Descrizione dei titoli dei progetti di ricerca / Titles’ description of research projects:

1) **Gender differences in social cognition (supervisor: Adenzato Mauro)**

The ability to decipher information about the intentions and affective states of social partners is crucial for the implementation of appropriate behaviour during social interactions. This complex process is part of the so-called social cognition domain, defined as the ability to construct mental representations of the relations that exist between oneself and others and to flexibly use these representations to function effectively in one’s social environment. 

The main aim of the present study is to shed light on the presence of gender differences in social cognition, analysing both its affective and cognitive dimensions. In particular, the following components will be investigated: (1) ability to correctly identify and regulate one’s own emotions; (2) empathic capacities; (3) recognition of other’s emotions through dynamic facial expressions; (4) ToM, distinguishing between its affective (i.e., representation of other people’s affective mental states) and cognitive dimensions (i.e., understanding of other’s intentions and beliefs).

2) **Binge Eating Disorder treatment and fMRI outcomes (supervisor: Amianto Federico)**

The BED has earned its psychopathological dignity by becoming one of the three major Eating Disorders. Neuroimaging techniques allowed clinicians to have a better view on some neurobiological circuits and systems involved in psychiatric pathologies; but in relation to BED these techniques are still not enough applied to for comprehending neurobiological mechanisms on which this pathology is based and even less as measures that can help evaluating the possible efficiency of therapeutic protocols under a neurobiological point of view.

The aim of this study is about evaluating at T0 (at the baseline in the moment in which the diagnosis is taken into account) and at T1 (after multidisciplinary and integrated treatments) a panel of patients with BED, comparing them to obese controlled subjects and to healthy controlled subjects, looking for possible modifications under a neurobiological point of view after the treatment.
3) **Determinants of motor and cognitive phenotypes of ALS (supervisor: Chiò Adriano)**

Amyotrophic lateral sclerosis (ALS) is the most common motor neuron disorder of the adult life, characterized by the loss of motor neurons at spinal, bulbar and cortical level. Its cause is still unknown, with the exception of genetically determined cases, which account for about 10% of published series. One recent acquisition is the large phenotypic heterogeneity of the disease, encompassing cases with a predominance of either upper motor or lower motor degeneration, different degrees of bulbar function involvement, different levels of cognitive impairment, going from normal cognition to clear-cut frontotemporal dementia. The determinants of these different phenotypes remain largely unknown. This PhD project will take advantage from the large wealth of patients’ clinical, genetic, neuroimaging and neuropsychological data collected from the ALS Expert Center in the last decade to dissect and reconstruct the phenotypic concept of ALS using advanced bioinformatics and machine learning approaches.

4) **Biomarkers of body awareness in healthy subjects and brain-damaged patients (supervisor: Garbarini Francesca)**

The starting point of the present project is the concept of body ownership, i.e. the feeling that our body parts belong to us. Capitalizing on several results acquired in pathological context, in which body awareness is selectively impaired, the next questions is: can we objectively measure the subjective experience of body ownership? To this aim, the project will be focused on investigating possible biomarkers of self/other body discrimination, by using different techniques, such as fMRI, EEG and MEG in both brain-damaged patients and healthy subjects. The successful candidate should have a degree in Psychology, Neuroscience, Biomedical Engineering (or related disciplines) and should be highly motivated to work in a multidisciplinary team. Candidates with previous experience in using experimental techniques, such as EEG, fMRI and/or MEG, are strongly encouraged to apply. Programming competences (Matlab) as well as a background in body awareness and multisensory integration will be appreciated.

5) **Aberrant sensory encoding in Autism Spectrum Disorders (supervisor: Giustetto Maurizio)**

Children and adults with autism spectrum disorder (ASD) suffer from social isolation, cognitive deficits, compulsive behaviour, and somatosensory deficits, including impaired multisensory integration ability and altered sensitivity to pain. However, neither the neural mechanisms underlying tactile sensory processing deficits and nociception in affected individuals nor the relationship between somatosensory deficits and social behavior are understood.

The prospective PhD student will be engaged in studies of molecular, cellular and circuit mechanisms involved in encoding sensorial inputs. CNS areas such as primary sensory and motor cortices, relevant for sensorymotor processing, will be in mice modeling autism (Shank3-KO mice) and RTT (Mecp2- and CDKL5-KO mice). Circuit organization and plasticity will be evaluated adopting high resolution imaging techniques (e.g.: in-vivo 2-photon and confocal microscopy) combined with in-situ detection of receptor/scaffolding proteins and electrophysiological analysis.
6) Understanding the behavior and the emotional brain circuits that mediate cognitive and affective processes in animal models for depression and PTSD (supervisor: Gotti Stefano)

Post-traumatic stress disorder (PTSD) is a stress-related psychiatric disorder; PTSD share many of the physiological mechanism found in the major depressive disorder (MDD) literature, which is thought to result from traumatic events and multiple molecular mechanism. Both PTSD and MDD are more prevalent in males than in females, suggesting a role of sexual hormones. Furthermore, animal models highlighted the importance of neonatal environmental for the development of the capability to react to stress in later life events and the role of many neuroactive steroids implicated in the management of anxiety and stress. The aim of this project is to analyze the molecular mechanisms underlying MDD and PTSD, considering the behavioral changes in adult life of animal consequent to neonatal traumas (like maternal separation, MS) and the role of neurosteroids and gonadal hormones.

7) Evaluation of effectiveness and safety for medical cannabis in palliative care patients (supervisor: Leombruni Paolo)

Although greater attention was raised over the last decades regarding the clinical applications of medical cannabis, studies revealed controversial results. This dispute is due to biased research methodologies adopted (i.e. heterogenous samples, not comparable routes of administration), and to legislative restrictions limiting the medical cannabis use. Recent developments in Italian regulation, allow now the medical cannabis experimentation for various indications, including chronic pain, chemo/radio-therapy side-effects, fibromyalgia and in palliative care setting. Moreover, based on previous studies, the main activity exerted by cannabis may be not exclusive to physical component of pain but also related to emotional aspects and opioid side-effects attenuation.

This project relies upon the consideration that the decoction, as proposed by the national guidelines, is not useful because its low titration, and that standardized capsules could be more effective. Defining the correct dosage is of paramount relevance to obtain the optimal balance between effectiveness and safety, and promote tailored interventions and further studies.

8) Relationship of cell proliferation and apoptosis in the postnatal and aging brain (supervisor: Lossi Laura/Merighi Adalberto)

A Ph.D. position is available to study the regulation of caspase 3 (CASP3) activity in cerebellar development and synaptogenesis and its relationship with neuronal proliferation. The successful candidate will use organotypic cultures of newborn and adult mouse cerebellum and cortex, biolistic transfection, electrophysiological recordings and confocal microscopy to assess the relationship of CASP3 activation (Lossi et al. 2016 Mol Neurodegen 11:34) and cell proliferation, H2AX phosphorylation, and DNA damage response.

Required previous experience: work in vivo/in vitro on CNS from laboratory rodents (mouse, rat). Additional preferred skills: patch-clamp recording from acute cerebellar slices, neuronal transfection.
9) **Tackling the amyloid clearance pathway in sporadic Alzheimer disease models (supervisor: Lossi Laura/Merighi Adalberto)**

A Ph.D. position is available to study the intervention of neprilysin (NEP) and insulin-degrading enzyme (IDE) in the clearance of amyloid β as a disease-modifying therapeutic strategy in sporadic Alzheimer Disease (SAD). The project consists of Phases. Phase 1 comprises a series of experiments to synthesize the new derivatives/agonists of NEP and IDE and test them using medium throughput-screening platforms. Optimization will follow the results of the analysis of cell death, and CASP3 activation on forebrain (cortex, hippocampus) and cerebellar organotypic cultures from wild type and transgenic mice. Full screening of molecules of interest will be complemented by whole-cell voltage-clamp analysis of neuronal excitability (resting membrane potential, number of action potentials, and after-hyperpolarization); and voltage-dependent Ca2+ currents in hippocampal slices. These data will be of importance in excluding any adverse effect on synaptic homeostasis. Phase 2 consists of in vivo preclinical testing experiments on mouse models.

10) **Staging in bipolar disorder: from theory to clinical utility (supervisor: Maina Giuseppe)**

Psychiatry has recently begun to use staging models as a template to model the sequence of vulnerability, at-risk states, prodrome, onset, progression, and end-stage chronicity, and to link these to outcome and choice of specific treatments. The body of data on this topic in bipolar disorder is steadily increasing, refining its applicability to targeted and individualized diagnostic, prognostic and therapeutic domains. Biological elements thought to be operative in bipolar disorder include a genetic diathesis, physical and psychic trauma, epigenetic changes, altered neurogenesis and apoptosis, mitochondrial dysfunction, inflammation and oxidative stress. The aims of this research project are to: 1) explore progressive biochemical, neuroimaging and cognitive changes in the disease process and potentially stage-specific differences in response to pharmacological and psychosocial treatments; 2) identify specific targets that could be amenable to intervention and a focus for health services and providers.

11) **Behavioural and Psychophysiological correlates of aesthetic appreciation (supervisor: Neppi-Modona Marco)**

The aim of the research project is to investigate the neurocognitive bases of aesthetic appreciation. Recent research in the domain of Neuroaesthetics has demonstrated that aesthetic appreciation emerges from the interaction between bottom up –implicit- and top down –conscious- processes. Within this framework, aesthetic experience is considered as a complex cognitive function with sensory, attentional, motivational and mnestic components. The research project will collect behavioural (Response Times) and neuropsychophysiological (EEG and TMS) data in normal and brain damaged subjects during the aesthetic evaluation of visual and auditory computer generated neutral stimuli. Through the analysis of these behavioural and psychophysiological indexes it will be possible to investigate the relationship among aesthetic appreciation, fluency of processing and the spatio-temporal dynamics of the underlying brain activation. By this means, it will be possible to better understand whether and how aesthetic experience can 1) modulate attention and learning processes in normal subjects and 2) potentiate
cognitive rehabilitation in brain-damaged patients suffering from spatial attentional and/or representational deficits.

12) Neurogenesis in the brain parenchyma: acquisition of neurogenic competence in astrocytes (supervisor: Peretto Paolo/Luzzati Federico)
We have previously demonstrated that neuronal progenitors are activated in the mammalian striatum in both physiologic and pathologic condition, and that these cells belong to a population of astrocytes. Astrocytes show a heterogeneous repertoire of responses to diverse brain insults, including detrimental states, generally associated with neurodegenerative and infectious diseases, and pro-reparative states, enriched in diseases such as stroke or trauma. Interestingly, the activation of a stem cell potential in resident astrocytes is specifically associated to conditions stimulating pro-reparative states. Yet, the mechanisms underlying neurogenic competence acquisition and lineage progression in astroglia, as well as the fate and role of newborn neurons are still largely elusive. This project will thus investigate the regulation of astrocytes in pro-reparative states and their mechanisms of actions, with particular attention to their neurogenic transformation, in order to foster the endogenous reparative potential of the adult brain and revert harmful astroglial states.

13) Owning a body + Moving a body = Me? (supervisor: Pia Lorenzo)
Whether and how body ownership (i.e., “this body is mine”; Gallagher, 2000) and sense of agency (i.e., “this willed action is mine”; Jeannerod, 2003) interact in giving rise to the sense of self (i.e., “this is me”) is still highly debated.
The main aim of the present PhD project is pinpointing the anatomo-functional mechanisms subserving bodily self-consciousness by means of an interdisciplinary approach. Indeed, the classical neuropsychological technique will be combined with physiology, neuroimaging and immersive virtual reality.
The whole project will take place at the SpAtial, Motor and Bodily Awareness Research Group (University of Turin). Any suitable candidate shall have a degree in Psychology, Neuroscience or related disciplines. Previous experiences within the field of neuropsychology, cognitive neuroscience or experimental psychology are strongly encouraged. Basic methodological skills and/or ability in stimulus presentation software are appreciated.

14) Investigating intra and inter-hemispheric contributions to emotional processing using non-invasive brain stimulation (supervisor: Ricci Raffaella)
The cerebral cortex is surprisingly plastic. Non-invasive brain stimulation (transcranial Direct Current Stimulation or tDCS and Transcranial Magnetic Stimulation or TMS) can be used to modulate the activity of brain areas/structures to explore their causal role in perceptual and cognitive processes. In the present research project non-invasive brain stimulation will be used to investigate intra-hemispheric neural circuits and putative hemispheric specialization underlying emotional stimuli processing. Behavioral and/or cognitive effects of brain stimulation will be investigated in healthy individuals. Neuroimaging techniques (e.g. functional Magnetic Resonance Imaging, EEG) will be also employed to study changes in
brain activation associated with cognitive and behavioral outcomes. These studies will allow to test the predictions derived from different theoretical models of emotion processing and might provide relevant information for the design of effective interventions in clinical population.

15) How to consolidate spatial associative memories: a behavioral and EEG study (supervisor: Sacco Katiuscia)
The project has two main aims: 1) studying the formation and consolidation of spatial memories in healthy and brain-damaged patients; 2) developing new possible protocols to train subjects’ navigation abilities. Recent studies showed that hippocampal theta oscillation may have a pivotal role in associative memories. The present project, by capitalizing on this previous research, through a series of behavioral and EEG studies, will investigate spatial memories formation and consolidation. Learning processes will be observed in different experimental scenarios, where stimuli will be delivered at different luminance/amplitude frequencies. Crucially, this novel stimulation protocol, following a first phase of testing on a population of young healthy subjects, will be employed with MCI (i.e. mild cognitive impairment) patients to prevent further declines in cognitive abilities and possibly restore spatial memory consolidation.

16) The experience of chronic pain: the role of the emotional and cognitive components in its pathogenesis, maintenance and modulation (supervisor: Torta Riccardo)
Pain is defined as an unpleasant sensorial and emotional experience, described in function of a present or potential damage to tissue. Chronic pain is frequently associated with medical and surgical conditions, but it can be considered as a disease itself. According to the biopsychosocial model, chronic pain is a complex multidimensional phenomenon that significantly affects patients’ quality of life and in which physical, psychological and social factors interact each other. Emotional aspects i.e. anxiety and depression are highly associated to chronic pain, but also the cognitive processes, the behavioral reactions to nociceptive stimuli, the traits of personality, the cultural aspects, and the existential and spiritual meaning attributed to the pain-related suffering have shown to be strictly involved in the chronic pain experience. The aim of the project is to deeply analyze the role of the emotional and cognitive components in the pathogenesis, maintenance and modulation of the chronic pain.

17) Implementation of a Intervention System based on Mindfulness aimed at the prevention of depression in patients with cancer within NEVERMIND research project (supervisor: Ostacoli Luca)
The Nevermind project (NEurobehavioural predictiVE and peRsonalised Modelling of depressive symptoms durinNg primary somatic Diseases with ICT-enabled self-management procedures), funded by European Community, is born from several research centers in order to implement a model of care that helps to prevent, recognize and treat patients’ depressive symptoms related to the burden of the somatic disease. In recent years personal technology health systems for the management of chronic diseases have seen major developments.
These systems allow the monitoring of breath and heart rate variability and the continuity of care even at home, but they do not provide support for promotion of adaptive lifestyles and for prevention of adjustment disorders. The aim of this research project is to contribute to the development of a Smartphone supported model of care including a mindfulness training and healthy life styles programs that helps people suffering from cancer to prevent and treat depressive sympotms. The intervention program integrates 1 personal training and 1 group meeting and then will be supported by a smarphone based System which “learns” from the user developing a personalized training. It will be integrated in different steps of patients’ health care.

18) Physiological roles of the fatty acid elongase ELOVL5 in cerebellar Purkinje cells (supervisor: Tempia Filippo)
Long-chain fatty acids are a major component of neurons and of glial cells. Their composition in phopholipids affects membrane stiffness, making them necessary for the formation and maintenance of myelin, dendritic spines and axons. In addition, unsaturated fatty acids serve as precursors of signaling molecules like endocannabinoids and eicosanoids. ELOVL5 is enriched in Purkinje neurons and its loss causes cerebellar motor deficits. The aim of the project is to discover the functional role of ELOVL5 in such hypothesized functions: myelin formation and action potential conduction, membrane curvature in dendritic spines, generation of active messenger molecules important for the function of Purkinje cells. The techniques utilized for the study will be immunohistochemistry, single cell labeling to study dendritic spines, confocal microscopy, patch-clamp in cerebellar slices.

Gliomas are an unsolved problem and despite the best available therapies, prognosis remains poor. The mainstay of therapy is the maximal safe resection. Many studies have proved the correlation between the extension of resection (EOR) (more than 80% of the enhancing tumor) and the overall survival (OS) in High Grade Gliomas (HGG). Moreover, Duffau have proved, in Low Grade Gliomas (LGG), the possibility to obtain a supratotal resection thanks to the awake surgery. This technique gives the possibility to spare subcortical connections and to recovery contingent post-operative deficits. Indeed post-lesional neuroplasticity have been largely described in slow-growing tumors, but there are no evidences about it in the HGG. This project investigates the reliability of awake surgery to obtain the best onco-functional balance in patient with HGG. Potential neuroplasticity of brain in patients suffering HGG will be evaluated with functional neuroimaging and neurological/neuropsychological tests, with specific attention to speech tasks. The results will be analyzed and linked to patients’ survivals.