPRM1 is polymorphic in the general population for the missense mutation Asn40Asp (A118G, rs1799971). The minor allele 118G results in decreased levels of OPRM1 mRNA and protein. As a consequence, G carriers are less responsive to opioids. The aim of the study was to test the hypothesis that hypnotizability is associated with the presence of the OPRM1 polymorphism. A sample of 43 highs and 60 low hypnotizable individuals (lows) as well as a population sample of 162 controls (umbilical cords) were typed for the A118G polymorphism of OPRM1. The frequency of the G allele was significantly higher in highs compared to both lows (Odd Ratio = 4.2,  $p < 0.001$ ) and controls (Odd Ratio = 2.75,  $p < 0.01$ ). This finding suggests that an inefficient opioid system may be a distinctive characteristic of highs and that hypnotic assessment may predict lower responsiveness to opioids.

## Event Related Potentials recorded by intracerebral electrodes

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

generators of P300, Mismatch Negativity and also N140 (a long latency SEP that is modulated by attention manipulations). We studied 7 pediatric patients with drug resistant epilepsy. Intracerebral electrodes were implanted in frontal, temporal and parietal lobes at different sites, depending on seizure types. Auditory ERPs (MMN, P300) and N140-SEPs (to median nerve stimulation) were recorded from the intracerebral electrode contacts referred to the nose (ERPs) or to the earlobe ipsilateral to the stimulation (SEPs). The analysis was addressed to the electrode contacts where an inversion of neurophysiological component polarity was observed or where the EP amplitude was higher. P300 was recorded by electrodes located in hippocampus with a clear inversion of signals in posterior hippocampus in one patient, while N200 was recorded in insular cortex. MMN (N100/P140) was recorded by electrodes placed in opercular-insular cortex without a clear inversion of signal. SEPs N120/N140 wave increased in amplitude during attention condition, showing the maximum amplitude in the frontal electrode contacts. Numerous investigations revealed that generators of Event Related Potentials are independent and also with a cortical-subcortical distribution. In this short case series, we could show some brain areas clearly involved in the generation of P300, MMN and N140 components.

## Are omitted targets the best suited for eliciting purely endogenous ERPs? Source modelling of emitted potentials based on simultaneous EEG-fMRI recordings

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ERPs occurring independently of any specific sensory event are purely endogenous (emitted potentials): as a consequence, their neural generators can be univocally linked with cognitive components. In the present EEG-fMRI study, the subjects performed two similar visual tasks: a standard two-stimulus oddball, and an omitted-target oddball task, characterized by the physical absence of the target stimulus. The main goal of the present investigation was to localize and compare the cortical and subcortical neural sources of the scalp-recorded ERPs from the two oddball paradigms. Our assumption was that the source analysis of ERP components obtained from the standard and the omitted-target oddball tasks provides an accurate and reliable identification of the brain functional anatomy subtending target detection. Thirteen healthy right-handed

volunteers (5 females; mean age 26 years, range 22-29), participated in the study. To optimize the sources localization, the high temporal resolution of electrophysiology was combined with the fine spatial information provided by functional MRI. In addition, the source modelling (dipole analysis) of ERPs was seeded to the clusters of fMRI activations. The simultaneous recording of EEG and fMRI guaranteed that the cognitive states of the subjects were the same for the two techniques during the experimental session. The results of both the omitted-target oddball and the standard oddball task were unanimous in depicting an antero-to-posterior neural circuitry for the detection of rare, task-relevant events. P300 (P3b) was generated in the frontal, temporo-parietal and parietal areas (these latter only in the standard oddball), namely the Temporo-Parietal junction (TPj), the premotor and motor area (M1) and the anterior Intraparietal sulcus (aIPs). Anterior Insula contributed to the pP2, a recently described prefrontal component (different from the well known P3a) associated with the stimulus-response mapping. The anticipatory (i.e. pre-stimulus) negative slow waves, also endogenous in their nature, were produced by anterior areas, namely the inferior and middle frontal gyrus over the lateral brain surface and the SMA-CMA areas over the medial cortex. We provide evidence for the possibility to record emitted ERPs from omission of target stimuli in a simultaneous EEG-fMRI event-related paradigm. Such a procedure allowed a detailed spatio-temporal modeling of the neural generators of purely endogenous late potentials.

## **Standardized neuropsychological assessment vs. clinical neuropsychological assessment: in search of potential residue in a case of severe bilateral brain damage**

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This paper describes evaluation, rehabilitation training and re-evaluation of a 69 years old patient, accountant, with cognitive and motor serious disabilities arose due to extended bilateral lesions in the brain. It illustrates a neuropsychological “functional” evaluation because neuropsychological standard assessment is not applicable in this case due to total absence of expressive verbal language, significant supervisory fluctuations, lack of trunk control and severe deforming rheumatoid arthritis in the hands. This evaluation allowed to reveal not only the obvious cognitive deficits acquired but primarily the residual potential. The assessment, conducted through a clinical protocol for patients with absence of verbal language, allowed to design a functional rehabilitation in accordance with ICF criteria and in accordance with needs expressed by patient and by his family to ensure the return home. Rehabilitation sessions were set following a protocol that uses the few resources available in order to recover and gradually stimulate as many skills as possible. The re-evaluation of this case has confirmed that even if a severe patient cannot be measured according to standard neuropsychological protocols he can still be examined and rehabilitated achieving significant improvements in his quality of life.

## Habituation of Gamma band oscillations after repetitive laser stimulation in migraine patients and healthy controls

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The migraine brain is characterized by a lack of habituation of evoked responses to repeated stimuli including the nociceptive ones. The nociceptive pathways are studied through the Laser Evoked Potentials (LEPs). The vertex N2-P2 complex expresses the cortical response to the salient painful stimuli. In migraine patients reduced LEPs habituation may express an enhanced attention toward relevant painful stimulus. Several study have demonstrated that brief painful stimuli induce Gamma oscillations (30-120 Hz) in somatosensory cortex, which likely reflect the local processing of sensory information and subjective pain perception, independently from stimulus salience. In this study we aimed to check if the reduced LEPs habituation is associated to increased Gamma band oscillation and subjective pain perception in migraine patients. Thirty migraine without aura patients and 10 healthy control subjects were evaluated. The right hand was stimulated by 30 CO<sub>2</sub> laser stimuli delivered in trains of three identical stimuli (S1, S2, S3) with constant ISI of 1 s, and 20 s between consecutive trains. The S1 S2 and S3 related N2 and P2 components were averaged. Similarly we analyzed S1, S2 and S3 related gamma oscillations, in the 200-600 msec time window. In control subjects the amplitude of cortical responses decreased from S1 to S3, indicating the presence of habituation, while the repetition of the stimulus did not reduce the size of the Gamma band. In migraine patients we found that both the LEPs and the Gamma band amplitude increased from S1 to S3. Thus we confirmed that when a laser stimulus is shortly preceded by another identical one, the amplitude of the N2-P2 response is greatly reduced in healthy control, while the Gamma band amplitude, expressing the subject pain intensity, was not affected by the reduction of the novelty that is derived from stimulus repetition. In the migraine group both GBO's and LEPs amplitude are not affected by habituation phenomena suggesting that the lack of attention decline to pain concurs with subjective pain feeling.

## tDCS polarity-dependent neuroplasticity changes in physiological brain aging: a multimodal study

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Physiological brain aging is characterized by synaptic dysfunctions with consequent neuroplasticity alterations. A challenge in neuroscience is to identify the patterns of neuronal activity underlying the neuroplasticity changes and the cognitive impairment during the life span, and to extract the neurophysiological markers on the cortical areas firstly impacted by physiological aging, i.e. prefrontal cortex. Our study aimed to understand the neuroplasticity mechanisms in healthy young and elderly subjects, evaluating

their changes at cortical network level, as well as their effects on behavioural outcomes. Transcranial Direct Current Stimulation (tDCS) was used as neuro-modulation technique targeting neuroplasticity of prefrontal cortex, whereas TMS-EEG recordings and working memory task (n-back) were performed to monitor the tDCS age- and polarity-dependent effects, respectively on cortical and behavioral measures. Fourteen healthy young and elderly subjects received anodal, cathodal and sham tDCS in three separate sessions, in a counterbalanced order. tDCS was applied for 13 min at 1.5 mA over the left Dorsolateral Prefrontal Cortex (DLPFC). Before and after each tDCS session, the participants performed a 3-back (young subjects) or a 2-back (elderly subjects) task. Moreover, combining TMS-EEG during resting state, cortical reactivity evoked by 80 single TMS pulses was assessed over the DLPFC. Before and after tDCS, accuracy rate and reaction times were evaluated in task performance, whereas the cortical reactivity was assessed by calculating the Global Mean Field Power (GMFP). Although tDCS polarity-dependent changes were not reported in task performance in both groups, we observed age- and polarity-dependent cortical plasticity changes. Specifically, we observed a cortical reactivity increase after cathodal tDCS and a decrease after anodal tDCS in young subjects. Interestingly, opposite cortical patterns were found in elderly subjects, with a cortical reactivity increase after anodal and a decrease after cathodal tDCS. Our findings demonstrate that tDCS is able to induce prefrontal cortical reactivity changes, which can be assessed by TMS-EEG measures, even when behavioral data are not sensitive enough to reveal functional modifications, but more importantly that the cortical modulations are not linear during the life span. Empirically measuring cortical plasticity in physiological aging may provide critical predictors and early physiological markers of cognitive decline and might represent the starting point for development of neuro-rehabilitation strategies.

## **Negative emotions modulation by means of anodal transcranial Direct Current Stimulation over right Ventrolateral Prefrontal Cortex**

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It is well established that a chronic incapacity to regulate negative emotions may be a key factor in the genesis and maintenance of many psychiatric and psychopathological diseases and that such regulatory deficit might be associated with multiple and distributed structural and functional brain abnormalities. In the past decades, both Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS) have emerged as adjuvant treatment of psychiatric and mood disorders with promising, although sometimes controversial, results. In the present study, we explored the possibility of modulating emotion regulation in healthy subjects by applying anodal tDCS over the right Ventrolateral Prefrontal Cortex (rVLPFC). The aim of the study was twofold. First, we aimed at exploring the use of tDCS as a tool to improve emotion regulation. Second, we wanted to assess which specific emotion can be regulated with this brain stimulation approach. We chose the rVLPFC as the target of tDCS because there is evidence suggesting that this region seems to play a role in detecting emotional salience, prompting the need to regulate. To achieve these objectives we designed a double-blind, between-subjects, sham-controlled study. Healthy participants were randomly subdivided

into an anodal and sham tDCS groups. After stimulation, participants viewed five short video clips eliciting, respectively, anger, sadness, fear, happiness and neutral emotions. Emotional reactions to the video clips were then assessed with self-report scales, assessing a wide range of emotions (anger, happiness, hurt feelings, anxiety, sadness, fear, disgust, indignation, interest, surprise, warmth, calm, embarrassment, guilt, boredom, pain). Results showed that anodal tDCS over rVLPFC successfully reduced, in comparison to sham condition, the perceived extent of negative emotions, thus confirming the usefulness of this approach to improve emotion regulation. Considering that participants were not explicitly instructed to apply any regulation strategy, we argue that tDCS affected mostly unconscious and autonomic emotion regulation processes. Regarding the effect of the stimulation on specific emotions, our results indicate that across and within the five video clips, anodal tDCS over rVLPFC mainly affected negative emotions but not neutral or positive ones. In particular, regardless of the video clip inducing it, anodal tDCS moderated most of all pain, anxiety and fear.

### **Visuomotor Prismatic Training modulates visual detection thresholds in normal subjects**

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Prismatic adaptation is obtained through a Visuomotor Training (VPT) procedure consisting in a series of ballistic movements of the dominant arm aimed at a visual target while wearing prismatic goggles. Initially, pointing errors ipsilateral to the prismatic deviation of the visual field are apparent, but after a few trials participants adjust movement trajectories and correctly reach for the target (adaptation, PA). Once prisms are removed, subjects commit pointing errors contralateral to prism deviation (aftereffects). The exact cause of such aftereffects is not yet fully clear, but it is thought to have an attentional component. Indeed, if employed with neglect patients, right-deviating prisms are effective in transiently restoring spatial awareness for the (left) neglected field. In normal subjects, however, there is conflicting behavioural evidence of PA effects on spatial attention, as Response Times (RTs) and visual search performance seem to be mostly unaffected by PA. A possible explanation for these negative findings might be related to a lack of sensitivity of some behavioural measures employed to detect PA aftereffects. To measure the attentional effects of PA we used a visual detection threshold paradigm, a method widely employed in psychophysical research for its sensitivity to attentional modulations. Forty healthy subjects participated in the study, consisting in a visual detection task performed before and after VPT. Twenty subjects performed VPT with prisms deviating the visual field 11° to the left (VPT), the remaining 20 subjects underwent the same visuomotor training procedure without prisms (Sham). The detection task consisted in 194 rectangular visual stimuli (0.4 × 0.6 cm) randomly presented on a computer screen for 50 ms around participants' subjective visual threshold level in 18 different screen locations. Subjects had to press the spacebar of the computer keyboard as fast as possible upon stimulus detection. We compared the Detection Rates (DRs) and RTs collected pre and post training in each condition (VPT, Sham). Following VPT, we evidenced significantly



higher DRs and faster RTs bilaterally (DT and RTs:  $p < 0.001$ ), as compared to both the pre training and the sham conditions; conversely, Sham pre and post training measures did not differ (DT:  $p = 0.726$ ; RTs:  $p = 0.942$ ). Our results demonstrate that VPT to left-deviating prisms strongly modulates visual attention by lowering visual detection thresholds and RTs bilaterally. This finding suggests that in healthy subjects: (1) PA attentional aftereffects in the visual domain are related to a general arousal enhancement effect, rather than to a unidirectional reorientation of the attentional focus such as that observed with neglect patients following PA; (2) visual detection threshold paradigms are sensitive to PA attentional aftereffects. Ongoing research of our group, employing tactile detection threshold, evidenced PA attentional aftereffects also in the somatosensory domain.

## Relationship between impulsivity traits and awareness of motor intention

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Electrophysiological and neuroimaging studies suggest that our actions are initiated by unconscious mental processes long before awareness of intention to act. However, the interval between conscious intention and movement onset seems to be sufficient to allow a conscious “veto” of the impending action. Deficient voluntary control of action and intentional inhibition are key aspects of impulsive behaviour. Impulsivity is a multidimensional construct characterized by the inability to inhibit or control actions and thoughts. We hypothesize that the time in which awareness of the intention to act occurs may represent a crucial aspect for an efficient intentional inhibition process. The objective of the present study was to evaluate the relationship between self-report and behavioural measures of impulsivity and the awareness of voluntary action. Seventy-four volunteers completed the Barratt Impulsiveness Scale (BIS-11), a go/no-go task, and a task using the Libet’s clock, in which they were requested to report the time of a self-initiated movement (M-judgment) and the time they first felt the intention to move (W-judgment). A subgroup of subjects also performed the task using the Libet’s clock during Event-Related Potential (ERPs) recording to examine components of the Readiness Potential (RP) waveform in relation to individual differences in trait impulsivity. A positive relationship between W-judgment and impulsivity measures emerged. In particular, the higher was the score in the attentional and motor impulsivity subscales of the BIS-11, and the number of inhibitory failure responses in the go/no-go task, the lower was the difference between the intention and the actual movement. We found also variability in the rate of growth of the RP between subjects as a function of the impulsivity measures. Present findings suggested that impulsivity might be related to a delayed awareness of voluntary action. We hypothesize that in impulse control disorders, the short interval between conscious intention and actual movement may interfere with processes underlying the conscious “veto” of the impending action.

## **An atypical course of Amnesic Mild Cognitive Impairment: neither Alzheimer's Disease nor Vascular Dementia?**

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Amnesic Mild Cognitive Impairment is associated to a high risk for developing Alzheimer's Disease (AD) or Vascular Dementia (VD). In typical forms, patients with AD manifest early deficit in a single domain (usually memory deficit), while patients with VD manifest early deficit in multiple domains. This study describes a case of Amnesic Mild Cognitive Impairment with single domain compromise (memory) and neuroimaging evidence (Magnetic Resonance and Computed Tomography) for frontal vascular lesions in early stage. During a period of five years, the patient had three neuropsychological and clinical evaluations. Neuropsychological tests were used for assessing cognitive abilities, i.e. global cognition (e.g. Mini Mental State Examination), memory (e.g. Digit span, Corsi test, Auditory Verbal Learning Task, Rey-Osterrieth Complex Figure), language (e.g. Boston Naming Test), attention (e.g. Trail Making Test), executive functions (e.g. Frontal Assessment Battery), whereas clinical aspects (i.e. depression, anxiety and hostility) were evaluated by patient interview and the Symptom Checklist 90. Results show progressive deterioration in all domains with marked deficits in memory and language, as well as executive deficits. The case studied here does not present the fluctuating, stepwise course that is typical of VD. It also differs from AD in that it lacks hippocampal volume or medial temporal atrophy, that are typical features of AD. Based on the aforementioned typical forms, a question might arise: does the case fit with Alzheimer's Disease? It is here suggested that further research, especially by neuroimaging, is required to answer this question.

## **Neuropsychological assessment in Mild Cognitive Impairment: targeted to the comparison analysis between MMSE and MoCA**

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This work borrows from the desire to highlight the value and the role that neuropsychology assume in the evaluation of Mild Cognitive Impairment (MCI), a neurological syndrome characterized by a state of MCI that does not fulfil criteria for dementia and leaves preserved the main everyday activities of the subject. In order to investigate and observe the state of the border between physiological aging and severe cognitive impairment it is not only relying on the study of Neuroimaging and genetic testing, but also on a concrete assessment of brain functions that it is provided by standardized tests. In this sense, that project wants to highlight the main screening tools to underline the concept of "discrepancy" respect to the comparison of MMSE and MoCA test's cut-off scores (cut-off of 24 for MMSE and a cut-off of 26 for MoCA). Although there were found a sensitivity and a greater application function of the Montreal Cognitive Assessment respect to the Mini Mental State Examination, both tests evaluate in a general way different cogni-

tive domains allowing to detect early signs of the syndrome. In the end the purpose is the propose the review of additional diagnostic tools integrated with the analysis of the emotional sphere of the subject.

## The clash of frames of reference: modality switching knocks out the Simon effect

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In this study, we addressed stimulus-response spatial compatibility effects via Simon tasks, within and across sensory modalities (vision, touch and audition). When tested in isolation, vision operates in an external spatial frame of reference (left-right hemi-field), whilst spatial reference frame in touch is defined anatomically (left-right body parts). Interestingly, when vision and touch were intermingled unpredictably, hence relevant spatial reference frames mixed, we found that the Simon effect disappeared for the visual modality, but persisted (in its native anatomical reference frame) for touch. However, when modalities operating within the same reference frame were intermixed, as in the case of audition and vision, we found the Simon effect for both modalities. In a further EEG experiment, we replicated the behavioural effects (absence of visual Simon effect in the visuo-tactile modality switching Simon task) and analyzed the P300 and the Lateralized Evoked Potentials (LRP) associated with Stimulus-Response (S-R) compatibility conditions in the single and modality switching Simon tasks. The aim was to show possible residual neurophysiological correlates of the visual Simon effect, not evident at behavioural level. In the single modality Simon task, we found a shift in latency of the visual P300 between incompatible and compatible trials, thus replicating the existing literature. The visual P300 latency effect disappeared in the modality switching version of the task. On the contrary, the LRP to visual trials showed no differences between the single and modality switching Simon task, that is the irrelevant spatial location automatically activates the wrong hand response (according to task instructions) in the incompatible trials despite no behavioural effects were evident for the visual trials in the modality switching version of the task. Our findings suggest the modality switching Simon task prevents preparation or pre-activation of a particular frame of reference and, implies re-calculating the weights assigned to different sources of spatial information on the fly, deeply affecting how relevant S-R compatibility patterns are orchestrated. To the best of our knowledge we are the first who unpredictably mixed frames of reference to address how spatial representations are formed considering both the alternations among sensory modalities and the intimate relationship between stimulus and response as it is in the Simon task. We believe that these findings are an important step forward towards understanding the format of spatial representations and their interrelation for action goals in the human brain. We contend that a comprehensive theory on spatial representations should consider situations in which different spatial codes arise not only from stimulus location and response/effector location, but also from the various potential sensory modalities in which the stimulus may appear, as it happens in real-life environment.

## Functional correlates of perceptual, motor and linguistic representations of complex actions: electrophysiological and optical imaging data

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Similarities between action observation and action execution processes – as well as action imagination and simulation ones – have been consistently reported to date by electrophysiological, neuroimaging and brain stimulation studies. According to the common coding hypothesis, perceptual and motor representations are associated and ground on a common computational code. Observing an action, then, would prime the relative action representation, and executing an action would facilitate relative representations of its perceivable effects. Furthermore, a link has been suggested between motor and conceptual-linguistic representations of actions and supported, for example, by behavioural evidences on the action-sentence compatibility effect. The present study aims at extending existing observations on simple actions and at investigating electrophysiological (EEG) and hemodynamic (functional Near-Infrared Spectroscopy, fNIRS) correlates of the execution and observation of complex common actions. So to explore potentially shared encoding processes with respect to conceptual-linguistic representations of those actions, we also looked at cortical correlates of listening to their relative verbal descriptions. Twenty healthy young adults took part in the study and were asked to: observe realistic complex actions (e.g. to pour some wine), actually execute them, or listen to their verbal description (brief verb and object phrases, e.g. “pour some wine”). We also included two combined tasks (observation and listening; execution and listening) so to investigate potential cross-facilitation effects. The integrated recording setup included 15 evenly distributed EEG electrodes and 16 fNIRS channels (over bilateral prefrontal and pre-motor regions). The analysis of EEG data highlighted the role of contralateral sensorimotor areas in all experimental tasks, as marked by a modulation of the upper-alpha band, and task-specific modulations of oscillatory activity over midline electrodes. Conversely, fNIRS prefrontal and pre-motor hemodynamic responses mainly highlighted task-specific peculiarities, with greater contralateral activity during action execution, lower activation during action observation, and no relevant hemispheric asymmetries during the listening conditions. To sum up, electrophysiological findings pointed out interesting similarities in motor and somatosensory cortical activity during observation, execution and listening conditions even when focusing on realistic actions, in line with common coding theories. Task specificities revealed by fNIRS measures might instead mirror the differential role of anterior cortical structures.

## Role of the Premotor Cortex in the action monitoring: an rTMS study in healthy volunteers

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A key challenge for cognitive neuroscience is the understanding of the conscious and unconscious mechanisms underlying the construction of willed actions. Although the Premotor Cortex (PMC) and the Parietal Cortex have been previously described as involved in action monitoring, their precise role in the construction of Motor Awareness (MA) is still to be clarified. With the present study, we investigated the role of the PMC in MA in thirteen healthy subjects through the application of the inhibitory repetitive Transcranial Magnetic Stimulation (rTMS). To this aim we used a motor task in which participants were instructed to trace either with the right or with the left hand, hidden under a box, straight lines, to a given target. During the task execution, participants received a visual feedback on a computer screen. In most of the trials (96%), the lines shown on the screen were deviated either to the right or to the left of the actual trajectories by a variable angle (Perturbed Trials, PT), so that, in order to keep the trajectories as requested by the trial, the subject had to perform a deviation movement in the opposite direction. At the end of each trial, participants were asked to report if the line they saw on the computer screen was congruent with the line they actually traced. Furthermore, they were requested to give a judgement on the congruency between the line seen on the screen and the own line, using a -3/+3 Lickert's scale (-3 = "totally different with respect to my movement", +3 = "totally equal to my movement"). Participants were tested in three different condition: (I) *baseline condition*; (II) *rTMS condition*, after the application of inhibitory rTMS (1 Hz, 900 pulses at 90% of resting Motor Threshold) over the right PMC, according to the 10-20 EEG system; (III) *sham condition*, after the application of sham rTMS over the PMC. The order of conditions was balanced across subjects. Results show that in the baseline condition subjects did not recognize the deviation of the seen line with respect to the actually traced line until a certain degree of angle. Importantly, active, but not sham, rTMS over the PMC significantly modulated motor monitoring, decreasing the amplitude of the angle at which participants became aware of the correction of their trajectory in the right and left PT, when the task was performed with the right hand. The results of the Lickert's scale indicate that subjects demonstrated more uncertainty in their judgement related to the congruence between the own line and the line seen on the screen. These results indicates that the PMC may play an important role in motor awareness. Future studies, also targeting different areas, are necessary to further investigate the neural bases of action self-monitoring.

## **A randomized double blind placebo-controlled trial of transcranial Direct Current Stimulation for Chronic Migraine with Medication Overuse: preliminary findings**

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Chronic migraine arises from a complex mixture of interconnected biological, psychological and social factors; it is a disabling condition that is worsened when associated with medication overuse. Transcranial Direct Current Stimulation (tDCS) is a innovative

non-invasive neurostimulation technique which can induce changes in brain activity; it has been already used in different chronic pain conditions which encouraging results. Few studies with preliminary results have been conducted with migraine patients. We hypothesize the efficacy of tDCS also in modulating pain in migraine. We report a clinical experience with the application of tDCS in a group of patients suffering from Chronic Migraine (CM) with Medication Overuse (MO). Our trial explore the effects of tDCS of the left primary motor cortex (M1) compared to placebo in this clinical condition. 32 patients, diagnosed as CM with MO (IHS-3 beta 2013 criteria), are presently enrolled. After baseline, all patients complete a standardized medication withdrawal in a day hospital setting. Patients are then assigned random in 1 of 2 conditions: tDCS real and tDCS placebo; the protocol consists of five consecutive sessions, each consisting of twenty minutes of stimulation in a quiet setting were the patient instructed to keep their eyes closed and stay relaxed. All patients are providing follow-up data before and 3, 6, 12 months after sessions, using daily pain diaries and measures of disability (MIDAS), quality of life (HIT-6), state and trait anxiety (STAI X1-X2), depression (BDI-II), pain catastrophizing (PCS), leads dependence (LDQ), allodynia (ASC). Preliminary results obtained with a small group of patients at short follow up (3 months) evidence that the treatment was well tolerated, without any particular side effect; all patients showed good adherence to treatment and they did not miss any session of the protocol. Although we can't confirm the efficacy of the technique as the limited group of patients treated and the short follow up, we can confirm that the technique seems to be well tolerated: patients did not report without any adverse events, and reported good treatment adherence and compliance.

## The more I like you the faster I am: aesthetic appreciation speeds up response times

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Recent neuroaesthetic research hints at the existence of a relationship between aesthetic pleasure and the quality of the perceivers' neural processing: the fluency of stimulus processing has been hypothesized to be positively correlated with individual aesthetic response. In particular, it is suggested a possible facilitatory effect of aesthetically pleasant stimuli on cognitive performance. However, the correlation between aesthetic pleasure and fluency of processing has not been directly demonstrated yet. In the present study, we specifically aimed at measuring the relation between aesthetic pleasure and visual processing. 31 healthy subjects participated in the experiment and were asked to perform a visual search task. Subjects had to identify a grey dot against a noisy background by pressing the keyboard spacebar as fast as possible with their right dominant hand. Background stimuli were 2d black and white noise stimuli randomly generated by the computer, according to the power law  $1/f^B$  which enabled us to specify the chosen  $B$  exponent, in order to control the stimuli spatial frequencies spectral power. 21 different categories of stimuli were generated with  $B$  exponents ranging from 0.8 to 2.8. It is widely accepted that humans find more pleasant stimuli with spatial frequencies conforming to a power

law with a  $B$  value close to 2. At the end of the experiment subjects were asked to give an aesthetic evaluation of the background stimuli on a 8 points Likert scale. Subjective aesthetic judgements replicated the data present in the literature, peaking for stimuli with a  $B$  value equal to 2. Furthermore, we showed that response times were inversely correlated to aesthetic judgements. We performed a multiple linear regression with response times as a dependent variable and  $B$  exponents and aesthetic judgements as regressors. The regression model was overall significant in explaining the observed reaction times variability (adjusted  $r$ -squared = 0.66). Moreover both regressors showed correlation coefficients significantly different from zero. Specifically, aesthetic judgements were negatively correlated to reaction times ( $p$ -value < 0.05). Further research is needed to determine the nature of the relationship between RTs and aesthetic judgements. Three interpretative hypotheses can be advanced: (1) aesthetic appreciation is mainly determined by the fluency of stimulus processing; (2) aesthetic pleasure is the major determinant of stimulus processing fluency; (3) bottom up perceptual features and top down aesthetic factors jointly contribute to stimulus processing fluency.

## The pathological laughing and crying: a three-cases study

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The pathological laughing and crying is a rare and underestimated syndrome that is often misinterpreted for mood disorders. It is characterized by brief episodes of stereotypical, intense and relatively uncontrollable laughs, cries, or both. The aims of the present work is to present and analyze the disease, and to define some clinical manifestations by reviewing relevant literature on the theme. To do so, in the first part the phenomenon, its epidemiology and its incidence will be described. In a second step the causes and the diagnostic criteria will be analyzed, as well as two different types of treatment (both pharmacological and cognitive treatments). In the last part, then, three different clinical cases will be presented and described in order to identify the clinical expression of the disease in three different patients. In conclusion, this work shows the importance of a detailed assessment to distinguish pathological laughing and crying from other disorders. This is the first step for a correct diagnosis and the following taking-charge procedures with the adoption of adequate rehabilitation therapies.

## Recovery of the Peripersonal Space around the feet in complete paraplegics people: phenomenology and autonomic correlates

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Peripersonal Space (PPS), i.e. the space where we can interact with objects, may be modulated by a variety of factors ranging from tool use to ability to act in it. For example, people with paraplegia consequent to spinal cord injury exhibit profound alterations of



the PPS around the feet, i.e. the body parts that cannot be moved because of the lesion. Importantly, however, 15 minutes of passive mobilization of the lower limbs may restore PPS in paraplegics. The aim of the present study is to understand if the feet PPS recovery is an effect of the vision of the motion, or if actual motion of the lower limbs is necessary. Moreover, the study aims to illuminate the role of the autonomic system, if any, in the recovery of feet PPS. To achieve this objective we recorded Skin Conductance Level (SCL) and the Respiratory Sinus Arrhythmia (RSA) as indexes of the sympathetic and parasympathetic systems, respectively. In two experiments we studied the modulatory role of visual-motor stimulation on feet PPS. The first experiment started with a baseline condition after which participants observed through a Virtual Reality (VR) device videos with passive movements of lower limbs, while an unseen experimenter could move or not move their real lower limbs (2 counterbalanced conditions). The second experiment started with a baseline condition after which participants observed in VR still lower limbs, while an experimenter could move or not move their real lower limbs. During the observation of the videos, each lasting 2', we recorded the SCL and RSA. After each video, the extension of feet PPS was estimated through a visuotactile crossmodal paradigm. In each experiment we tested 3 groups of 14 participants (Paraplegic Complete, PC, Paraplegic Incomplete, PI, and Healthy Controls, HC). Data analysis, conducted within the Bayesian framework, show that in PC the recovery of feet PPS is linked to visual stimulation, while in HC is always present. Interestingly, in PI the results depend from the neurological level of lesion. Importantly autonomic reactivity in the PC group correlated to feet PPS during the vision of still legs, while their legs were actually moved. Our results suggest that visual feedback can lead to a feet PPS recovery in PC. Importantly, although these patients are not consciously aware of lower-limbs motion, their autonomic functions respond to visual-motor incongruities.

## **fMRI investigation of brain activity in motor and language brain areas in Friedreich's Ataxia after rehabilitation**

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Friedreich Ataxia (FRDA), the most common of the hereditary ataxias, is an autosomal recessive disease. It is due to mutations in frataxin gene which ultimately results in a reduction of frataxin, a mitochondrial membrane protein involved in iron sulfur protein production, storage and transport. FRDA is a multisystem neurodegenerative and rare disorder, affecting approximately 1:29.000 individuals. The first signs of the disease usually occur in adolescence: cerebellar ataxia (incoordination), dysarthria, fixation instability, impaired vibration sense and proprioception are the main symptoms. The most affected individuals have absent lower limb reflexes, and may have spasticity. Also, patients are affected by non-neurological features: scoliosis, diabetes, foot deformity and cardiomyopathy. No specific therapies have been identified that can arrest the course of this devastating disease and the only available therapy, to contain symptoms, is the maintenance of muscle tone and speech by means of neurorehabilitation. The aim of this work is to investigate, by means of fMRI, brain activity before and after physiotherapy and speech therapy. We will observe which classes of patients will be more susceptible

to the different therapies. As well as in the pre-surgical fMRI, with fMRI, we see the motor areas and speech in patients with FRDA, both before and after speech therapy and physiotherapy treatment. The fMRI is a non-invasive technique that takes advantage of the changes in the ratio of oxygenated to deoxygenated hemoglobin in capillary beds because of their different magnetic properties during the execution of the tasks. During fMRI, the motor tasks have to be done are: finger tapping and movement with the feet, about finger tapping the subject are asked to perform a finger tapping task with the right hand if see on monitor “right”, move the left hand if the subject see “left”, the process for the movement of feet is the same. To investigate the language area I use generation of words (WGEN) or verbs (VGEN). Instructions of VGEN are simple: given a word, the subject think of the associate verb. WGEN: given a letter the subject must generate a series of consecutive words starting with a letter shown. We must to regard the time of presentation of stimuli and the response times, which are longer, because of the pathology. About data acquisition, anatomical imaging and task fMRI, i would use a 3.0 tesla scanner and about data analysis i would use the Brain voyager program. I expect activation quantitatively and qualitatively increased during cycles of therapy, compared to the same without therapy.

## Active limb movements and functional specialization in the human Medial Parietal cortex

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The Parieto-Occipital sulcus (POs) is a crucial node of the dorsal visual stream and the origin of several pathways for visuo-spatial processing. Neurophysiological studies on macaques have suggested that in the territory between the POs and the precuneus there exist at least three cytoarchitecturally, retinotopically and functionally distinct regions: the visual motion area V6, the visuomotor and pointing-selective area V6A, and the somatomotor area PEc responding to active limb movements. In humans, we have identified putative homologue regions (V6 and V6A) using wide-field retinotopy and brain mapping fMRI techniques. However, little is known about the possible location and functional properties of the human PEc (hPEc). In this study we used a combination of fMRI brain mapping methods in order: (1) to map the PEc area in humans by means of active limb movements and (2) to study the functional specialization along the POs and the precuneus respect to visual, visuo-motor and motor tasks. For these purposes, 20 participants completed a series of fMRI scans during: (1) a visual stimulation paradigm, FlowFields, which we have previously proposed as a functional localizer for human V6 area; (2) a delayed hand pointing, foot pointing and saccadic task, designed to maximally activate the arm-movement-related cells with spatial tuning in area V6A and to reveal any foot-related neural responses in the POs and precuneus; (3) a pure motor task implying active movements of the inferior (leg) and superior (shoulder) limbs designed to reveal effector-related somatomotor responses in V6A and precuneus regions. We found a functional

difference along the POs between two regions: a posterior area (V6) responding more to both coherently moving stimuli and saccades than to hand/foot pointing movements, and a pointing selective anterior region (V6A) with an opposite functional profile. In addition, while V6 was inhibited during both limb movements, V6A was activated for shoulder movements as in the macaque. We have also identified a region in the anterior precuneus (likely the human PEc), which responds more to pointing than to saccades, and even more to foot pointing movements. Differently to other medial parietal regions, hPEc responds more to leg than to shoulder movements. Our data show a visuo-motor gradient on the medial wall along the postero-anterior direction with regions responding to visual motion located posteriorly and regions responding to visuo-motor or somato-motor tasks located anteriorly. In conclusion, the functional properties of the described regions suggest a good correspondence with macaque V6, V6A and PEc.

### **Decisional impairment (IOWA Gambling Task) in Parkinson's Disease patients with active and remitted Pathological Gambling behavior**

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Among the non-motor features of Parkinson Disease (PD), impulsive-compulsive behaviours such as Pathological Gambling (PG) have been described in the last decade. These abnormal behaviours occur in about 14%-25% of the patients and their relation with Dopamine Replacement Therapy (DRT) and cognitive features of PD is still debated. Stable remission from PG has been described in about 40% of the PD PG patients but few studies explored this topic. We studied the decisional process in non demented PD patients with PG, patients who remitted from PG and those who never gambled (CNTR) using the IOWA Gambling Task (IGT). We also evaluated electrophysiological activity (EEG) during the performance. We included in the study non-demented patients with PD treated with stable DRT. We enrolled 14 patients with PG, 10 patients who developed PG in the course of the disease but that were in stable remission (ex-PG) and 18 patients who never gambled. Gambling behaviour was evaluated by clinical interview and QUIP rating scale for the assessment of impulsive compulsive behavior in PD; we also asked to caregivers about patient's gambling attitude. A short cognitive and behavioural assessment was conducted in order to generally evaluate cognitive status. Decision making abilities were evaluated using the IGT and electrophysiological correlates were recorded. The analysis of IGT performances revealed many differences between groups: PG group had worse performances in the IGT total score and did not show any learning effect among blocks. PG showed also a tendency to prefer disadvantageous decks and they more frequently chose the most disadvantageous compared to the other two groups. Interestingly, ex-PG group results were similar but not as good as those of CNTR. However both ex-PG and CNTR showed a good learning trend and had better total scores than PG. Therefore, whereas the performances of PG group were clearly pathological in

term of decisional processes, the data on ex-PG are new and interesting since it seems they are more close to PD who never gambled than to active gamblers as if the decisional process could be partially restored.

## **Cortical correlates of a priming-based learning enhancement task: a Brain Computer Interface study**

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Priming is an automatic cognitive mechanism according to which the exposition to a certain kind of stimulus can modify the response to a subsequent stimulus. Even if literature has widely dealt with this phenomenon, experiments that analyses effects of priming in learning and their neural correlates are still few. The main aim of this project is to evaluate whether semantic priming could be considered as a useful method to improve the performances of subjects involved in a learning task. In particular, we expected that the subjects, which received semantic priming, would show faster behavioral patterns and that the priming effect would result in a lower cognitive load correlated to a lower engagement of anterior cortical areas. We then hypothesized that during tasks primed by semantic-related cues beta and gamma frequency bands will show a lower activation with respect to non-primed ones. Thirty right-handed volunteers (age range 18-26) with normal or corrected to normal visual acuity and without neurological illness nor learning disabilities participated in the study. We designed an experiment with three groups (semantic prime; neutral prime; no prime) and three conditions (letter recognition, word recognition, word definition). A NeuroskyMindwave BCI device was used to collect frontal EEG data. The use of the open source OpenVibe stimulation software allowed us to implement a Python code to build the experiment. Significant differences were found in all conditions. In the first task (Letter recognition), the prime-group reported an average RT of 0.63 seconds while the other two groups (neutral-prime and no-prime) reacted slower (respectively, 0.92 s and the 0.85 s). In the second task (Word recognition), the prime-group RTs had an average of 0.44 seconds vs. 0.84 and 0.81 of the other groups. In the third task (Definition), the prime-group answered took an average of 4.73 seconds to respond, versus 6.38 and 6.86 of other 2 groups. Finally, to analyze EEG correlates of behavioral results a Matlab's tool (EEGLab) was used to analyze the data recorded by the BCI. As expected, primed-subjects reported a less average activation of Beta and Gamma waves, immediately before and after the onset of the stimulus ( $F [2, 27] = 20.123, p < .001$ ;  $F [2, 27] = 20.002, p < .001$ ). Our EEG data showed in the frontal areas the priming effect is correlated to a reduced activity, showing a cognitive discharge. These data suggest that is possible to structure education material so to increase learning performance and/or reducing the cognitive load. These achievements are particularly wishful in case of learning disorders or when many information have to be learned in a brief time. The use of a BCI device might then be used to assess the cognitive load providing specific feedback when excessive, less-functional level of cortical activity is reached. We believe that a systematic use of BCI devices will foster the implementation of cognitive-driven education and enhancement programs.

## **Cognitive task to differentiate between visual field deficit and neglect**

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Neglect patients are able to process visual stimuli even if they do not have an overt perception of them. Indeed, since first studies at the end of 80 s lot of works demonstrated the presence of an implicit information processing, specifically part of them focused on the presence of a semantic activation effect due to the onset of a prime (either word or picture) in neglected space. This kind of effect was not found in patient with visual field deficits. Actually hemianopia determines a variable reduction of visual field width and a consequent partial blindness for the patient. Even though there are different neuro-anatomical substrates between neglect and hemianopia, we know that clinical examination (including neuropsychological assessment) may provide confounding results. Not so many studies tried to disentangle neglect from hemianopia even using an implicit information processing task to discriminate. In our previous works we hypothesized that a prime-word in the neglected field should determine a semantic activation effect differently for what expected by prime in hemianopic field. We discussed a single case patient with bilateral brain lesion causing both left neglect and right hemianopia. Our results confirmed a strong repetition priming effect only when prime occurred in neglect hemi-field. In this work we will describe the performance of 8 patients with a unilateral brain lesion which causes the presence of left visual neglect or left homonymous hemianopia. The experimental procedure was identical to those one described in our previous work. The patients were required to press the space-bar when the target word belonged to a living category after a prime word onset on six different possible positions of the monitor. We collect data on a small group of patients but our first results have confirmed the hypothesis concerning semantic activation in the space affected by neglect but not in hemianopic field. This test gives than promising results as a tool for differential diagnosis, even if it requires minimal levels of attention to be executed.

## **Fronto-temporo-parietal connection as network for awareness: a clinical case description of anosognosia for blindness**

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Anosognosia for visual deficit is mainly associated to cortical blindness and refers to the complex description of the Anton-Babinski Syndrome (ABS). As widely known patients with ABS present occipital bilateral lesions causing cortical blindness and lack of awareness about this deficit. We here discuss the case of a patient presenting visual impairment, anosognosia for blindness and spare of primary visual cortices. Our patient is a 65 y.o. woman suffering from a massive subarachnoid hemorrhage involving a large part of right hemisphere. In particular, CT scan documented an extensive damaged area mainly

involving right temporal lobe, part of right frontal areas, right basal ganglia. Moreover an extension of lateral ventricle as effect of blood reabsorption is seen (ex-vacuo suffering). After acute hemorrhage, she presented a 1-month period of unresponsiveness and gradually achieved full levels of consciousness. At time of first assessment in our ward, namely 2-months after the vascular event, her clinical conditions were characterized by the presence of general ideo-motor slowness, confusive state, left hemineglect and severe visual deficits. Indeed she was suffering of a bilateral Terson Syndrome which is known as a intraocular hemorrhage mainly associated with subarachnoid haemorrhage as reaction to artery rupture. Such condition was the cause of her blindness, she was not able to perceive nothing excluding light flashes. A neuro-ophthalmological examination confirmed the severe visual impairment. Despite she showed total unawareness of her blindness pretending to behave as a normal-sight person. She used to verbal denying her blindness, confirming a perfect sight ability, in grasping task she tried to reach objects without any effectiveness. After grasping behavior she used to react in two main different ways: sometimes she looked aware of her failure and justified it as a consequence of a sudden trick by the examiner. In other occasions she pretended to have correctly execute the object grasping simulating a congruent behavior (i.e. at the order “please, grab the pen” she executed the movement but, even though she was not able to do it, she successively imitated a writing movement). The peculiarity of this case concerns the fact that this woman was undoubtedly describing as patient with ABS in which no occipital involvement can be found. We conclude and discuss these clinical sings as a strong confirmation of neurophysiological theories concerning the involvement of right fronto-temporo-parietal connections in anosognosia and self-awareness.

## Assessment of executive functions and attention in children with developmental disabilities: a cases study

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This paper aims to help the assessment of attention and executive functions in developing through the creation of an early screening in a group of preschool children with developmental disorders, at a rehabilitation center in Bari. Executive functions play a fundamental role in cognitive development. In the last 15-20 years the study of the executive functions in developmental disorders (psychopathology and neuropsychology of the development) has gradually assumed a central role: the ability to monitor and regulate behavior and cognitive processes is an important predictor of adaptive functioning and school performances of children. Executive functions are defined as the cognitive skills needed to plan, implement and bring to a successful conclusion a conduct aimed at a goal; they include cognitive processes, and self-regulation which allow the monitoring and control of thoughts and actions, such as the inhibition, planning, attentional flexibility, the identification and correction of errors, the resistance to interference. The development of executive functions in children is closely linked to the development of attention. The evaluation of the attention and the executive functions has importance not only for diagnostic purposes, but also and especially for therapeutic purposes to set any treatment program that can focus directly on them or, if primarily focused on other objectives,

however, must keep into account their level of functioning. Therefore, the present work aims to make an early screening of a group of preschool children with developmental disorders (autism spectrum disorder, learning disabilities, speech disorder), identifying cases at risk. Therefore it has a preventive aim. It is divided into four phases: interview with family of the child and observation; psychological assessment using cognitive tests, and tests that investigate aspects related to attention and executive function, tests of the learning prerequisites; next scoring and processing of results; realization of a specific individual training on the functions impaired at the rehabilitation center with the children evacuate. Particularly in autism spectrum disorders are registered limits in cognitive flexibility, perseverative responses and rigid use of rules, falls in the ability of planning. In language disorders, there are deficits in phonological working memory and visual-spatial, impaired cognitive flexibility, impairment of verbal and non-planning. Children with intellectual disability present executive performance globally lower than children of the same chronological age as compared to children with their mental age showing deficit of inhibition planning, working memory nonverbal.

## Neurophysiological correlates of cognitive control and food-related attentional bias: a longitudinal study in obese candidates for Laparoscopic Sleeve Gastrectomy

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Laparoscopic Sleeve Gastrectomy (LSG) is a bariatric surgery procedure to promote weight-loss in severe obese individuals. Beyond homeostatic needs, several non-homeostatic mechanisms contribute to overeating, which may in turn lead to weight gain and obesity. Attentional bias toward food-related cues has been suggested in obese individuals, possibly reflecting altered reward-sensitivity within the brain reward network. From the other hand, cognitive control exerted by frontal brain regions is necessary to inhibit overeating and pursuit long-term goals (i.e. weight loss), and reduced frontal activation has been shown in obese individuals. Both attentional processing and top-down cognitive control might correspond to a decrease in impulsive symptoms after bariatric surgery and contribute to successful weight-loss. Initial evidences for cognitive improvement after bariatric surgery exist, however neurophysiological correlates of these processes are poorly investigated and longitudinal studies are needed. Thus, the aim of the present study was to assess changes following LSG in 17 obese individuals, evaluated in fasted state before LSG (pre-LSG) and one year after-surgery (post-LSG). Cognitive control and attentional bias toward food were investigated with a modified Simon task with central presentation of distracting food and non-food images, and a neutral condition without distractors. Stimulus-response spatial compatibility was assessed analyzing spatial corresponding and non-corresponding trials. Behavioral measures and Event-Related Brain Potentials



(ERPs) were recorded during task execution. Behavioral results showed reduced cognitive control in trials with food, with longer reaction times and lower accuracy in the non-corresponding condition both pre- and post-LSG. Frontal N2 showed an increase in amplitude from pre- to post-LSG, in all conditions. Furthermore, in pre-LSG N2 latency for distractors was shorter than neutral whereas this difference was no longer present post-LSG. P3 analysis did not reveal any significant effect of surgery, however, a significant difference between corresponding and non-corresponding trials was detected only for food. Increased N2 amplitude after surgery may suggest higher recruitment of frontal resources during conflict detection processes post-LSG, whereas changes in N2 latency post-LSG can be interpreted as an overall reduction of attentional bias during conflict detection. In contrast, higher P3 amplitude for food may indicate a food-specific attentional bias in severe obese individuals, persisting after LSG. P3 results are in line with behavioral findings, showing lower control of interference in presence of food distractors both pre- and post-LSG. In conclusion, the present findings suggest motivational and attentional bias toward food-stimuli in severe obese, which is not modulated by LSG. By contrast, cognitive control in presence of distracting food and non-food stimuli is improved after surgery.

### **Active control of a virtual arm as a proxy to embodiment and action monitoring in people with Spinal Cord Injury: an EEG study in immersive virtual reality**

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Acting efficiently in the world depends not only on the integrity of motor and somatosensory systems but also on the sense that our body belongs to us (i.e. Feeling of Ownership, FO). Recent studies on healthy subjects show that simply observing a virtual arm in first-person perspective (1PP) induces illusory FO over it and activates the error monitoring brain systems when the virtual arm performs an erroneous action (indexed by Medial-Frontal Theta activity). Here we investigated whether similar phenomena are elicited in people who sustain a Spinal Cord Injury (SCI), i.e. a condition that brings about a massive disconnection of the below-lesion level body from the brain. We combined Immersive Virtual Reality and EEG to record the brain activity of an SCI patient (with injury at C4 level) and a control group (12 healthy subjects) during the observation of virtual arm's movements in 1PP. In particular, using a 4-screen CAVE system we created a virtual arm (in continuation of the participant's right shoulder) that performed a correct or an incorrect reach-to-grasp movement toward a virtual mug. In addition, by measuring the Electromyographic (EMG) activity of the participant's right shoulder and lips, we implemented a simple EMG-based Body Computer Interface through which SCI patient and healthy participants were able trigger the start of the virtual arm's actions. Thus, in three different blocks the virtual arm was (1) passively observed or actively triggered by fast muscle contraction of the (2) shoulder or (3) the lips. At the end of each action, participants reported verbally how much they embodied the avatar's arm. EEG activity

was recorded during the experiment. Results obtained in healthy participants show high levels of illusory FO over the virtual arm during the passive observation as well as the active control and a clear Medial-Frontal Theta activity during the incorrect movements. Moreover, results from the SCI patient show that the passive observation was not sufficient to elicit FO and to activate the error monitoring brain systems. Conversely, the active control of the virtual arm with muscle's contraction activated a cascade of events ultimately leading to the induction of FO. Such a change of FO paralleled Medial-Frontal Theta activity in reaction to observation of incorrect movements of the virtual limb. Thus, the voluntary muscle's contraction is necessary to enhance the embodiment and the electrocortical markers of error detection in the SCI patient. These findings shed new light on the role of Ownership and cerebral systems for action monitoring in people with SCI and have important implications for (i) understanding how the brain can control the external world and thus contributing to create new brain-computer interfaces and (ii) to develop new rehabilitation treatments using Virtual Reality and EMG-based Body Computer Interface.

## Oculomotor control in children with Cerebral Palsy

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Cerebral Palsy (CP) refers to non-progressive syndromes resulting from peri-/post-natal injury of the central nervous system. Children suffering from this neurological disorder show limitations in oculomotor control that are often thought to affect the executive functioning. In the present study, we assessed the attentional skills of CP children during the execution of lower-order cognitive tasks. To this end, we recorded ocular movements from 10 CP children (5 females, mean age: 11 years and 4 months  $\pm$  2 years and 10 months) during the execution of both a simple visually guided saccade task and a spatial cueing paradigm. In the cueing paradigm, 150 ms before the onset of an eye target, one of four placeholder around a central fixation cross briefly flashed (cue). The target randomly occurred at the same location of the cue (valid condition) or at a different one (invalid condition), and subjects had to direct the gaze towards it as fast as possible. Latency and accuracy of saccades recorded from CP subjects were compared with those of 13 children (6 males and 7 females, mean age: 13 years and 1 month  $\pm$  2 years and 6 months) with Typical Development (TD). Interestingly, the ocular performances during the simple visually guided saccade task did not differ between CP and TD subjects, being both groups quick to react to the onset of the ocular target. In the spatial cueing task, a coupling between cue location and gaze direction emerged, being saccadic latencies faster towards valid targets, both in TD and CP groups. However, CP children often executed gaze movements to the cue, suggesting a difficulty to inhibit an eye shift towards a task-irrelevant visual stimulus. Moreover, CP children frequently executed eye

movements during the fixation of the central cross. Interestingly, these intrusive saccades were mostly aimed to one of the placeholder displayed in the visual scene. This behavior clearly suggests a difficulty of CP children to suppress eye movements towards locations exogenously and endogenously activated by visuo-spatial attention. By combining eye-tracking techniques and cognitive protocols, the present study offers a new approach for studying executive function in patients suffering from limitations of voluntary motor control.

## Venlafaxine and oxycodone have different effects on spinal and supra-spinal activity in man

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This study aimed to explore how oxycodone (opioid) and venlafaxine (SNRI) modulate somatosensory processing. Twenty volunteers were included in this randomized, cross-over, double blinded experimental study comparing treatment with venlafaxine and oxycodone to placebo. Spinal and full scalp cortical Somatosensory Evoked Potentials (SEPs) to median nerve stimulation were recorded before and after five days of treatment. In the venlafaxine arm, the P11 and N60-80 latencies were reduced ( $p < 0.01$ ), whereas the P25 amplitude was decreased ( $p = 0.01$ ). Oxycodone increased the P14 ( $p = 0.03$ ) and N30 ( $p = 0.04$ ) amplitudes and the N60-80 latency ( $p < 0.05$ ). The brainstem and primary somatosensory cortex source strengths were increased in oxycodone arm, whereas the primary somatosensory cortex strength was decreased in venlafaxine arm ( $p < 0.05$ ). Our results show that venlafaxine determines changes in the non-nociceptive somatosensory pathway at both spinal and cortical level, while oxycodone acts at brainstem and cortical level. It can be concluded that opioids and SNRIs exert different central effects.

## Cooperation and competition in the brain: cortical and personality components

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In the present research cooperative and competitive tasks were compared to explore their temporal and spatial dynamics in the brain through electrocortical (EEG) and hemodynamic (functional Near-Infrared Spectroscopy, fNIRS) measures. Two distinct groups of subjects were submitted to a joint cooperative (experiment 1) or competitive (experiment 2) game in the form of a sustained attention task. Participants were required to synchronize their behavioral responses in exp 1, and to perform better than the competitor in exp 2, considering both accuracy (Error Rate, ER) and Response Times (RTs). During the experiment subjects constantly received feedbacks about their performance, which

was experimentally manipulated. In addition, a personality trait measure (Behavioral Activation System, BAS) was submitted and used to qualify participants according to their rewarding attitude. Also, subjects were required to assess their self-perception of social ranking during the task. Their behavioral performance was calculated to assess the relation between all these different measures. Results showed increased left prefrontal cortical responsiveness in high-BAS participants in case of both cooperation and competition. Moreover, high-BAS participants showed greater left frontal activity during the cooperative task, in parallel with the perception of increased social ranking and better performance. Such results demonstrate that cooperation is related to the highest cortical responsivity within the left prefrontal cortex, especially for high-BAS subjects. This left hemisphere effect, in fact, is related to the individual approach attitude in a way that individuals with higher BAS profiles were more likely to show dominant and proactive attitudes in situations that produce positive and rewarding effects. Indeed, personality traits proved to affect the representation of social hierarchy and to improve the behavioral outcome.

## Perceiving emotions in Autism Spectrum Disorders: cortical and peripheral effects during intra- and inter-species social interactions

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Convergent evidence showed that children with Autistic Spectrum Disorders (ASD) have often to deal with some social deficits and their consequences, such as rejection, social anxiety, and negative peer interactions. Thus, the need to develop alternative strategies to improve social communication has recently emerged and become an important goal. One recent possibility consists in the introduction of therapies based on human-animal interactions: it has been largely demonstrated, in fact, that animals can improve social exchange among humans. This effect could be of primary relevance for individuals with disabilities, to encourage a positive experience and reinforce socio-emotional development. Nonetheless, it's still largely unknown what are the psychological and neural mechanisms that can mediate the emotional and empathic processes related to such effects. To explore cognitive and affective components related to these research questions, a multi-method approach with electroencephalographic (EEG) and autonomic activity recording was applied to explore central and peripheral responsivity of ASD children during an emotional task. It has been proven, in fact, that they typically show impaired autonomic responsivity to social cues and anomalies in electrocortical patterns during emotional tasks. A small pilot group made up of 8 children with ASD (M age = 8.5, SD = 1.9) was shown 144 affective pictures (positive vs. negative vs. neutral) depicting both Human-Human (HH) and Human-Animal (HA) interactions. For what concerns EEG data, a decreased activity in alpha power was found with respect to HH stimuli (increased cortical activity). Similar results in ASD have been interpreted as the recourse to more voluntary-driven mechanisms to process and interpret affective stimuli (higher/controlled mental functions), instead of recruiting phylogenetically ancient structures

responsible for the execution of automatic brain functions. For what concerns autonomic activity, cardiovascular indices (both Blood Volume Pulse, BVP, and Heart Rate, HR) showed increased activity for positive stimuli. Finally, SCL showed increased responses for negative HA stimuli, which probably triggered significant automatic orienting/defensive responses. Such results will be compared to those obtained by a matched control group. The present work provided significant neuroscientific evidence on emotion perception in ASD to different social agents, with important highlights for future therapeutic support and interventions.

## Intra and inter-brain connectivity during cooperation: a fNIRS-based connectivity analysis

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Research suggested that during social interactions typical forms of synchronization in two individuals' brains can occur in the form of an alignment of neural activity (brain-to-brain coupling). To explore these issues hyperscanning paradigms emerged thus permitting the simultaneous recording of the cortical activity from two or more participants interacting together. Nonetheless, new neurophysiological techniques are required to monitor these processes to allow flexible and ecological settings, such as functional Near-Infrared Spectroscopy, which is portable and constraint-free to acquire data during the interactional setting. In the present study intra and inter-brain connectivity was calculated during a social interaction proposed as an attentive joint task including a social feedback, experimentally manipulated. Halfway, in fact, a feedback was provided artificially to participants assessing the goodness of behavioral synchronicity scores. The aim was to compare subjective and inter-subjective brain contribution in the joint-action with respect to the social reinforced cooperation and perception of a good joint-action. Partial correlation coefficients were used as a functional connectivity index for computing both intra and inter-brain coherence, by quantifying the relationship between the two different signals. For what concerns intra-brain coherence, results showed a significant difference ( $p < 0.05$ ) between the first and the second half of the task in the connectivity of channel F2-F4, corresponding to Premotor Cortex (PMC), and F2-FC2, corresponding to Frontal Eye Field (FEF). The link between these two areas account for the subjective efforts during the first part of the task to accompany the detection of visual stimuli with synchronized motor responses. A similar result was found for inter-brain coherence, with higher connectivity between two premotor areas (FC4-FC2 and F2-FC2;  $p < 0.05$ ) before the social feedback, related to motor planning and imaginary. Finally, higher inter-brain coherence emerged after the social manipulation for FC3-F3 and FC4-F4 ( $p < 0.05$ ), which correspond to left and right Dorsolateral Prefrontal Cortex (DLPFC). With respect to previous brain networks, this area has been proved to be involved in social cognition. Thus, the presence of enhanced emotional and social processes related

to empathy and bonding could be hypothesized after the feedback. The present results provided new insights in the identification of brain areas with specific functional roles in intra and inter-brain coherence during interpersonal coordination. Importantly, the social feedback permitted to distinguish brain networks specifically related to motor synchronization and emotional/social tuning.

## **Hemianopiain stroke patients: a new software for the rehabilitation**

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Unilateral homonymous hemianopia is the most frequent visual deficit after acute neurological events (es. stroke). This deficit has an important impact on functional level and quality of life of the patients. Patients with hemianopia show a reduction of visual field and problems to do saccadic movements spontaneously, which are essential to compensate the deficit. Recent studies suggest that compensatory trainings are effective to improve the deficit. Specifically, NeuroEyeCoach (NEC) software trains patients to compensate visual field deficits increasing the efficacy of their saccadic movement. The aim of this study is to evaluate the effects of NEC on recovery of hemianopia disability in stroke patients. Ten stroke patients with unilateral homonymous hemianopia has been recruited (M = 9). Before (T0) and after (T1) treatment each patients has been evaluated by computerized (specified in NEC) and paper and pencil (visual search, copy of figures, spontaneous drawing, bisecting lines and lecture) tests. The training software, composed of 12 levels (3 sections each) of increasing difficulty, included 3 sessions a week of one hour each. The duration of training depended on patient's ability to overcome each level. The software adapted to subject's performance, repeating, in case of poor performance, the previous level with some facilitation (es. longer permanence of stimuli on the screen). Two patients dropped-out during the treatment. Eight patients have completed the treatment with NEC. The analysis shows an increase of performance post treatment. Specifically, computerized outcome measures reveal improvements both in accuracy and execution time. Paper and pencil test post treatment reveal slight increase of accuracy, while execution time is significantly reduced. These preliminary data suggest that NEC software should be an effective compensatory tool for the rehabilitation of visual field deficits.

## **Facilitation of cognitive process during gait in normal subjects**

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Neuroimaging research has shown that acute aerobic exercise improves cognitive performance and produces neurophysiological changes, particularly in frontal lobe regions, during tasks requiring selective attention. The circuitry of the Prefrontal Cortex (PFC) is complex with extensive reciprocal corticocortical and thalamocortical connections. The

process of normal walking is complex, consisting of voluntary and automated sequences of motor patterns. The aim of our study was to explore the effect of walking on cognition by recording brain activity during a dual task paradigm. We realized EEG registration in 30 healthy subjects aged 18-65 years and we performed an acoustic P300 oddball paradigm in standing condition and during walking. The P300 amplitude increased during walking compared to standing condition, while there were no significant changes in latency. A correlation analysis showed a P300 amplitude reduction with age in the standing condition, but this negative correlation was not found during walking. A topographic analysis showed increased amplitude of P300 during gait in the anterior regions of the scalp. Walking seems to facilitate cognitive process, offsetting the age-related deficits, and selectively up-regulates excitability in anterior lobe regions, thereby promoting greater top-down attentional control during executive functioning tasks. Our results are in line with the growing number of human studies that reported the beneficial influences of acute as well as chronic exercise on cognitive functions, highlighting the possible modulatory effect of the motor cortex activation on the prefrontal cortex functions. These aspects may be relevant for the formulation of rehabilitation programs in subjects with cognitive impairment.

### **The detection of psychophysiological parameters in vegetative state patients: a response to sensory stimulation?**

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This study aims to find psychophysiological markers of state of consciousness in response to sensorial stimuli addressed to vegetative state patients. A set of stimuli is presented to a sample of 18 vegetative state patients; stimuli belong to four categories, different for sensorial channel used: visive, uditive, tactile, olfactory. For visive and uditive stimuli there is a distinction between autobiographical and not-autobiographical stimuli, id est patients' photos and name versus others' photos and names. Instead tactile stimuli are a close to the wrist and the application of ice on the wrist, while olfactory stimuli are vanilla and cinnamon fragrances. Visive and uditive stimuli are presented by a event-related paradigm, while tactile and olfactory stimuli are presented as single trial. During the entire stimuli presentation, cortical activity and physiological activation are recorded by electroencephalography and biofeedback. Data showed a significative ERP P300 component in response to autobiographical visive and uditive stimuli. Subjects seem to be able to recognise an autobiographical stimulus between various non autobiographical stimuli. P300 ERP occurs only during attentional involvement in a cognitive task and seems to be linked to attentive and conscious processes. We could infer the presence of preserved cognitive abilities, even without significant behavioral responses. It can be assumed that associative cortex in vegetative state patients is partially active and involved with sensory cortex, since P300 ERP (as well as all potential registered more than 100 ms after stimulus presentation) typically reflects the activation of the associative cortex. However, the thalamus-cortical and cortico-cortical disconnection remains massive in this type of patients, in fact there is no ability to perform voluntary actions and



there is an absolute predominance of the delta band for cortical activity, typical of neurological diseases and cortico-cortical and thalamic-cortical disconnections. Moreover, any evidence of awareness is shown by behavioral data and autonomic responses.

## **Social issues vs. commercial advertising, differences in psychophysiological activation during multimedial artefact fruition**

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This study aimed to investigate differences in neurophysiological activation during different types of multimedial artefact fruition. In particular we wanted to verify cortical activation during the vision of both social issues and commercial advertising videos. 10 videos of 30 seconds of duration were presented to a sample of 15 healthy subjects. Half of them was commercial advertising videos and the other half dealt with social issue. Advertising videos were selected identifying 5 categories comparable by a commercial or pro-social point of view, and they were: money, health, technology, nutrition and clothing. During videos vision, cortical and physiological activation were recorded by electroencephalography and biofeedback. Data showed an increasing of Alpha power in central brain areas, greater during social issue advertising fruition and a higher Delta power in frontal brain areas for social issue advertising except for nutrition category, in which there is a greater activation for commercial advertising. Physiological data showed an increasing of heart-beat during commercial advertising fruition, in particular for money, technology and nutrition categories. Data suggest a greater disposition to action and involvement in subjects due to commercial advertising features. This is showed by heartbeat increasing during commercial videos and alpha band increasing in central areas while watching prosocial videos, that means a de-activation of central areas, involved in movement and tension to action. During social issue advertising, instead, we can see an activation of frontal area, linked to motivation processes. Finally, starting by the point that frontal lobe is related to evolved social functions linked to adaptation to social environment, we could imagine that commercial advertising touches more ancestral and instinctual processes related to movement and action, with lower central Alpha power; social issue advertising, on the other side, with higher frontal Delta power, activates higher functions related to motivation, adaptation to the environment, and thus to prosociality.

## **Brain oscillations implications in Parkinson's Disease patients with or without remitted gambling behavior**

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Among the non-motor features of Parkinson Disease (PD), impulsive-compulsive behaviours such as Pathological Gambling (PG) have been described in the last decade. We studied the decisional process in non demented PD patients with PG, patients who remitted from PG and those who never gambled (CNTR) using the IOWA Gambling Task (IGT). We evaluated electrophysiological activity (EEG) during the performance, by computing the power spectra. The present research focused on the decisional processes by using IGT. We included non-demented patients with PD treated with stable DRT: 14 patients with PG, 10 patients who developed PG in the course of the disease but that were in stable remission (ex-PG) and 18 patients who never gambled. The frequency band analysis showed significant differences among the groups. Specifically low-frequency bands (mainly delta and theta) showed an increased delta activity within the posterior (occipital) areas for PG compared with the other two groups, mainly during erroneous decisions (disadvantageous options). In contrast remitted PG group revealed a similar power distribution as compared to CNTR. The low-frequency bands prevalence may underline an anomalous cortical response by PG patients with regard to their ability to monitor and control emotional behavior during a decisional task where “gambling” feature is relevant.

## Structuring cortical bistability in sleeping DOC parallels the recovery of consciousness

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To date little is known about sleep in Disorders of Consciousness (DOC). A few studies showed that sleep macrostructure is often altered, but NREM sleep graphoelements (i.e. Sleep Slow Oscillations, SSOs, and spindles) could be sometimes observed in the EEG of patients with DOC. Recently some studies suggested that the presence of such sleep features correlate with the prognosis of DOC patients and could help in the diagnosis between Vegetative State (VS) and Minimally Conscious State (MCS). SSOs and spindles are the EEG graphoelements of a fine tuned interaction between cortical neurons, excitatory thalamocortical cells and the reticular thalamic nucleus. SSOs are bistable processes of hyperpolarization/depolarization occurring during NREM sleep that engage cortex and thalamus, whereas spindles derived from the rhythm imposed by reticular thalamic nucleus on the cortex. Last years the study of consciousness in both healthy people and DOC patients focused on the emerging properties of complex bidirectional thalamo-cortical connections; hence the study of sleep could be an optimal window to study thalamo-cortical circuits involved in consciousness and to verify the role of thalamo-cortical connectivity in the recovery of consciousness. Here, we aim at studying the EEG of a sample of patients with DOC in different recordings along the recovery of consciousness (VS, MCS and Exit From Minimally Conscious State, EMCS) to see how it changes in the different levels of consciousness. We also applied the same criteria on

the sleep EEG of two healthy volunteers. We recorded high density EEG (128 ch) during night and we selected as Events of Interests (EOI) graphoelements having the characteristics and morphology of SSOs according to the features already published. We found that in two patients that improved their clinical conditions spindles were not present in VS but they became evident in MCS and EMCS. Regarding the study of SSOs features we found that the amplitude increased in the recovery of consciousness, reaching values close to the normality; and the SSOs became more expressed in the frontal lobes, as it can be observed in healthy subjects. Moreover the measure of steepness (positive and negative slopes) changed in their values becoming more similar to the normal ones. It has been shown that amplitude measures are mainly related to membrane potential amplitudes and to the size of the local neuronal pool showing a synchronized SSO behavior. The slopes measures are inherent to synchronization of the underlying neuronal pool during the transition towards the down state (negative slope) and during the transition between down and up states (positive slope). Since these features depend on the correct interaction between thalamus and cortex, we corroborate the hypothesis of the pivotal role of thalamocortical interaction for consciousness and we show that the study of sleep can provide relevant information about the integrity of thalamo-cortical system, that is crucial for consciousness.

## Perceptual and physiological consequences of dark adaptation: a TMS-EEG study

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In this study we assessed changes in phosphene perception and Transcranial Magnetic Stimulation (TMS) - Evoked Potentials (TEPs) after light and dark adaptation. The primary aim was to link a direct neurophysiological correlate of cortical excitability (i.e. TEPs) to the subjective report (i.e. phosphene perception) in order to evaluate whether environmental light changing induced modifications in visual cortex excitability or only at retinal level, as previously reported. Ten young healthy participants underwent three conditions: baseline (environmental light), 30 minutes of Light Adaptation (LA) and 30 minutes of and Dark Adaptation (DA) in counterbalanced order. After each condition, we assessed the TMS-induced phosphenes perception by single pulse TMS over the visual cortex (V1) while 32-channels Electroencephalogram (EEG) was recorded. Coil position was maintained stable across conditions through a stereotaxic neuronavigation system. Phosphenes threshold was calculated through the method of constant stimuli, in which TMS pulses were delivered at different TMS intensities ranging from 46 to 76% of the maximal stimulator output. The participants were asked to report whether they perceived or not a phosphene after each TMS pulse. A Weibull function was fitted to phosphenes report for each condition and participant separately, in order to estimate the threshold and slope of the psychometric functions. Results confirmed that DA modulated

visual perception: the slope of the psychometric function after DA significantly increased ( $p < 0.05$ ) compared to LA and baseline, whilst the estimated threshold for phosphene perception did not change across conditions. A preliminary analysis of TMS-EEG data shows a reduction of TEPs amplitude after DA compared to LA, thus suggesting that a period of prolonged DA is able to decrease cortical excitability. This modulation could explain the reduction of sensitivity indexed by the increased slope of the psychometric function.