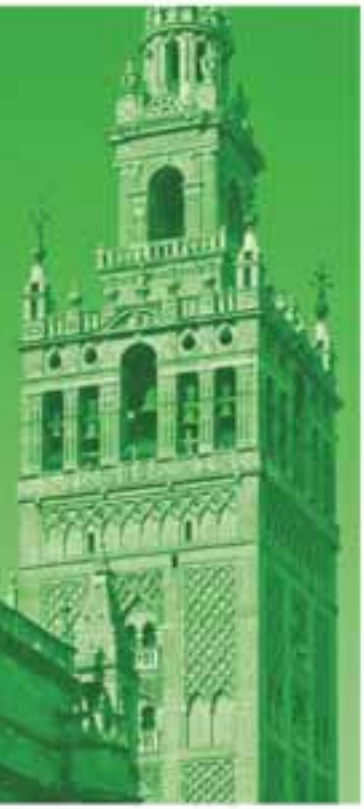

43rd European Brain and Behaviour Society Meeting

Seville (Spain)

EBBS

Abstracts

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43rd European Brain and Behaviour Society Meeting

Abstracts Plenary Lectures

ABSTRACTS
Plenary Lectures

L.1. Opening Plenary Lecture

AWARE OR UNAWARE: HOW DOES THE BRAIN DECIDE?

Alan Cowey[1]
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From being a neglected and derided backwater, explored only by 'fools', the nature of consciousness is now at the forefront of brain research. Theories of what makes us consciously, and selectively, aware abound. Common examples are: the sheer amount of activity in particular cortical areas; top-down pre-frontal activity targeted on different cortical areas; whether cortical activity in relevant cortical areas is in particular frequency bands, e.g. the gamma-band range; whether that cortical activity is phase-locked in neurons dealing with the stimuli of which we are aware; whether particular cortico-thalamic pathways are involved and necessary and whether some are irrelevant; whether the activity reaches or exceeds a particular duration. In an attempt to illustrate work on these ideas the talk will focus on neurological conditions where awareness is impaired or abolished. A prime example is 'blindsight', which is the paradoxical ability of patients with destruction of part of the primary visual cortex (V1) to detect, localise and discriminate between a variety of visual stimuli presented in the cortically blind visual field defect despite the fact that the patients deny seeing them. They claim either to be bewildered and therefore just guessing (pure blindsight) or to be experiencing a non-visual event (an amodal experience that guides them to a correct response (Type-2 blindsight). Blindsight has been studied by means of visual psychophysics to reveal its properties, by magnetoencepahlography (MEG), functional magnetic resonance imaging (FMRI), tractography by diffusion tensor imaging (DTI), pupillometry, reaction times, and more cognitive procedures like having the subject place bets on the correctness of his/her discriminatory response (post-decision wagering). In some rare instances all of these techniques have been used on the same patient. The results are intriguing. Finally, monkeys too have 'blindsight', which is especially helpful because most of our knowledge of the behaviour of single neurons and their connexions comes from studies of macaque monkeys in which parts or all of striate cortex (V1) have been removed or reversibly inactivated. Such monkeys can tell us a lot about awareness and its neural basis.

L.2. *Colegio de América* Special Lecture

CHANGING FEAR

Elizabeth Phelps[1]
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Studies of fear learning have demonstrated that the mechanisms of fear acquisition are shared across species and extend to the social learning of fear in humans. More recently, this research approach has been extended to techniques to diminish learned fear. In this talk I review how we can extend the basic neural mechanisms of fear acquisition and regulation identified in research in non-human animals to the human brain function. Specifically, I explore the neural systems mediating human how fears are diminished through extinction, emotion regulation and altering reconsolidation.

L.3.

BRAIN MECHANISMS FOR COMPUTING SPACE

May-Britt Moser[1]
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Self-location is represented by hippocampal and parahippocampal cells that are active at certain places in the environment. Grid cells, place cells and border cells are examples of such cells. In the first part of my talk, I will discuss fundamental properties of grid cells, including its topographical organization along the dorsal-ventral axis of the entorhinal cortex. Grid cells fire selectively at regularly spaced positions in the environment such that, for each cell, activity is observed only when the animal is at places that together define a repeating triangular pattern tiling the entire environment covered by the animal, much like the holes of a Chinese checkerboard. The scale of the grid map is topographically organized in that the spacing of the grid increases from the dorsal to the ventral end of medial entorhinal cortex. I will show that the organization of the grid map is modular, and that grid cells co-localize with other functional cell types such as head-direction cells and border cells. Together these cell types contribute to a dynamically updated metric representation of current location in the medial entorhinal cortex. Based on studies using a virus-mediated approach to selectively express photoresponsive channel proteins in entorhinal cells with projections to the hippocampus, I will suggest that grid cells, head direction cells and border cells all provide direct input to the hippocampus, with grid cells providing the principal contribution. The second part of my talk will deal with the representation of space in memory. An important difference between grid cells and place cells is the tendency for place cells to form orthogonal representations in different environments. This orthogonalization process is thought to depend on the formation of attractor states in recurrent neuronal networks. While several experimental observations are consistent with the presence of attractors in the entorhinal cortex and hippocampus, the dynamic processes supporting attractor dynamics, at the time scale of behaviour, are not well understood. I will show that, in response to an instantaneous transition between two familiar and similar spatial contexts, hippocampal CA3 networks undergo short periods of flickering between pre-formed representations before settling in on the representation most consistent with the new cue configuration, several seconds after the cue change. During the flickering period, convergence to each representation may take place within a single theta cycle and fully expressed representations may alternate at theta time-scale frequencies. The data suggest that, in CA3, pattern completion dynamics repeats within each individual theta cycle. The repetition may facilitate error correction, thus enhancing the discriminative power of the system in the presence of conflicting input cues from spatial representations in entorhinal cortex and stored representations within the hippocampus.

L.4. DANA Alliance Public Lecture

THE NEUROSCIENTIFIC REVOLUTION

Francisco J. Rubia[1]
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In the history of humanity one speaks of 3 revolutions: The Copernican revolution, which put to rest the notion that the earth is the center of the universe, the revolution of Darwin and his theory of evolution, which dethroned man from the center of creation, and the Freudian revolution, which stated that we are not in control of ourselves but that our behaviour is controlled by unconscious processes. Currently, however, we are facing a fourth revolution: the neuroscientific revolution. Neuroscientific knowledge is acquiring unprecedented importance, which can be observed in the fact that other classical disciplines add the prefix “neuro” to generate new disciplines which aim to apply knowledge from neuroscience to traditional subjects (i.e. neurophilosophy, neuroeconomics, etc). One needs to distinguish between an objective revolution, which is the result of recent advances in our knowledge of the nervous system, due to technological advances, from molecular biology to modern brain imaging techniques, and a subjective revolution that will transform our conceptions of the world and human being. Examples of the applications of objective findings are the use of neuroimaging techniques in the judicial system, in intelligence services, in business in relation to decision making, in the study of cognitive functions in healthy subjects, in the manufacturing of commercial products, and even in military services. We have entered what has been labeled the “neurosociety”. For some time the public’s attention was centered on possibilities brought about by the discovery of the genome and expectations of cure for degenerative disorders. Today this attention is focused on the potential discoveries in the area of neuroscience. There are many important mysteries to solve, such as the mystery of how nervous cell firing translates into the experience of consciousness and other cognitive functions. In other words, the most difficult problem in neuroscience is the qualitative jump between the objective and the subjective. However, the most important revolution is the so-called subjective revolution which will change the image we have of the world and of ourselves. Subjects such as the external reality, the Self, freedom, consciousness and spirituality are being studied with scientific methods thanks to the fact that neuroscience has overcome the Cartesian dualism that was responsible for the study of these issues within the disciplines of philosophy, psychology and even theology. The findings which so far have been made in these subjects already hint at another blow to human pride destroying many concepts we have of the world and of ourselves which are most likely completely wrong.

L.5. Elsevier BBR Lecture

DEPRESSION AND RESILIENCE: INSIGHTS FROM COGNITIVE, NEUROIMAGING AND PSYCHOPHARMACOLOGICAL STUDIES

Barbara J Sahakian[1]
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Unipolar depression is the leading cause for global burden of mental, neurological and substance use disorders (Collins, et al, 2011), affecting an estimated 121 million people worldwide. In addition to the enormous emotional burden to the individual and their family, depressive disorders cost an estimated £7.5bn in the UK alone and this figure is projected to rise by 62% by 2026 (McCrone et al, 2008). Mood disorders are unlikely to stem from aberrant function of a specific gene, brain region or cognitive process. Rather, the top-level phenotype (symptoms) should be seen as an end-point of underlying dysregulation of distributed networks and cognitive-emotional control processes. Cognitive abnormalities are core to depression as evidenced by the daily life experiences of patients with mood disorders and are integral to the diagnostic criteria for depressive episodes according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV). Indeed, these cognitive problems may impair performance of everyday functioning and prove the biggest barrier for rehabilitation and return to paid employment (Beddington et al., 2008). For example, affective processing and feedback sensitivity are likely contributors to negative impact on quality of life and everyday functioning in depressed patients. The results from cognition, neuroimaging and psychopharmacological studies indicate that general underlying processes such as negative attentional bias and abnormal response to negative or error feedback are core cognitive impairments in major depressive disorder (MDD) which may account for the broad-ranging cognitive deficits observed in MDD. Furthermore, results from event-related fMRI studies in unmedicated MDD patients suggest that disrupted top-down control by the prefrontal cortex of the amygdale underlies the hypersensitivity to negative feedback in MDD. Additional findings indicate the role of serotonin in the modulation of performance on tests of attentional bias and response to error feedback. It is concluded that negative attentional bias and abnormal response to negative or error feedback may be useful cognitive biomarkers in early detection of symptoms and monitoring of relapse in MDD and in assessing the efficacy of current and novel pharmacological and psychological treatments for MDD.

References:

- Beddington, J., Cooper, C.L., Field, J., Goswami, U., Huppert, F.A., Jenkins, R., Jones, H.S., Kirkwood, T.B.L., Sahakian, B.J., & Thomas, S.M. (2008). The mental wealth of nations. Nature, 455, 1057-1060.
- Collins, P.Y., Patel, V., Joestl, S.S., March, D., Insel, T.R., Daar, A.S., Bordin, I.A., Costello E.J., Durkin, M., Fairburn, C., Glass, R.I., Hall, W., Huang, Y., Hyman, S.E., Jamison, K., Kaaya, S., Kapur, S., Kleinman, A., Ogunniyi, A., Otero-Ojeda, A., Poo, M-M., Ravindranath, V., Sahakian, B.J., Saxena, S., Singer, P.A., Stein, D.J., Anderson, W., Dhansay, M.A., Ewart, W., Phillips, A., Shurin, S., & Walport, M. Nature, 475, 27-30.
- McCrone, P., Dhanasiri, S., Patel, A., Knapp, M., & Lawton-Smith, S. (2008). Paying -the price: The cost of mental health care in England to 2026. King's Fund Report. [Online] http://www.kingsfund.org.uk/publications

L.6. Frontiers in Behavioral Neuroscience Lecture

TINKERING WITH THE MOLECULAR MACHINERY OF LONG-TERM MEMORY IN CORTEX

Yadin Dudai[1]
[1] Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel.

While much has been learned in recent years about the molecular and cellular mechanisms of the memory encoding, consolidation and reconsolidation, rather little is known about the neuronal mechanisms that permit memory to persist over long periods of time. I will describe how transient inhibition of the atypical protein kinase isoform PKMzeta in the insular cortex of the behaving rat, by the use of a cell-permeable pseudosubstrate peptide, rapidly blocks long-term conditioned taste associations even several months after encoding, without affecting the ability to acquire new memories. Inhibition by competition with a dominant negative mutation of the enzyme has a similar effect. In contrast, overexpression of PKMzeta in the insular cortex enhances long-term memory long after encoding. The implication of these findings for models of maintenance and expression of long-term memory will be discussed.

L.7

SOCIAL EMOTIONS FROM THE LENS OF SOCIAL NEUROSCIENCE

Tania Singer[1]
[1] Department of Social Neuroscience, University of Zurich, Switzerland.

With the emergence of social neuroscience, researchers have started to investigate the underpinnings of our ability to share and understand feelings of others. After a definition of the concepts 'cognitive perspective taking', 'emotion contagion', 'empathy' and 'compassion' I will shortly revise the main results of neuroscientific studies investigating empathic brain responses elicited by the observation of others in pain and show how these empathic brain responses are modulated by several contextual and stimulus intrinsic factors such as perceived fairness or ingroup/outgroup membership. I will then show results of studies exploring the relationship between interoceptive awareness, empathy and pathologies such as Alexithymia and Autistic Spectrum Disorder (ASD). Furthermore, I will present data from a novel paradigm on empathy for pleasant and unpleasant touch allowing the investigation of the neural mechanisms underlying affective egocentric bias in adults. These data will be complemented with developmental findings showing age-differences in egocentric bias, social emotions such as envy and Schadenfreude as well as strategic decision making during childhood. These data will be discussed in lights of their relevance for recent models of social cognition.

L.8.

GENETIC AND ENVIRONMENTAL RISK MECHANISMS FOR SCHIZOPHRENIA

Andreas Meyer-Lindenberg[1]
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Multiple genetic and environmental risk factors for the multifactorial brain disorder, schizophrenia, have been identified through epidemiological and genetic research in the preceding decades. A major translational research strategy is to try and elucidate how these confirmed risk factors act on brain to increase risk for the disorder.

In this talk, we will review this strategy, using both genetic and environmental risk factors as examples. In genetic risk, we will focus on genome-wide identified single nucleotide polymorphisms in or near the genes ZNF8O4A and CACNA1C. In environmental risk, we discuss recent work relating urbanicity and migration status to risk for schizophrenia. Our data show that neural effects of epidemiologically validated risk factors can be elucidated in human brain that mirror intermediate phenotypes found in subjects with the illness and their relatives. Specifically, connectivity of lateral prefrontal cortex with striatum, midbrain and hippocampus can be shown to be impacted by genetic risk, and a medial prefrontal circuit regulating amygdala and be extended limbic system, previously implicated in the processing of negative emotion, can be linked to environmental risk factors. Taken together, this research begins to define a neurogenetic and neuroenvironmental risk architecture for schizophrenia that improves our understanding of the pathophysiology of the illness and may point the way to new treatment targets.

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Abstracts
Satellite Symposia

NEUROBIOLOGY OF TIME PERCEPTION: FROM NORMALITY TO DYSFUNCTION
Valérie Doyère (FR)
Argiro Vatakis (GR)
Elzbieta Szelag (PL)

The 'Neurobiology of Time Perception: from normality to dysfunction'satellite event is an emergence of the COST ISCH Action "TIMELY" (Time In MEntaLactivitY: theoretical, behavioral, bioimaging and clinical perspectives). The meeting explores time perception in humans and animals from different disciplines from philosophy to psychology and neurosciences. The meeting is composed of four main themes: A. Concepts will cover philosophical issues on timing and meta-cognitive processes in prospective timing; B. Constructed Time will introduce issues on multisensory synchrony perception and temporal recalibration of audiovisual stimuli, as well as research methodology and new results on perceptual learning in time perception; C. Neuropathology and Rehabilitation will open the discussion in terms of neuropathology in humans and animal models by covering timing in an animal model of Huntington disease and the application of temporal training in neuropsychological rehabilitation; D. Networking and Modeling will emphasize on the different models of timing by comparing the Scalar Expectancy Theory and the Learning-to-Time hypothesis, reviewing evidence on the striatal beat-frequency models of interval timing, and introducing incorporation of time in ACT-(R)[$_{ES1}$].

TIME PERCEPTION IN META-COGNITIVE PROCESSES
Dan Zakay[(1)]
[(1)] Department of Psychology, Tel Aviv University, Tel Aviv, Israel.

Meta-cognitive processes are taking place continuously and are used for monitoring and regulating cognitive behaviour. It is argued that prospective time perception processes are part of these meta-cognitive processes. Prospective time judgments are used as important parameters in processes which result in meta-cognitive judgments such as feeling of knowing, rapid don't know judgment, familiarity judgments and feeling of retrospective confidence in the accuracy of knowledge retrieved from memory. Other judgments in which prospective time estimation play an important role are causality judgment and control of human communication. It is claimed that as part of the general meta-cognitive processes prospective time judgments of brief durations are taking place automatically and on a continuous basis. The above mentioned arguments will be demonstrated and a general model which integrates time perception with meta-cognitive processes will be presented.

NEWTONIAN AND PRIGOGINEAN CONCEPTS OF TIME: PHYSICAL, PSYCHOLOGICAL AND CULTURAL PERSPECTIVES
Anna D. Eisler[(1)]
[(1)] Department of Psychology, Stockholm University, Stockholm, Sweden.

Physical time is defined on the basis of periodic events in the outside of the world. The theories about the physical world in general, and space and time in particular, seem often to be conflicting elaborations of human conceptions of time and space. The present paper considers mainly Newton´s and the Prigogine´s theories and perspectives about physical time and about the concept of time as seen in the psychology, the sense of time, namely, 1) the biological and 2) the cognitive clock. Furthermore, the relation between psychological (subjective, perceived) time and universal objective (physical) time is dealt with. Psychological time depends not only on the biological time sense, but also on learning, cognitive ability, experience, personality and the physical, social and cultural environment. The psychological and cultural aspects of the concept of time are taken up in several contexts and general implications will be presented from my empirical research.

***TEMPORAL RECALIBRATION:*ASYNCHRONOUS AUDIOVISUAL SPEECH EXPOSURE EXTENDS THE TEMPORAL WINDOW OF MULTISENSORY INTEGRATION**
Argiro Vatakis[(1)]
[(1)] Department of Natural Language and Knowledge Extraction, Institute of Speech and Language, Athens, Greece.

An examination was conducted regarding whether monitoring asynchronous audiovisual speech induces a general temporal recalibration of auditory and visual sensory processing. Participants monitored a background (adapting) continuous audiovisual speech/music stream. This background stream was superimposed over target simple or complex audiovisual stimuli. The background speech/music stream could either be presented in synchrony, or else with the auditory stream lagging by 300 ms. A dual task was completed: temporal order judgments regarding whether the target auditory stream or the target visual stream occurred first; monitored the background stream for targets. In two experiments, the targets were composed of simple auditory and visual stimuli with a speech/music background. The results showed that, while monitoring desynchronized speech/music, participants required a longer interval between the auditory and visual streams in order to perceive their temporal order correctly, suggesting a widening of the temporal window for audiovisual integration. Given that this outcome could have been driven by the use of speech as the background stimulus, an investigation was conducted on the consequences of monitoring asynchronous audiovisual speech on the temporal perception of simultaneously-presented vowel-consonant-vowel stimuli. Similar results were obtained suggesting that the consequences of adapting to asynchronous speech extends beyond the case of simple stimuli and can even affect the perception of more complex speech stimuli.

NEURAL BASIS OF MULTISENSORY SYNCHRONY PROCESSING

Toemme Noesselt[1]
[1] Department of Neurology, Otto-von-Guericke University, Magdeburg, Germany.

In our everyday life many events stimulate more than one of our sensory modalities and our brain needs to integrate or segregate the incoming information. Temporal proximity is one key factor which determines how information should be handled. In this talk I will focus on the neural basis of audiovisual synchrony processing in the human brain when confronted with simple non-semantic stimuli. In particular, the involvement of putative unisensory cortex in multisensory temporal perception will be reviewed. In addition we will focus on the temporal dynamics of these integration processes, and we will discuss whether temporal integration occurs early or late in the human brain. Finally, we will review recent animal studies on audiovisual temporal perception and compare those results with the outcomes of human studies.

PERCEPTUAL LEARNING IN RESEARCH OF TIME PERCEPTION

Daniel Bratzke[1]
[1] Department of Cognitive and Biological Psychology, University of Tübingen, Germany.

Perceptual learning is a prominent research paradigm to elucidate the mechanisms underlying the perception of time. In this paradigm, participants are usually trained to discriminate the duration of a target stimulus against the duration of a standard stimulus. For example, the target and the standard could be auditory stimuli of 220 msec and 200 msec duration, respectively. After several training sessions, participants are probed with different stimuli (e.g., stimuli with different standard durations, different sensory modalities, or different intensity characteristics) in order to examine whether the acquired performance on temporal discrimination transfers to these newly experienced stimuli. Transfer effects in this paradigm are employed to address the question whether or not range-specific timing mechanisms exist and whether timing mechanisms are amodal or not. In this talk, I will briefly review and evaluate previous and current research and the conclusions that have emerged so far from this paradigm. I will also critically review previous research methods of perceptual learning and make some suggestions on research designs, psychophysical measures of discrimination performance, and statistical issues, which may help to improve future research.

TIMING IN AN ANIMAL MODEL OF HUNTINGTON DISEASE: PRESYMPTOMATIC INDICATOR OF ALTERATION IN PREFRONTO-STRIATAL PROCESSING

Valérie Doyère[1]
[1] Center Neurosciences Paris-Sud, CNRS University Paris-Sud, Paris, France.

Prefronto-striatal circuits are thought to play a critical role in temporal processing. Huntington's disease (HD) is a neurodegenerative disease linked to an extended CAG repeat expansions within the coding region of the huntingtin gene, and results in a progressive neurodegeneration of the GABAergic medium-sized spiny neurons of the striatum. Cognitive decline and psychiatric disorders precede motor symptoms. Thus, we sought whether disruption of temporal processing in the supra-seconds range may be one of the presymptomatic impeded cognitive functions that precede motor deficits. We used a transgenic rat model of HD with 51 CAG repeats which closely resembles the human late onset HD phenotype. Supra-second temporal bisection tasks and in vivo electrophysiological studies show disruption of temporal processing related to prefronto-striatal dysfunction at a presymptomatic stage. Our results suggest that disrupted executive function may be linked to dysfunctional fronto-striatal network at a presymptomatic stage of HD. Timing, as a presymptomatic marker of the disease, may therefore be a valid tool for testing efficiency of candidate therapeutics in the next future.

THE APPLICATION OF TEMPORAL TRAINING IN NEUROPSYCHOLOGICAL REHABILITATION: PSYCHOPHYSICAL, ELECTROPHYSIOLOGICAL AND NEUROIMAGING EVIDENCE

Elzbieta Szelag[1]
[1] Laboratory of Neuropsychology, Polish Academy of Sciences, Nencki Institute of Experimental Biology, Poland.

Timing provides a structure for human cognition. A developing consensus among researchers is that cognitive deficits are characterized by timing deficits. Furthermore, research indicates that specific temporal training has a great impact in neurorehabilitation. In our studies we focused on following questions: (1) can the temporal training reduce comprehension deficits in aphasic patients; (2) can temporal training ameliorate cognitive function in healthy volunteers? (3) are there any changes in brain activation following this training? The specific temporal training was applied in aphasic patients, healthy elderly volunteers or young students. In all these groups we observed significant improvements in cognitive function after temporal training. In aphasics, ameliorated auditory comprehension was evidenced. In elderly volunteers improvements were observed in associative learning, memory span, vigilance and divided attention. In young students improvements in associative learning, alertness, divided attention, short-term and working memory were accompanied by electrophysiological correlates (increased amplitude of evoked potentials 330–600 ms after stimulus presentation observed in timing task). Using fMRI, we found in young students additional activation after temporal training in right prefrontal cortex (BA 10) in timing task. These results indicate that timing studies are crucial for neurorehabilitation.

TIME, MEMORY, AND CONTEXT: SET OR LET? PLACE YOUR BET

Armando Machado[1]
[1] Instituto de Educação e Psicologia, Universidade do Minho, Portugal.

I will contrast two models of how animals learn to time arbitrary events in the range of seconds to minutes. The first, Scalar Expectancy Theory or SET, is an information-processing model that has influenced significantly the psychological and neurobiological studies of timing. SET accounts well for an impressive range of results obtained with animals and humans, children and adults, under normal and abnormal conditions; it is therefore a strong and worthy null hypothesis. The alternative hypothesis is the Learning-to-Time, or LeT, model. In contrast with its rival, LeT stresses the distributed, context-dependent nature of temporal memories. In this talk I will describe the structure of each model and how it accounts for simple temporal learning tasks. Then I will summarize some experiments that tested the models' different conceptualizations of temporal memory. Finally, I will argue that the results strongly suggest that we reject the null hypothesis – perhaps like all memory, temporal memory also is context dependent.

NEUROBIOLOGICAL MODELS OF INTERVAL TIMING

Warren Meck[1]
[1]Department of Psychology and Neuroscience, Duke University, USA.

The ability of the brain to process time in the seconds-to-minutes range is a fascinating problem given that the basic electrophysiological properties of neurons operate on a msec time scale. Neuropsychological studies of subjects with damage to the basal ganglia have indicated that these structures play an important role in timing and time perception. Parkinson's patients, for example, show evidence of a slowed internal clock and the "coupling" of durations stored in temporal memory when tested off of their dopaminergic medication. These studies have shown that the normal cognitive functions of the basal ganglia are heavily dependent upon dopamine-regulated neuronal firing in the cortex and striatum. Moreover, the electrophysiological properties of medium spiny neurons within the basal ganglia suggest that networks of these cells may serve as a coincidence detector of cortical and thalamic oscillatory/ beat frequency input in order to provide the basis for duration discrimination. Recent electrophysiological data obtained from the prefrontal/cingulate cortex and the anterior dorsal striatum indicate that spiny neurons are able to encode specific durations in their firing rate in a "perceptron-like" manner. These findings correspond well with functional neuroimaging data and lend support to striatal beat-frequency models of interval timing.

AN INTEGRATED THEORY OF PROSPECTIVE TIME INTERVAL ESTIMATION: THE ROLE OF COGNITION, ATTENTION AND LEARNING

Hedderik van Rijn[1]
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A theory of prospective time perception is presented that extends existing theories by incorporating it as a module in an integrated theory of cognition, allowing predictions about attention and learning. First, a time perception module is established by fitting existing datasets (interval estimation, bisection and impact of secondary tasks on attention). The module is subsequently used as a part of the ACT-R architecture to model a new experiment that combines attention, learning, dual tasking and time perception. Finally, the model predicts learning and attention in a new experiment. The model fits and predictions demonstrate that the proposed integrated theory of prospective time interval estimation explains detailed effects of attention and learning during time interval estimation.

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Abstracts Symposia

S1A

HORMONAL REGULATION OF LEARNING AND MEMORY PROCESSES

Acquisition and consolidation of stressful memories is largely modulated by cortisol (humans) and corticosterone (rodents) which are released from the adrenal glands after exposure to a stressful learning event. In interaction with other stress hormones, corticosterone promotes successful behavioral adaptation via two receptors: the high-affinity mineralocorticoid receptor (MR) and the lower affinity glucocorticoid receptor (GR). In this symposium we will highlight recently identified molecular mechanisms that underlie the effects of stress hormones on synaptic transmission, synaptic plasticity; and learning and memory. We focus a.o. on AMPA receptor trafficking – which is critically involved in synaptic transmission and plasticity – is rapidly but also persistently regulated by stress hormones.

S1A.1

HORMONAL REGULATION OF LEARNING AND MEMORY PROCESSES

Benno Roozendaal[(1)]
[(1)] University Medical Center Groningen, The Netherlands.

Extensive evidence indicates that stress hormones released from the adrenal glands are critically involved in memory consolidation of emotionally arousing experiences. Epinephrine or glucocorticoids administered after exposure to emotionally arousing experiences enhance the consolidation of long-term memories of these experiences. Our findings indicate that adrenal stress hormones influence memory consolidation via interactions with arousal-induced activation of noradrenergic mechanisms within the basolateral complex of the amygdala (BLA). In turn, the BLA regulates memory consolidation via its efferent projections to many other brain regions. In contrast to the enhancing effects on consolidation, high circulating levels of stress hormones impair memory retrieval and working memory. Such effects also require noradrenergic activation of the amygdala and interactions with other brain regions. These apparently dual effects of glucocorticoids on memory consolidation versus memory retrieval and working memory appear to be related in terms of function and neurobiological substrate. The BLA is a key structure in a memory-modulatory system that regulates, in concert with other brain regions, stress and glucocorticoid effects on these different memory functions.

S1A.2

AMPA RECEPTORS AND LEARNING AND MEMORY PROCESSES

David M. Bannerman[(1)], *R. Sprengel*[(2)], *P.H. Seeburg*[(2)], *D.J. Sanderson*[(1)]
[(1)] Department of Experimental Psychology, University of Oxford, UK.
[(2)] Max Planck Institute for Medical Research, Heidelberg, Germany.

The development of glutamate receptor subunit-specific knockout mice has revealed important dissociations between different psychological processes within the domain of learning and memory, and has provided important clues about the neurobiological mechanisms that underpin these processes. Genetically modified mice lacking the GluA1 AMPA receptor subunit display impaired spatial working memory (e.g. win-shift maze tasks like the radial maze) but normal long-term associative spatial reference memory (e.g. discriminating between always baited and never baited arms on the radial maze, finding a fixed location, hidden escape platform in the watermaze). An explanation for these findings is that win-shift performance reflects a non-associative short-term habituation process in which animals choose more novel arms in preference to more familiar options. In contrast, spatial reference memory acquisition, on tasks like the Morris watermaze, is likely to reflect associative, long-term memory processes. These results are potentially accommodated by Wagner's Dual process model of memory in which short and long-term mechanisms exist in parallel and, under certain circumstances, can compete with each other. Thus, GluA1$^{-/-}$ mice lack a short-term memory or a sense of familiarity for recently experienced spatial and non-spatial stimuli, but as a consequence, these stimuli remain surprising and so should be better able to form long-term associations. Indeed, under certain conditions long-term memory is enhanced in GluA1$^{-/-}$ mice. Taken together, these results support a role for GluA1-containing AMPA receptors in short-term habituation to recently presented stimuli, and are consistent with a role for these receptors in modulating the attentional intensity or perceived salience of stimuli. These results have important implications when considering the neurobiological substrates that might underpin spatial working memory performance on win-shift maze tasks, and on the role of AMPA receptor trafficking in memory processes. They also have implications for the use of these spatial working memory tasks in rodents as models of human working memory processes.

S1A.3

HORMONAL REGULATION OF HIPPOCAMPAL AMPA RECEPTOR DYNAMICS AND FUNCTION

Harm. J. Krugers[1]
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Memories for emotionally arousing and stressful events are generally well retained. The memory enhancing effect of stress and emotion is largely modulated by hormones, peptides and neurotransmitters which are released during and after exposure to stressful conditions. One of the core reactions in response to a stressful situation is the rapid activation of the autonomic nervous system (ANS), which results in the release of norepinephrine in the brain. In addition, stressful events stimulate the hypothalamus–pituitary–adrenal (HPA) axis which slowly increases the release of glucocorticoid hormones from the adrenal glands. An import question that remains to be addressed is which molecular mechanisms mediate the effects of stress-hormones on learning and memory. The current view of how memories are formed is that neurons are activated during the learning process thereby changing synaptic communication. AMPA type glutamate receptors mediate most of the fast excitatory synaptic transmission in the brain and controlling the number of synaptic AMPA receptors on the postsynaptic membrane is an essential mechanism to regulate synaptic transmission, synaptic plasticity (such as long-term potentiation and long-term depression) and memory formation. Data will be presented showing that glucocorticoids regulate synaptic insertion of AMPA receptors, AMPA receptor mobility, and activity-dependent recruitment of synaptic AMPA receptors as well as synaptic plasticity in the hippocampus. Second, some of the molecular mechanisms that are involved in synaptic regulation of AMPA receptors by glucocorticoids will be addressed. Finally, recent data suggests that AMPA receptors are dynamically regulated by glucocorticoids interacting with other neuromodulators such as norepinephrine. These effects of glucocorticoids on excitatory synapses may explain how these hormones can facilitate the storage of relevant information.

S1A.4

STRESS-INDUCED REGULATION OF WORKING MEMORY AND AMPAR FUNCTION IN THE PREFRONTAL CORTEX

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Corticosteroid stress hormones have a strong impact on the function of prefrontal cortex (PFC), a central region controlling cognition and emotion, However, the molecular and cellular mechanisms underlying the action of stress remain elusive. We found that AMPAR-mediated synaptic transmission in PFC pyramidal neurons was strongly potentiated in rats exposed to acute stress, while it was markedly reduced in rats exposed to repeated stress. Concomitantly, the surface expression of AMPAR subunits was significantly increased in acutely stressed animals, while it was decreased in repeatedly stressed animals. The effect of acute stress depended on the induction of serum- and glucocorticoid-inducible kinase (SGK) and the activation of Rab4, while the effect of repeated stress relied on activation of glucocorticoid receptors and the subsequent enhancement of ubiquitin/proteasome-mediated degradation of GluR1 subunits. Moreover, cognitive processes controlled by PFC, such as working memory or recognition memory, was enhanced in acutely stressed animals via a SGK-dependent mechanism, and was impaired in repeatedly stressed rats. These results suggest that stress, by converging on AMPARs, exerts a biphasic effect on PFC, which may underlie the adaptive or maladaptive changes induced by acute or chronic stress, respectively.

S1B

INDIVIDUAL DIFFERENCES IN COGNITION AND BEHAVIOR, DO THEY INTERFERE WITH MEASURING?

Whereas we are all aware that we as humans are different individuals, do we take this into account when we measure behavior in rodents? We know that different strains of mice have distinct behavioral profiles, but do all mice of the same strain act similarly? The answer is, no, not all rodents act or react similarly when faced with the same problem or situation. Not only are there individual differences in behavior within a group of mice (even when they are genetically identical), these differences are not constant, for instance they can change depending on the time of day or can change with age. Furthermore, differences between individual mice can be compounded by variance in the genetic background of transgenic animals. While these confounds should be taken into account when planning behavioral measurements, careful analysis of these differences can increase our understanding of behavioral functioning.

S1B.1

HOW SMART IS MY MOUSE? PITFALLS IN MEASURING BEHAVIOR

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An important pitfall in the study of animal and human behavior is to confound the measurements that we make with the underlying processes. For example, it is impossible to measure processes or states like learning and memory or anxiety directly. What we are measuring are certain movements or reactions and from these we infer that these processes or states occur. This inferential process is of necessity subjective and may be biased by our own expectations. As an example, an elevated plus maze is often used to “measure anxiety” in rodents. However, what is measured is not anxiety, but the amount of time that an animal spends on the open or closed arms. From this measurement we then infer conclusions about the anxiety level of the animal. The validity of the test therefore hinges on the assumption that the proportions of time spend on the open and closed arms are exactly correlated with anxiety levels. If for some reason this assumption is not fulfilled, the validity of the test disappears. In this presentation, I will show several examples of tests that are supposed to measure a certain process, but perhaps do not do so. I also present work from my laboratory on the genetic dissection of learning behavior in the radial maze. In a radial maze we presumably observe the ability of an animal to orient itself in space. In a series of experiments we have tested whether this is indeed the case. These experiments also show the power of using genetically-defined animals from the many different inbred strains that are nowadays available for the urgently-necessary cross-validation of many behavioral tests.

S1B.2

INTER-INDIVIDUAL VARIABILITY IN A MOUSE MODEL FOR AUTISM: THE IMPORTANCE OF THE GENETIC BACKGROUND

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Autism spectrum disorder (ASD) is a developmental disease with multi-genic bases and a highly complex symptomatology, for which effective treatments are still lacking. Several mouse models for ASD have been proposed in the last years: these include the Fmr1-KO mouse, a model for Fragile X syndrome, i.e., a human disease that is highly associated to ASD. Multiple studies have evaluated the presence of ASD-like behavioural deficits in the Fmr1-KO line, but mixed results were reported. It has been suggested that differences in the genetic background on which the Fmr1 deletion is implemented may contribute to these discrepancies. In this presentation data from our and others’ laboratories are summarized and discussed to evaluate the validity of this hypothesis. Results from the analysis of ASD-like behaviours in Fmr1-KO mice of multiple backgrounds are presented, as well as some pharmacological studies. The case of the Fmr1-KO model is then used as an example to highlight the crucial importance of taking into account the role of the specific genetic background in mouse models of neuropsychiatric disorders.

S1B.3

TIME OF DAY AND INDIVIDUAL DIFFERENCES

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To study the effect of day-time on inter-individual variability in response to innate anxiety, 2-, 12- and 20-months aged male Wistar rats were exposed, over four consecutive days, to a battery of tests based on novelty stress (open field, elevated-plus maze, light-dark and object novelty test) in the morning (8:30-10:00), early afternoon (13:00-14:30) and late afternoon (18:30-20:00). In all the tasks, anxiety-related exploratory behavior, general exploratory activity, grooming activity and elimination behavior were measured. Although there are differences between tasks, we can conclude that: 1) the time-of-day effects on tested behavior decrease with the age, 2) the correlation between the tested parameters, in each task, highly depend on the age and the period of the day, 3) the highest general and anxiety-like explorative behavior were found in young animals, and 4) the end of the light phase seems to be the less stressful period of the day. Furthermore, independently of the age and time of the day, only few animals expressed consistent level of anxiety, suggesting great individual variability in response to different novel situations.

S1B.4

INDIVIDUAL DIFFERENCES, DO THEY CHANGE WITH AGING?

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Whereas we are all aware that we as humans are different individuals, do we take this into account when we measure behavior in rodents? We know that different strains of mice have distinct behavioral profiles, but do all mice of the same strain act similarly? The answer is, no, not all mice act or react similarly when faced with the same problem or situation. Not only are there individual differences in behavior within a group of mice (even when they are genetically identical), these differences are not constant, for instance they can change depending on the time of day or they change with age. While these confounds should be taken into account when planning behavioral measurements, careful analysis of these differences can increase our understanding of behavioral functioning. Individual differences within and between groups of mice are a significant problem, for instance when testing a young group of mice in the water maze, there is at least one that does not swim, but freezes, and floats. On the other hand, when all animals have learned the task, they have learned different strategies to find the platform. One set does as it is "supposed to do", it knows where the platform is and "directly" swims to the location. On the other hand, the other set of animals uses a search strategy, searching for the platform in looping circles at the correct distance from the wall. The consequence of these strategies is that the first group will perform well in the probe trial but the second will not. In younger mice the majority of mice is normal, with a smaller group of searchers, in contrast, older groups of mice tend to have much higher numbers of mice that search for the platform, and who do not know its exact location compared to young mice. Similarly, whereas young mice have no problem learning the water maze task, older mice take a much longer time to learn the task, but they do learn!

S2A

FEAR-BASED ANTICIPATION: ONTOGENESIS, NETWORKS AND MECHANISMS

Knowledge about temporal relationships between significant events and memory for durations underlie the building of a general knowledge base and the development of adaptive anticipatory behaviour. The neural circuits and mechanisms sustaining the encoding and memorization of temporal information are still a matter of debate. Timing in the seconds to minutes range may be mediated by networks involving the striatum, the prefrontal cortex and the dopaminergic systems. Recent data suggest that the amygdala also processes and stores the temporal architecture of the emotional associations. The proposed symposium brings together experts in timing and in the neurobiology of animal fear memory. Convergence of behavioural and neurobiological approaches from a developmental perspective both in humans and animals will help delineate the critical phases at which timing capacities are formed, and the neural networks and mechanisms involved in temporal memory, prelude to anticipatory behaviour.

S2A.1

ROLE OF THE AMYGDALA IN MEMORY OF TEMPORAL STRUCTURE IN FEAR CONDITIONING

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When a conditioned stimulus (CS) is paired with an unconditioned stimulus (US) the CS then comes to elicit fear responses. The subject not only learns that the CS predicts the arrival of the US, but also the time when the US is expected to arrive (US-ETA). Here, we asked whether the amygdala, which is crucial for fear conditioning, processes the CS-US interval. We used a reconsolidation paradigm in rats to test whether a change in the CS-US interval is detected and triggers the updating of fear memory. Rats with bilateral cannulae in the lateral amygdala (LA) were submitted to a strong auditory fear conditioning training paradigm. The next day, they were presented with a single CS-US trial with the same CS-US interval or an interval different than during training. Immediately, a protein synthesis inhibitor or vehicle was infused into the LA. The next day, freezing to the CS was tested. The long-term memory test indicated that, in this strong training condition, a protein synthesis dependent reconsolidation was triggered in the amygdala only when the CS-US interval was different, either earlier or later than during initial training. No loss of fear memory was observed in the animals for which the CS-US interval was the same in the test as in training. The same result was obtained with weak training (2 CS-US training trials). Rats exposed to a different CS-US interval during retrieval showed an increase in the number of Zif-positive cells. These results suggest that a change in US-ETA triggers an updating of the fear memory in the amygdala through a reconsolidation process, and rats can learn the time of US arrival in very few trials. Thus, not only the association between the CS and US is learned but also the US-ETA. Moreover, a change in the expected time of the US arrival triggers plasticity mechanisms in the lateral amygdala. LA is involved not only in the acquisition and storage of the CS-US association but also in temporal properties of the association.

S2A.2

IT'S TIME TO FEAR: TIME INTERVAL ENCODING IN ODOR FEAR CONDITIONING

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Time perception is crucial to survival, and interval timing guides fundamental behaviors in humans and other animals. In Pavlovian fear conditioning, an initially neutral stimulus acquires the ability to predict the arrival of an aversive unconditioned stimulus at a fixed time interval. Accumulating evidence indicates that temporal relations between events are also encoded. However the neural networks underlying the encoding and memory of time interval learning are poorly understood. The aim of the present study was to explore this question using a fear conditioning paradigm where animals received 10 pairings of a 20-s odor with a mild (0.4-mA) footshock during the last second of the odor, using a 4 min intertrial interval. Although the fear response is characterized by a large repertoire of behavioural and physiological responses, freezing is often the sole parameter used for quantifying fear. Interestingly, respiratory changes and ultrasonic vocalizations (USV) can also occur during fear response. We implemented an experimental procedure allowing the simultaneous recording of respiration, USV and freezing in rats. The data show that after only a few odor-shock pairings, an anticipatory response develops, characterized by a decrease in respiratory rhythm and an increase in USV emission just prior to shock delivery. In order to identify the structures involved in this time encoding, we used high temporal resolution microdialysis to monitor amino acids changes in amygdala and olfactory cortex during odor fear acquisition. We observed an increase in amino acids in the amygdala during the first odor-shock pairing, while in the olfactory cortex increases were detected for each pairing, and were also observed after the end of training, at the predicted time of occurrence of an anticipated trial. This suggests that the olfactory cortex might be involved in interval timing. Current experiments are being carried out to identify some of the other structures involved in time interval encoding in odor fear conditioning.
Funding: ANR-07-NEURO-O48 Memotime; CNRS PICS program; PUF program Emotion & Time; COST ISCH Action TD0904 TIMELY

S2A.3

THE NEUROBEHAVIORAL DEVELOPMENT OF FEAR-BASED ANTICIPATION IN INFANT RATS

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Time is fundamental to learning and memory and for the elaboration of temporal maps that permit the proper evaluation of ongoing and past events. For example, in the fear conditioning paradigm, a conditioned stimulus (CS) is paired with an unconditioned stimulus (US), so that the CS comes to elicit conditioned responses. What is learned is not only that the CS predicts the arrival of the US, but also when the US is expected to arrive. It is not known from what age rat pups are able to memorize the duration of the interval separating two events. Here we explore the age at which rat pups begin to anticipate the arrival of a shock and which brain areas are correlated with its emergence. To assess the development of timing we used an olfactory fear conditioning paradigm in rats during infancy and adulthood. Pups were conditioned in a 45 min session: Paired (peppermint odor-0.5mA shock), Unpaired, and Odor-only. The odor (peppermint) was presented for 30 sec with the 0.5mA shock overlapping with the last sec of the odor presentation. An intertrial interval (ITI) of 4 min was used. The ontogeny of timing was assessed through behavioral observations during the odor presentation over the 10 trial conditioning session. In parallel, using 14C 2-deoxyglucose autoradiography, we assessed the neural activity of brain areas associated with timing in adulthood, including the amygdala, piriform cortex and striatum. Results suggest that 12 day old pups show no signs of timing, while weaning aged pups (PN23) appear to show some signs of timing. Assessment of 2-DG autoradiography suggests that emergence of timing is associated with the functional activation of an expanded learning circuit.

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S2A.4

EMOTION AND TIME PERCEPTION: THE DIFFERENCES AS A FUNCTION OF THE TEMPORAL TASK

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A number of studies have reported that the perception of an arousing emotional stimulus, such as an angry face, results in temporal overestimations, which are probably due to the speeding up of an internal clock-like system. The aim of the present study was to examine whether this emotional effect can be generalized to all temporal tasks irrespective of the underlying cognitive processes involved in each task. Five different temporal tasks involving the presentation of neutral and angry faces were therefore tested: bisection, generalization, verbal estimation, production and reproduction. Our results showed an overestimation of time for the angry compared to the neutral faces in the temporal bisection, verbal estimation and production tasks but not in the temporal generalization and reproduction tasks. Moreover, the results obtained in the temporal verbal estimation and production tasks suggest that this temporal overestimation of the angry faces was associated with relatively more accurate estimates. The involvement of both arousal and cognitive mechanisms in the effect of emotional facial expressions on time perception is discussed in the light of the differences in the impact of the same emotional stimulus as a function of the temporal task considered.

S2B

NEURAL PROCESSING OF COMMUNICATION SOUNDS ACROSS THE SPECIES

Speech is a recent evolutionary adaptation, but spoken language must have emerged from neural mechanisms at least partially available in nonhuman animals. Investigating the neural processing of species-specific vocalizations across several species can thus help us to understand the neural mechanisms underlying human speech perception. The presenters at this symposium will illustrate the latest findings on how the brain processes vocal communication signals in various models including human beings (Katharina von Kriegstein), non-human primates (Chris Petkov), rodents (Robert Liu) and songbirds (Colline Poirier). The speakers will relate their findings to results from other species to highlight the common neurobiological processes shared by humans and animals for auditory communication.

S2B.1

NEURAL MECHANISMS OF HUMAN COMMUNICATION

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One of the most important sensory signals in human communication is auditory speech. Traditionally it is assumed that specialisation for processing of speech can only be found beyond the primary sensory cortices. In this talk I will present evidence challenging this assumption and argue that the brain works differently to obtain its robustness in auditory-only communication. I will present findings that modulation of subcortical sensory structures (i.e. auditory thalamus) serves the processing of specific features of speech sounds and is behaviourally relevant for speech recognition. The findings will be integrated into a predictive coding account of thalamo-cortical interaction in auditory communication.

S2B.2

OF MICE AND MOMS: AUDITORY PROCESSING OF BEHAVIORALLY RELEVANT VOCALIZATIONS

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Species-specific acoustic communication requires a receiver to interpret a vocalization's biologically important message in order to act. What happens in the brain as the meaning of such a message is acquired? What enables this meaning to be maintained in the brain so that future experiences with the sound can be correctly interpreted? Our studies of the ultrasonic communication between mouse pups and mothers are helping to shed light on these questions of how behaviorally relevant auditory signals are processed in the mammalian auditory system. Mouse pups emit ultrasounds when they are isolated from their nest. Mothers recognize the behavioral relevance of these calls and search out these pups to retrieve them to the nest. However, pup-naïve virgin females do not prefer pup calls over a neutral sound, while virgins actively caring for pups (cocarers) do, suggesting that experience facilitates behavioral call recognition in this model. Our earlier studies established electrophysiological correlates of this recognition within the auditory cortex of anesthetized and awake animals by comparing call-evoked responses in mothers to pup-naïve virgins (Liu et al, 2006; Liu and Schreiner, 2007; Galindo-Leon et al, 2009). By studying cocarers at the same post-weaning time point at which we recorded in mothers, we have now found that the prolonged nature of the mother's auditory cortical correlate of pup call recognition after pup-rearing ends depends on more than just the experience with pups, and likely involves hormonal influences. Hence, this model system is beginning to reveal how both extrinsic experiences and intrinsic physiological states work together to establish the long-term auditory memories of behaviorally relevant vocalizations in a mammal.

S2B.3

NEURAL PROCESSING OF BIRDSONG: NEW INSIGHTS FROM fMRI

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Songbirds share with humans the ability to learn their vocalizations. Both juvenile birds and human infants form long-term memories of adult vocalizations and subsequently try to match their own vocalisations to these memories. The first phase thus depends on auditory perception of the adult vocalization while the second one depends on auditory perception of the own vocalization via auditory feedback. The neural bases of both types of auditory experience are still poorly understood. In a first fMRI experiment, we have shown that bird's own song selective responses, suspected to support the auditory feedback, emerge at a very early stage of the ascending auditory pathway, at the midbrain level (Poirier et al., 2009). Interestingly, these selective responses were restricted to the right auditory midbrain nucleus, whereas the left nucleus was found selective for conspecific song recognition. In a second fMRI experiment, we have now found that the right auditory midbrain nucleus is not only selective for the bird's own song but also for the tutor song, the adult song that the birds previously used as a model to develop their own vocalization. This result suggests that the right auditory midbrain is (part of) the neural substrates for tutor song and bird's own song memories, which are activated when the adult birds are exposed to these songs. In support to this interpretation, the strength of bird's own song and tutor song selectivity was found positively correlated with the strength of song learning, measured by the amount of song that juvenile birds copied from their tutor. Altogether, these results suggest that the right auditory midbrain nucleus plays a crucial role in vocal learning. Since this structure is well conserved among vertebrates, we hypothesize that the central nucleus of the inferior colliculus, the homologue region in human beings, could play a similar role in speech acquisition.

S2B.4

RELATING HUMAN AND NONHUMAN PRIMATE BRAIN FUNCTION FOR COMMUNICATION

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Traditionally, neurobiological work on human communication has focused on the unique aspects of speech acoustics and perception and on how the human brain has specialized for processing speech. More recently, human brain imaging ('neuroimaging') work has evaluated the 'stimulus-bound' aspects of speech and there has been greater interest in the non-linguistic processing of voice information. These approaches are much easier to relate to the processing of the acoustical structure in animal communication sounds. To obtain new insights into the relationship of the systems processing communication signals in primates, we summarized the results from several neuroimaging studies in human and nonhuman primates. While some differences across the species remain, our observations suggest a general cross-species correspondence in how the primate temporal lobe analyzes species-specific vocalizations. A striking correspondence is seen in the function of a region in the right anterior-temporal lobe of both humans and macaque monkeys, where sensitivity to the acoustics associated with voice identity (of, respectively, different human speakers and monkey callers) is observed. We have recently been using macaque fMRI-guided electrophysiology to understand how neurons might support the fMRI activity response associated with voice-sensitivity and have potentially identified 'voice cells' in the primate brain. In summary, the accumulating human neuroimaging evidence for, in particular, the processing of voice acoustics reveals interesting correspondences to the neuroimaging evidence available in nonhuman primates. Upon a proposed functional homology, the study of nonhuman animals can be extremely informative with regards to understanding the neurophysiological bases of the fMRI activity response involved in the processing of communication signals.

S3A

COMPLEXITY IN THE RESPONSE TO STRESS: THE ENVIRONMENT AND THE INDIVIDUAL

Life stress can be an important risk factor for health in some, but not all, individuals leading to metabolic or psychiatric disorders. The symposium will address the mechanisms through which individual differences in neurobiology and behavior, with a special emphasis on the response to stress, emerge during development and the role of the adult environment in revealing these differences. We will focus on studies performed on laboratory rodents, which illustrate the role of the early environment in shaping stable variation in gene expression and behavior. This discussion includes maternal effects and the influence of peer interactions during infancy and the juvenile period of development. In addition, we will discuss the role of gene-environment interactions and epigenetic mechanisms in mediating the variation in behavior that emerges across the life span and accounts for stable individual traits in different species, ranging from rodents to non-human primates.

S3A.1

STRESS AND MEMORY SYSTEMS: FROM EARLY LIFE TO ADULTHOOD

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Stress and the effect of the glucocorticoid hormones on the brain have been envisioned as being mainly negative. This view emerged principally from animal and human studies showing that stress early in life and in adulthood or cumulative exposure to high levels of glucocorticoids can have a detrimental impact on hippocampal morphology and function: atrophy of dendrites and memory impairments were reported. Why some individuals develop cognitive deficits after stress, while other individuals improve their cognitive performance under similar adverse conditions is still unresolved. In animal models, various manipulations of the mother-pup interaction have produced lasting changes in neuroendocrine and emotional reactivity, as well as cognitive ability. Duration and frequency of maternal separation, the level of maternal care behaviour appears to differentially affect physical and mental health and well-being throughout life. Data from rodent studies (rats, mice) on immediate as well as long-term effects of disturbed mother-pup interactions will be discussed in relation to the degree of “matching” with environmental demands in later life. The ‘Predictive Adaptation Hypothesis’ therefore presents a conceptual framework to examine the role of glucocorticoids in understanding individual phenotypic differences in stress-related behaviours over the lifespan.

S3A.2

STRESS RESPONSE IS CONTEXT-DEPENDENT: THE ROLE OF EARLY EXPERIENCES IN SHAPING THE ADULT REACTIVITY TO THE ENVIRONMENT

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The early environment takes part in shaping the adult individual and its response to stressors. Starting from the seminal work by Seymour “Gig” Levine, several studies performed in animal models provided a clear picture of this phenomenon. Early experiences, as those associated with the handling procedure in rodents (15 min separation from the mother each day during the first two weeks of life), lead to a more efficient coping response to stress at adulthood. However, limited information is available on the role of the quality of the early experiences in determining the adult response to stress. Aim of the present study was to investigate whether early experiences, affecting primarily a selected behavioral domain, have specific effects on the adult coping response to stressors involving only such domain. To this purpose, we have exploited a novel experimental paradigm that provides the developing mouse pup with a highly stimulating social experience: the Communal Nest (CN). CN consists in a single nest where three mothers keep their pups together and share care-giving behavior from birth to weaning and mimics the natural ecological niche of the mouse species. CN pups, compared to mice reared in standard laboratory conditions (SN), received higher levels of maternal behavior, such as arched-back nursing and licking and grooming, and more frequent interactions with peers. At adulthood, we investigated the coping response to two stressors of different quality: social and physical. Results showed that, compared to SN, CN mice are more resilient to social stress, displaying reduced anhedonia and lower corticosterone levels. However, no difference in the response to physical stress was found between the two groups. The improved resilience to social stress was associated with more elaborate social competences, which in turn arise from the exposure to the early social enrichment provided by the CN, that involved both the interaction with the mother and with the peers. Overall, these findings illustrate that the quality of the early experiences determine selective vulnerabilities to different stressors at adulthood.

S3A.3

UNRAVELING THE MOLECULAR BASIS OF INDIVIDUAL STRESS VULNERABILITY

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Chronic stress is widely regarded as a key risk factor for a variety of diseases, including depression. Genetic predispositions are thought to interact with environmental demands such as chronic stress. However, the molecular mechanisms underlying individual susceptibility or resilience to chronic stress are still poorly understood. Corticotropin-releasing hormone (CRH) and CRH receptor 1 (CRHR1) are key candidate genes for modulating the risk for stress-related disorders. Polymorphisms in the CRHR1 gene have been shown to increase the risk for depression in traumatized individuals. To test the interaction of the CRH-CRHR1 system with individual stress vulnerability, we used two different approaches. First, we utilized animals with a forebrain specific deletion of the CRHR1 gene or with a conditional overexpression of CRH in combination with an exposure to early life stress. We could show that deletion of CRHR1 in forebrain regions was protective for a number of molecular, structural and behavioural consequences of early life stress, while CRH overexpression mimicked the phenotype of early life stress. In a second approach, we identified a mouse single nucleotide polymorphism (SNP) in the CRHR1 gene, which affects individual stress vulnerability. Risk allele carriers of this SNP display an enhanced CRHR1 expression, increased anxiety and a more robust and longer lasting response to chronic social stress exposure. Taken together, our results strongly support the important role of the CRH-CRHR1 system in stress vulnerability and depression.

S3A.4

GENETIC AND ENVIRONMENTAL MODULATORS OF RISK AND RESILIENCE IN RODENTS AND PRIMATES

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In humans, both genetic and experiential factors shape individual vulnerability to neurological and psychiatric illnesses. However, the extent and modalities of such interaction is far from being characterized. To answer these questions, animal models have been generated targeting experiential factors with robust effects that are relatively consistent across species. Procedures that disrupt or alter mother-infant or other early social relationships both in rodents and non-human primates have been instrumental in understanding the long-term consequences of the developmental context on adult stress reactivity and social functioning. This is certainly true for studies involving maternal separation and deprivation in mammals. Among the many neurobiological factors involved in brain development and function, neurotrophins, such as Brain-derived neurotrophic factors (BDNF) appear as good candidates for mediating long-term effects of experience on brain function as they are known to play a major role during brain development. We have recently characterized a single nucleotide polymorphism (SNP) in rhesus macaques, which results in a Val to Met transition in the pro-BDNF domain, similar to a well described variant in the human gene. We subsequently tested the hypothesis that peripheral levels of BDNF, which is involved in the response to stress and in the pathophysiology of anxiety and depression, might be differentially affected in a non-human primate model of early adverse rearing in a genotype-dependent manner. Males and females rhesus macaques reared either with their mothers (MR), in peer-only groups (PR), or in a “surrogate/peer-reared” (SPR) condition with limited peer interactions, were used as experimental subjects. Results from these studies indicate that a SNP, which results in a Val to Met transition in the pro-BDNF domain, is present in rhesus macaques and is able to affect BDNF peripheral levels in a gene x environment manner in non-human primates. Implications for such context-dependent changes in the expression of key genes affecting brain development and plasticity will be discussed.

S3B

NON INVASIVE TRANSCORTICAL ELECTRICAL STIMULATION

Non-invasive brain stimulation with electric currents (transcranial current stimulation, tCS) was recently re-introduced as a tool to modulate cortical excitability in the human brain. Depending on stimulation parameters, acute neuromodulation and longlasting neuroplastic effects on cortical excitability can been achieved. As a stand-alone technique, and in combination with non-invasive measures of brain activity (such as EEG and fMRI), it offers a potent new technique for studying human cortical function. Recently considerable progress has been made in understanding the mechanisms underlying the effects of tCS on neural excitability: in vivo animal studies and models of the interactions between applied electrical fields and neuronal systems are reviewed. Hitherto, tCS has been used in a rather empiric fashion, but the multifaceted approach presented in this symposium offers the realistic expectation of neuromodulation precisely controlled in time and space; a novel multichannel tCS/EEG device that exploits recent advances is presented.

S3B.1

COMBINING NON-INVASIVE BRAIN STIMULATION USING tCS WITH NON-INVASIVE BRAIN ACTIVITY MEASURES (SUCH AS fMRI AND EEG)

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Non-invasive brain stimulation with electric currents (transcranial current stimulation, tCS) was recently re-introduced as a tool to modulate cortical excitability in the human brain. Depending on stimulation parameters, acute neuromodulation and longlasting neuroplastic effects on cortical excitability can been achieved. Most commonly, trancranial direct current stimulation (tDCS) has been employed. Anodal tDCS is thought to cause slight depolarization of the membrane potentials of superficial cortical neurons. Such stimulation has been associated with increased excitability in motor and visual cortices. Cathodal tDCS is thought to hyperpolarize membrane potentials; such stimulation has been shown to decrease performance in tasks whose neural substrates include the stimulated cortex. Transcranial alternating current stimulation (tACS) may interact with physiological cortical rhythms to alter concurrent behaviours. As a stand-alone technique, tCS is being increasing used in experimental and clinical settings. However, the combination of tCS with non-invasive measures of brain activity (such as EEG and fMRI) offers a potent new technique for studying functional networks in the human cortex.

S3B.2

EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) ON CORTICAL ACTIVITY: INSIGHTS FROM COMPUTATIONAL MODELS

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The use of transcranial Current Stimulation tCS (either direct tDCS or alternating tACS) has considerably increased both in clinical and research studies as this non-invasive method was shown to modulate the activity and performance of the brain. Although many applications of tCS have been investigated over the two past decades, the exact mechanisms by which externally-applied fields influence the activity of neuronal populations in the cerebral cortex are not well described yet. Better understanding the impact of tCS on neuronal systems is fundamental and may lead to substantial improvement of stimulation devices and protocols, for both diagnostic and therapeutic purposes. The objective was to investigate how a neuronal assembly is affected by the electric field induced by tDCS, and how its response, as reflected in local field potentials (LFPs), relates to the applied electric field parameters. Methods: We elaborated a macroscopic neurophysiologically-relevant computational model of the somatosensory cortex. This neuronal population model i) can reproduce sensory evoked potentials as recorded in the rabbit sensory cortex in response to air-puff stimulation on the whisker pad and ii) accounts for the influence of tDCS on the mean membrane potential of subpopulations of neurons (main cells and interneurons). Results revealed that feed-forward inhibition must be included in the model for accurate simulation of actual EPs (peaks and latencies). In addition, we also investigated the “differential” effects of externally-applied fields on pyramidal cells and interneurons. Interestingly, we found that the features of simulated EPs became closer to those of real EPs when externally-applied fields also affected interneurons. In particular, under anodal tDCS condition, more realistic EPs could be obtained when pyramidal cells got depolarized and, simultaneously, slow (resp. fast) interneurons became de- (resp. hyper-) polarized. Finally, results suggested that geometrical characteristics of interneurons may explain observed changes in EPs and that modeling efforts can provide insights into the - less understood - behavior of non principal cells under tDCS.

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S3B.3

MODELLING THE SPATIAL AND TEMPORAL CHARACTERISTICS OF THE ELECTRIC FIELD IN TRANSCRANIAL STIMULATION

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In transcranial current stimulation (tCS), a weak electric current is applied to the head through two or more electrodes. The current source automatically adjusts the potential difference between the electrodes so that the current intensity reaches the desired value, typically 1 mA. The electric field in the brain alters the neuronal membrane potential thus modulating the neuron's activity. The effect of the applied electric field on the membrane potential depends on the magnitude of the electric field as well as on the relative orientation of the electric field and the neuron. We have developed a realistic model of a human head based on MR images, with an accurate representation of the cortical sheet and other surfaces separating five different tissues. This computational model was used to calculate the electric field on the cortical surface and throughout the brain. It showed a significant effect of the convoluted cortical geometry and of tissue heterogeneity on the field distribution, with considerable differences from the predictions of a spherical head model. The normal component of the electric field was high in narrow regions at the bottom of the sulci under the electrode and not on the crown of the gyri. The tangential component was largest on the crowns of the gyri between the electrodes. We also used this model to study the effect of electrode size on the field's focality. In tCS, the current intensity is most often constant in time (transcranial direct current stimulation or tDCS). Sinusoidal currents (transcranial alternating current stimulation or tACS) are being increasingly used due to possible frequency-specific effects. For slowly varying stimulus waveforms, such as those currently used in tCS and transcranial magnetic stimulation (TMS), the temporal variation of the electric field follows exactly that of the stimulator output at all points in the head, i.e., the spatial distribution of the electric field is the same as in tDCS and its amplitude is modulated by the stimulus waveform everywhere. We will describe some of the results on the electric field distribution in a realistic head model that were mentioned above.

S3B.4

NEW TECHNOLOGIES FOR DELIVERING MULTIFOCAL TCS IN MAN

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Advances in transcranial brain current stimulation (tCS) will play a key role in neuroscience research, diagnosis and clinical applications. HIVE (a FET Open EU project) is exploring new stimulation paradigms to design, develop and test a new generation of more powerful and controllable non-invasive brain stimulation technologies. Present tCS technologies suffer from poor focality and unknown spatial distribution of the generated electrical fields, making the effects of stimulation non-specific, hard to reproduce and interpret. To address this, the project has developed improved electric field and multi-scale neuron-field interaction models, and is currently carrying out experiments in humans and animals. Based on this work, we have developed a tCS multisite transcranial current stimulation device (MtCS) implementing online EEG feature extraction for visualization and control. This tCS device has novel characteristics: it is multichannel, portable and wireless; it uses EEG-like electrodes; it allows for the independent electrical current control of each electrode in terms of intensity, direction, frequency and phase. In particular, although it can be used as a coherent multichannel tDCS/tACS/tRNS system, arbitrary waveforms can also be input by the user. In addition, the system provides visualization of the generated electric fields and currents and it can capture and transmit EEG. EEG features extracted online can be used to tune stimulation parameters. These features include power spectra, connectivity maps and cortical and tomographic maps in different bands. The entire system is wirelessly controlled using a standard laptop. In this paper we provide the motivation and derived requirements for this device, an overview of its design and features and discuss future steps.

S4A

IT TAKES TWO TO TANGO - SPECIALIZATION AND COOPERATION OF THE TWO CEREBRAL HEMISPHERES IN HUMANS AND OTHER ANIMALS

Cerebral lateralization represents a core feature of information processing in vertebrate brains that impacts cognitive capacities. But lateralization cannot be successful without effective interhemispheric crosstalk. The symposium addresses the interplay between specialization and cooperation of the hemispheres combining structural, functional, developmental and evolutionary research in two outstanding models: humans and birds. Westerhausen will present recent data on the coupling of structural development of the corpus callosum and language lateralization in children. Hausmann will review his work investigating the role of sex hormones onto interhemispheric crosstalk and resulting gender differences in functional lateralization and cognitive strategies. Manns will present recent data from pigeons demonstrating that the ability to integrate information of both hemispheres for problem solving is not dependent on a corpus callosum but on a lateralized functional architecture of the brain. Regolin will present an overview about her work with chicken showing how hemispheric lateralization enables social cognition providing a comparative evolutionary view.

S4A.1

CALLOSAL STRUCTURE AND LATERALIZED SPEECH PERCEPTION: LONGITUDINAL DEVELOPMENT IN CHILDREN FROM THE AGE OF 5 TO 8 YEARS

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The maturation of the corpus callosum and the establishment of an efficient interaction between the cerebral hemispheres is of crucial importance in the developing functionally lateralised brain. Accordingly, altered maturation of the corpus callosum has been linked to developmental disabilities and psychiatric disorders, such as dyslexia, autism, or schizophrenia. Behavioural studies of inter-hemispheric integration indicate a critical age period for these maturational processes between the age of 6 and 10 years. At the beginning of this period the children's performance pattern in task measuring behavioural laterality and interhemispheric transfer appears to be comparable to the pattern found in subjects with callosal agenesis. However, towards the end of this period children yield results similar to those typically found in adults. The present talk will present longitudinal behavioural and structural magnetic-resonance imaging data which were collected by following a cohort of 20 children through this critical age period. In a speech discrimination task – based on dichotic presentation of consonant-vowel syllables – it was found that with increasing age the children's performance is increasingly determined by phonological aspects (voicing) of the syllables. Parallel to these functional changes, the children showed a continuing increase in thickness in most subregions of the corpus callosum, except for the isthmus subregion. Interestingly, correlating indices of structural and functional development revealed that children whose isthmus decreased in thickness, exhibited an increase in inter-hemispheric information transfer. Conversely, children exhibiting an increase in isthmus thickness showed a decrease in information transfer. Taken together, the above results indicate a refinement or re-organisation process of the callosal connections to optimise the neuronal communication between the developing cerebral hemispheres. Since axons running through the isthmus subregion mostly inter-connect the temporal lobes the changes might reflect the development of sound and speech processing. Furthermore, the observed effects temporally coincide with the children's enrolment into school so that it can be speculated that the present findings are related to the beginning literacy education.

S4A.2

SEX HORMONAL MODULATION OF INTERHEMISPHERIC CROSSTALK

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Hemispheric asymmetries are a basic principle of functional brain organization in humans and many other species. However, the degree of hemispheric asymmetries shows inter-individual differences and dynamically changes within relative short time periods. For example, it has been shown that hemispheric asymmetries are sex specific: While they are relatively stable in men, they change during the menstrual cycle in women, suggesting that sex hormones play an important role in modulating functional brain asymmetries. Sex hormones have indeed powerful neuronal actions in the brain and affect the interaction between functionally linked cortical areas within and across cerebral hemispheres. However, the underlying mechanisms are still not fully understood. It is unlikely that sex hormones selectively affect one hemisphere. Here it is suggested that sex hormones modulate interhemispheric interaction via the corpus callosum due to their neuromodulatory properties, which could diminish cortico-cortical transmission and thus reduce hemispheric asymmetries. Menstrual cycle-related dynamic fluctuations in functional cerebral asymmetries and interhemispheric crosstalk have been shown to be a useful experimental model to investigate the activating effects of sex hormones on functional connectivity in the brain. Besides a better understanding of sex hormonal effects on cognitive brain functions, this research may also contribute to addressing the question of whether sex differences in cognitive brain functioning truly exist and where they originate from.

S4A.3

HEMISPHERIC CROSSTALK IN A NATURAL-SPLIT BRAIN: THE AVIAN CASE

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Cerebral lateralization represents a core feature of information processing in vertebrate brains. But separation of function is presumably only advantageous when commissural systems that efficiently exchange and integrate information between both half brains are present. We address this problem by analyzing hemispheric cooperation in pigeons since their visual system is functionally and structurally lateralized in response to asymmetrical visual light stimulation. Recent data from our lab suggest that the ability to transfer and integrate hemispheric-specific information for problem solving is not dependent on a corpus callosum but on a lateralized functional architecture of the brain. We investigated information transfer in the visual system by training pigeons in a color discrimination task whereby each eye learned to discriminate a different color pair. Because of the total crossing of the optic nerves, occlusion of one eye restricts visual input primarily to the hemisphere contralateral to the seeing eye resulting in a pair of known and unknown colors for each eye/ hemisphere. A superior performance of the right eye in discriminating the unknown color pairs indicated a better information transfer to the left hemisphere. This can be explained by a stronger bilateral input from the ascending visual processing stream. But transection of the inhibitory mesencephalic commissural system significantly decreased the right eye performance in discriminating the unknown pairs only. Thus, information flow between the hemispheres is controlled by the mesencephalic commissures, which specifically enhance information transfer to the left hemisphere. Performance of dark-incubated pigeons suggests that the pattern of lateralized modulation develops in response to embryonic light stimulation. In order to analyze whether information is not only exchanged but also integrated, we confronted pigeons with problems that require knowledge from both hemispheres. These experiments demonstrated that normal but not dark-incubated pigeons were able to integrate information learnt separately with each hemisphere to solve a transitive reasoning task. Accordingly, asymmetrical visual experience enables hemispheric integration in the pigeon's visual system. However, in mean none of the hemispheres alone were successful in combining hemispheric-specific information to adopt transitive inference logic. This indicates that hemispheric integration only occurs after activation of both brain halves by ascending visual input. In sum, asymmetrical embryonic light stimulation does not only induce lateralization of the pigeon's visual system but also affects the efficiency of interhemispheric crosstalk and as a consequence, cognitive capacities.

S4A.4

HIGHER COGNITION IN A LATERALISED, CHICK, BRAIN

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Sophisticated cognitive abilities characterize social species whose members live in groups establishing stable hierarchies. These animals need to recognize other individuals and to have the capacity to assess their own (or their conspecifics') status. To this purpose, very advantageous for the individual would be the ability to deduce one's status on the basis of the observed interactions between other individuals. This can be obtained using a form of logical reasoning. We investigated the ability to master transitive inference learning in a bird species which forms social hierarchies, the domestic chick, in order to determine if this may be related to the possession of a lateralized brain, and if this ability is performed differently in the two hemispheres. Brain lateralization has in fact been linked to the selective pressures associated with social life. Lateralization was manipulated by exposing vs. non exposing eggs to light before hatching as light exposure modulates the development of lateralization of some visual functions. Chicks with strong (Light-incubated, Li-chicks) or weak (Dark-incubated, Di-chicks) lateralization were trained for food reinforcement to discriminate stimulus pairs and peck at the reinforced stimulus in each pair (es. A+ B-; B+ C-; etc), in order to build a hierarchy of five stimuli (A>B>C>D>E). Chicks were subsequently tested on stimulus-pairs never experienced before, in particular, as a test of transitivity the novel pairing BD was used (the expected correct response being B). As a control test of successful associative learning the non-transitive novel pairing AE was used (the expected correct response being A). Li-chicks performed the discrimination BD better than did Di-chicks. Moreover, lateralized chicks using their left eye only (right hemisphere) during test showed a better performance than did right eye-only (left hemisphere) chicks on the BD task. Females also tended to perform better than males. Results demonstrate that chicks with lateralized brain hemispheres show greater inference and this is under right hemisphere control, the brain hemisphere that is dominant in social interactions.

S4B

ADENOSINE RECEPTORS AS THERAPEUTIC TARGETS IN BRAIN DISORDERS

This symposium covers recent studies undertaken in animal models and humans revealing the actions of adenosine and related drugs in cognition and memory. We will particularly focus on various pathological situations such as ageing, psychiatric disorders and neurodegeneration. The presented data will highlight the promising potential of adenosine or adenosine receptor ligands as therapeutic agents in several brain disorders. We will cover the latest developments in the field and discuss novel strategies for intervention. The quality of the speakers, including younger as well as more established researchers, constitutes a major focus of attraction in the field of adenosine-based therapies. Their diverse backgrounds and broad range of expertise (molecular, behavioural and clinical) were critical aspects that guided our choices.

S4B.1

ADENOSINE A_{2A} RECEPTORS IN THE HIPPOCAMPUS: IMPLICATIONS IN AGEING AND STRESS

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Maternal separation is known to induce permanent changes in the central nervous system in adulthood, being associated to increased predisposition to chronic depression and anxiety. We hypothesized that these stress-associated effects could be an aggravating factor in situations of pre-existing cognitive decline, such as in aging. Our recent data show that stress induced in early-life has a long lasting impact on anxiety-related behavior and memory. The findings clearly indicate that a chronic stress, such as maternal separation, spans until old life and may exacerbate age-associated cognitive deficits. This is the first time that a link between early-life stress and age-related effects were demonstrated both at a neuronal level and in animal behaviour. We are now focused on unraveling the molecular mechanisms implicated in the observed deficits, which is of major importance for the identification of potential therapeutic approaches which could be beneficial in reversing the observed damages. It is still unknown the extent to which A_{2A} receptors are involved in the long-term, irreversible, effects of early life stress. There are, however, compelling evidences for a role of hippocampal A_{2A} receptors in stress-induced modifications related to cognition, thus opening a potential window for therapeutic intervention. Here we submitted rats to the maternal separation model, evaluated the long lasting molecular, electrophysiological and behavioural impairments at adult age. We then assessed the therapeutic potential of blocking endogenous activation of A_{2A} receptors, by administering a selective antagonist, KW 6002, orally for one month to stress-impaired animals. We report that the blockade of A_{2A} receptors was efficient in reverting the behavior and electrophysiological impairments induced by MS. This effect is associated with the reestablishment of the HPA-axis function, since both the plasma corticosterone levels and glucocorticoid expression pattern returned to physiological-like status after the treatment.
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S4B.2

ROLE OF A_{2A} RECEPTORS IN NEURODEGENERATION: FROM HUNTINGTON'S DISEASE TO TAUOPATHIES

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A_{2A} receptors are G-protein coupled receptors largely expressed in the central nervous system by neurons and glial cells. They are seen as a potential target in neurodegenerative disorders through their particular ability to modulate synaptic function and neuro-inflammation. However, whether they may represent a valuable target in Huntington's (HD) and Alzheimer's (AD) diseases, two proteinopathies affecting respectively the striatum and the hippocampus, remain unclear so far. In this context, we have obtained data supporting that A_{2A} receptor blockade would lead to an opposite outcomes in both disorders. Pharmacological and genetic blockade of A_{2A} receptor were found deleterious in phenotypic and transgenic mouse models of HD. We particularly observed that A_{2A} knockout worsened survival and motor function in the N171-82Q transgenic model. In accordance, in a retrospective study realized in 80 HD patients from the Huntington French Speaking Network, we found -after adjustment on CAG repeat length, tobacco and alcohol consumptions- that patients exhibiting higher consumption of caffeine (>190mg/d) -a non-selective A_{2A} receptor antagonist- had an earlier age at onset. Conversely, we obtained experimental data supporting a beneficial effect of A_{2A} receptor blockade against AD-like Tau pathology. Specifically, we found that A_{2A} receptor knockout prevented from memory defects, Tau hyperphosphorylation and hippocampal inflammation in the THY-Tau22 transgenic model mimicking the Tau-side of AD. This appears particularly relevant since cognitive deficits in AD are well correlated with the spatio-temporal progression of Tau pathology in the brain of AD patients. In conclusion, depending on the neurodegenerative context, the potential of A_{2A} receptor blockade is different. Complexity of relationships between underlying pathophysiological mechanisms and A_{2A} receptors makes its targeting questionable in HD while this approach deserves further investigation in AD field.

S4B.3

PROTECTIVE EFFECTS OF A_{2A} RECEPTOR BLOCKADE IN B-AMYLOID INDUCED DEFICITS

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Adenosine is a neuromodulator that can either inhibit or facilitate synaptic transmission through A_1R or $A_{2A}R$ respectively. Since noxious brain conditions enhance extracellular levels of adenosine, and blockade of adenosine $A_{2A}R$ prevents synaptic dysfunction and confers neuroprotection, it was explored if $A_{2A}R$ blockade prevented synaptic dysfunction and memory impairment characteristic of Alzheimer's disease. Alzheimer's disease (AD) is characterized by memory impairment, neurochemically by accumulation of ß-amyloid peptide (namely $Aß_{1-42}$) and morphologically by an initial loss of nerve terminals. In a rodent model of AD based on intracerebral administration of soluble $Aß_{1-42}$, the animals (rats or mice) presented, after two weeks, memory impairment and loss of nerve terminal markers without overt neuronal loss, astrogliosis or microgliosis; this was prevented upon pharmacological blockade with SCH58261 ($A_{2A}R$ antagonist) in rats, and genetic inactivation of $A_{2A}R$ in mice. To further study the influence of $A_{2A}R$ in $Aß_{1-42}$-induced synaptic loss, a nerve terminal preparation was used: SCH58261 prevented $Aß_{1-42}$-induced loss of viability and mitochondrial dysfunction; likewise, SCH58261 also prevented the initial synaptotoxicity and subsequent loss of viability of cultured hippocampal neurons exposed to $Aß_{1-42}$. Additional investigation was engaged to discover which signaling pathways were associated with this $A_{2A}R$-mediated control of neurodegeneration upon exposure of rat hippocampal cultured neurons to $Aß_{1-42}$. It was observed that the neuroprotection afforded by $A_{2A}R$ blockade is independent from cAMP/PKA pathway, but involves p38 MAPK. $A_{2A}R$ antagonists do not cause generic prevention of memory impairment in rodents. In fact, SCH58261 or KW6002 (another $A_{2A}R$ antagonist) failed to modify scopolamine- or MK-801-induced amnesia, and were only effective against Aß-induced memory impairment, where synaptotoxicity is known to occur. $A_{2A}Rs$ do not affect general processes of memory impairment, but instead play a crucial role restricted to neurodegenerative conditions involving an insidious synaptic deterioration leading to memory dysfunction.

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S4B.4

EPIGENETIC MODULATION OF ADENOSINE A_{2A} RECEPTOR: A PUTATIVE THERAPEUTICAL TOOL FOR PARKINSON'S DISEASE TREATMENT

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In the central nervous system, the most A_{2A}R-enriched brain region is the striatum, in which A_{2A}Rs are largely restricted to GABAergic neurons of the indirect pathway, projecting from the caudate/putamen to the external globus pallidus, which also expresses dopamine D_2 receptors (D_2Rs). A_{2A}Rs play out antagonistic interactions with D_2Rs and as a result of this interaction, antagonists of A_{2A}Rs have been proposed as non-dopaminergic anti-parkinsonian agents facilitating the availability of D_2Rs. Clinical trials have proven that A_{2A}Rs antagonists reduce the postsynaptic effects of dopamine depletion and lessen motor symptoms of Parkinson's disease (PD). Moreover, the A_{2A}R levels in PD have been reported to be upregulated in the post-mortem putamen of PD patients with diskynesias and A_{2A}R overexpression have been correlated with the typical parkinsonian motor symptoms. We recently described how DNA methylation is an epigenetic marker that regulates the basal gene expression of A_{2A}R (*ADORA2A*) in human brain. DNA methylation is associated with gene repression and it is present in human brain. Neuronal alterations of this epigenetic marker have been described in human neurodegenerative diseases. It remains to be seen whether there is a reduction of DNA methylation in *ADORA2A* to explain the protein upregulation in PD. However, we have shown that treatment with S-adenosylmethionine (SAM) reduced the A_{2A}R levels in SH-SY5Y and U87-MG cells. SAM is the major methyl-group donor molecule in the organism and it is reduced in PD patients. Moreover, reduced SAM levels are associated with hyperhomocysteinemia in PD and also following L-dopa treatment. Interestingly, SAM has been used for many years as an antidepressant with fewer side effects, and it was shown to present benefits in an open label trial in PD patients. Therefore, in light of the high content of A_{2A}R levels in the brain, its implication in the pathophysiology of PD and the role of DNA methylation in its gene expression, the design of DNA methylating drugs combined with A_{2A}R antagonists and/or L-dopa might be useful for future pharmacological intervention to reduce A_{2A}R activity in PD.

S5.1

NORADRENERGIC ACTIVATION OF THE BASOLATERAL AMYGDALA MODULATES CONSOLIDATION OF OBJECT-IN-CONTEXT RECOGNITION MEMORY

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Noradrenergic activation of the basolateral complex of the amygdala (BLA) is known to modulate the consolidation of memory for many kinds of highly emotionally arousing training tasks. Recent findings from our laboratory have demonstrated that posttraining noradrenergic activation of the BLA is sufficient to also enable memory consolidation of a low-arousing training experience, such as novel object recognition memory. The present experiments investigated whether such noradrenergic activation can modulate the consolidation of memory of object-in-context recognition training, a behavioral task designed for the investigation of episodic-like memory in rats. For training, male Sprague–Dawley rats were exposed to two identical objects in one distinctive context for either 3 or 10 min, immediately followed by exposure to two other identical objects in another distinctive context for the same amount of time. Immediately after the training session, they received intra-BLA infusions of norepinephrine (0.3, 1.0 or 3.0 ug in 0.2 ul), the beta adrenoceptor antagonist propranolol (0.1, 0.3 or 1.0 ug in 0.2 ul) or saline. On the 24-h retention test, rats were placed back into one of the training contexts with one copy of both training objects. Thus, although both objects were familiar, one of the objects had not been seen in this particular test context. Hence, if the animal generated a long-term memory for the association between an object and its context, on the retention test, it would spend significantly more time exploring the object that was in a novel environment. Saline-infused controls exhibited poor 24-h retention when given 3 min of training and good retention when given 10 min of training. Norepinephrine administered after 3 min of object-in-context training induced a dose-dependent enhancement of 24-h recognition memory, whereas propranolol administered after 10 min of training produced a dose-dependent memory impairment. These findings provide novel evidence that posttraining noradrenergic activation of the BLA modulates the consolidation of object-in-context recognition training, enabling enhancement of episodic-like memories.

S5.2

MENOPAUSE, HORMONE THERAPY, AND COGNITION: OPTIMIZING TREATMENTS BASED ON INSIGHTS FROM ANIMAL MODELS

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The question of whether to take hormone therapy (HT) will impact every woman as she enters reproductive senescence. In women, studies suggest that ovarian hormone loss associated with menopause has deleterious cognitive effects. Results from clinical studies evaluating whether estrogen-containing HT mitigates these effects, and benefits cognition, are varied and discrepant. The most commonly prescribed HT in the United States is conjugated equine estrogen (CEE, tradename Premarin). Using animal models, data will be presented regarding variables modulating the cognitive effects of CEE. First, whether CEE impacted cognition and the cholinergic system, via pharmacological challenge during memory testing and ChAT-immunoreactive cell counts in the basal forebrain, was tested. The doses of CEE tested were those commonly used by women, adjusted only for body weight of the rat. Next, using the 4-vinylcyclohexene diepoxide (VCD) rodent model of ovarian follicle-depletion, which mimics transitional menopause, we directly compared cognition in transitional versus surgical hormone loss. Finally, we investigated whether etiology of hormone loss (transitional versus surgical) influenced the cognitive effects of CEE. Findings indicated that CEE provided cognitive benefits on spatial tasks through cholinergic mechanisms in surgically menopausal rats. Transitional menopause benefited cognition only if residual ovarian hormones were removed, suggesting that initiation of transitional menopause before surgical ovary removal can benefit mnemonic function. CEE benefited surgically menopausal rats, but, in contrast, impaired transitionally menopausal rats. Taken together, findings suggest that the deleterious effects of hormone loss may be obviated by CEE HT. However, these beneficial effects were only evident after surgical menopause. The current findings have wide implications for future research and optimizing HT treatments for menopausal women.

S5.3

STRESS-INDUCED MODULATION OF INSTRUMENTAL ACTION

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Instrumental action can be controlled by two functionally and anatomically distinct systems: (i) a prefrontal cortex-dependent goal-directed system that encodes the causal relationship between an action and an outcome and (ii) a dorsolateral striatum-dependent habit system that learns associations between responses and preceding stimuli, without any link to the outcome that the response engendered. Given the well-known effects of stress on learning and memory processes, we asked whether stress may also modulate the systems controlling instrumental action. In a series of experiments, participants were trained in two instrumental actions that were associated with two distinct food outcomes. After learning, one of the food outcomes was selectively devalued by feeding participants to satiety with that food. Stress, either before or after learning, rendered participants' responding in a subsequent extinction test insensitive to the change in the value of the food outcome. In other words: Stress rendered behavior habitual. Using a pharmacological approach, we could demonstrate that this stress-induced shift towards habit behavior requires concurrent glucocorticoid and noradrenergic activity. Our findings show that stress and stress hormones favor habits over goal-directed action and may have important implications for drug addiction and other compulsive disorders that have been related to an aberrant engagement of habit processes and can be promoted by stress.

S5.4

SEROTONIN AND PROSOCIAL BEHAVIOUR: NEURAL AND PSYCHOLOGICAL MECHANISMS

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Humans are selfish, but also care about the welfare of others. Counter to the predictions of influential economic models, humans often act against their own self-interest, incurring personal costs to help cooperators and punish cheaters. These so-called 'altruistic' behaviours are highly variable, both between individuals and across situations, and the mechanisms that drive this variability are not well understood. One potential mechanism governing the context-dependent variability of altruistic behaviour is neuromodulation by the neurotransmitter serotonin (5-HT), which responds to environmental stressors and shapes activity in brain regions implicated in social decision-making. Supporting this hypothesis, decades of research have linked 5-HT to prosocial behaviour across species; however, the specific motivational processes mediating this relationship have not yet been elucidated. In this talk, I will present a series of studies designed to examine the influence of 5-HT on altruistic punishment. Our first experiment indicated that temporarily lowering 5-HT function increases the occurrence of altruistic punishment. Additional analysis suggested that the effects of lowering 5-HT on altruistic punishment are partly mediated by concurrent increases in preference for immediate rewards, an effect that may depend on interactions between 5-HT and dopamine. In a second study, we showed that enhancing 5-HT function decreases the occurrence of altruistic punishment specifically through effects on harm aversion. Finally, a third study demonstrated that the social context critically moderates the impact of 5-HT depletion on altruistic punishment, raising new questions about the role of different decision-making systems in motivating punishment. Neuroimaging data indicated that 5-HT depletion reduced the response of the ventral striatum to fairness, while simultaneously enhancing the response of the dorsal striatum to punishing unfairness, suggesting that changes in 5-HT neurotransmission mediate tradeoffs between the rewards of cooperation and the satisfaction of revenge. Overall, these findings provide strong evidence implicating 5-HT in human altruistic behaviour, and begin to clarify the influence of interacting neuromodulatory systems on social decision-making.

S5.5

ENDOCANNABINOIDS: NEW PLAYERS IN EMOTIONAL MEMORY CONSOLIDATION

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The activation of neuromodulatory systems affecting the amygdala plays a key role in enabling emotionally significant experiences to be well remembered. The endocannabinoid system is essential in regulating several brain functions, including emotionality and cognition. Extensive evidence indicates that the basolateral complex of the amygdala (BLA) modulates the consolidation of memories for emotionally arousing experiences via interactions with other brain regions (i.e. hippocampus and prefrontal cortex (PFC)). The BLA, the hippocampus and the PFC express high densities of cannabinoid CB1 receptors. My talk will focus on the role of the endocannabinoid system in the modulation of memory consolidation for emotional experiences. Indeed, we have recently shown that the CB1 cannabinoid receptor agonist WIN55,212-2, infused bilaterally into the BLA of male Sprague-Dawley rats immediately after inhibitory avoidance training, enhances memory consolidation, and that this effect depends on activation of CB1 cannabinoid receptors. Furthermore, we have shown that there is a bidirectional crosstalk between the endocannabinoid and the glucocorticoid systems in the regulation of emotional memory, demonstrating that CB1 activity within the BLA mediates glucocorticoid effects on memory consolidation. Nowadays, more innovative and selective pharmacological approaches exist to enhance endocannabinoid signalling in the brain. Indeed, indirect cannabinoid agonists, that prolong endocannabinoid activity by interfering with endocannabinoid deactivation, have emerged as a novel therapeutic approach for the treatment of central nervous system disorders. I will present recent results showing that post-training infusions of the indirect cannabinoid agonist URB597 into the BLA, hippocampus and PFC, modulate emotional memory in rats. I will complement these findings by presenting data on changes of endocannabinoid levels in these brain areas following inhibitory avoidance training. Overall, my results will show that endocannabinoids are essential new players in the consolidation of memory for emotional salient events.

S5.6

THE SEARCH FOR THE NEURONAL SIGNATURE OF EPISODIC MEMORY: A NOVEL DEVELOPMENTAL APPROACH

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Episodic memories are spontaneously formed memories for unique events that occur in our everyday lives. They involve a unique combination of rich contextual features; for example where we were, what we were doing and who we were with. Episodic memory typically develops late in childhood and is often one of the first cognitive functions to decline in old age. The limitations that arise when studying episodic memory in humans, however, are twofold. Firstly, imaging studies in healthy individuals are not currently able to visualise brain activity at the cellular and mechanistic level. Secondly, deficits in episodic memory can only be studied in patients who are lacking the brain regions critical to its function, thereby precluding the study of intact and impaired memory in the same subjects. In order to elucidate the neural mechanisms of episodic memory therefore, animal models in which these memory processes can be studied and manipulated at a neuronal level within the same subject are necessary. Accumulating evidence is beginning to suggest that laboratory rodents show a differential ontogeny of memory, as is the case in humans. This suggests that the late postnatal development of episodic-like memory in laboratory rodents could provide an opportunity to examine its behavioural and neural correlates concurrently within the same animal during the critical period in which it develops. This longitudinal design is powerful as it avoids the caveats of neurotoxic interventions which are required to induce the absence of episodic-like memory in adult subjects. The juvenile rodent is therefore a novel and previously unexploited model in which to potentially identify the neural signature of episodic memory and correlate this neural-level activity with behaviourally measurable memory performance at the systems level. I have recently shown that simple novelty recognition memory develops earlier than associative recognition memory in young rats and am currently working to pinpoint when episodic memory characteristics appear and, with the use of immediate early gene imaging, to show which brain networks are active at this critical developmental time point.

S6A

BRAIN OSCILLATIONS AND HIPPOCAMPAL MEMORY PROCESSING

Brain oscillations are essential for maintaining synchrony amongst neuronal ensembles both within- and across different brain structures. In the hippocampus, The activity of pyramidal neurons (place cells) forms a spatial representation of the environment, a supposed element of episodic memory. Besides space, place cell activity is modulated by distinct frequency bands of the local field potential (LFP)- theta and gamma oscillations, together with sharp wave/ripple events. This forum will highlight recent advances in understanding the different roles of these oscillations in hippocampal memory and information processing. 1)Distinct gamma oscillation bands (~40/~80 Hz) and their role in streaming the information flow between cortical and hippocampal areas. 2) Theta oscillations (5-11 Hz)- their importance for pattern completion and segregation between different memory states. 3) Replay of stored neuronal activity patterns during sharp wave/ripple complexes as a suggested mechanism for memory consolidation. 4) Discoordination of the relationships between hippocampal ensemble discharge and LFP oscillations in schizophrenia-related animal models.

S6A.1

DISTINCT FREQUENCIES OF GAMMA OSCILLATIONS AND THEIR ROLE IN STREAMING INFORMATION FLOW IN THE HIPPOCAMPAL NETWORK

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Gamma oscillations occur throughout many brain regions, including the hippocampus, a region critical for spatial and episodic memory. In the hippocampus, gamma frequency varies widely (~25-140 Hz), and recent evidence suggests that these frequency variations are functionally relevant. Slow gamma (~40 Hz) synchronizes hippocampal subfield CA1 with CA3, an area required for memory retrieval. Fast gamma (~80-100 Hz) couples CA1 to the entorhinal cortex, a region providing information about the current environment. I hypothesize that slow gamma facilitates internal streams of information, such as memories of past experiences, and that fast gamma promotes transmission of information from the external world during memory encoding.

S6A.2

TRANSITION BETWEEN DISTINCT HIPPOCAMPAL MEMORY STATES AND THEIR ORCHESTRATION BY LOCAL THETA OSCILLATIONS

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Theta rhythm (6-10 Hz) is a prominent oscillation in various cortical and subcortical brain structures. In hippocampal networks it modulates activity of most neurons during exploratory behaviour and REM sleep. Its role in dynamics of memory expression on neuronal population level is poorly understood, however. Hippocampal CA3 is viewed as recurrent collateral network capable of storing large number of independent memory states. Recently we found that transition between hippocampal spatial representations evoked by sudden change of external cues is followed by transient period of flickering between the original and new network state. Rather than expressing progressive transformation, the network quickly jumps between competing attractors, often by complete replacement of the active cell population from one theta cycle to the next. Within individual cycles, segregation between representations for past and present environment is strongest in the second half of the wave. This suggests that theta cycle might serve as a temporal unit for retrieval of attractor states in the hippocampus.

S6A.3

REPLAY OF STORED NEURONAL ACTIVITY PATTERNS DURING SHARP WAVE/RIPPLE COMPLEXES AS A SUGGESTED MECHANISM FOR MEMORY CONSOLIDATION

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It is thought that the hippocampus participates in the formation of new memories by temporarily storing labile memory traces of waking experience and later replaying them, leading to consolidation. Several lines of evidence support the hypothesis that 150-250 Hz Sharp Wave/Ripples (SWR) events play a role in the network mechanisms underlying these mnemonic processes. During periods of active waking behaviour, hippocampal neurons fire in relation to space, so that different regions of the environment are represented by different combinations place cell activity. Such cell assembly activity patterns are then "reactivated" in immobility and sleep, predominantly during SWR while neuronal activity is independent of sensory input. This SWR-reactivation has been shown to reflect features of the previous behavioural experience and predict future memory performance. In addition to the participation of SWRs in offline stage of memory consolidation, recent evidence suggests that they also participate in the initial 'online' stabilisation of memory traces. Indeed, SWR activity is also observed during brief interruptions of active exploratory periods at times when the increased network activity overlap with the ongoing place-selective activity. This suggests that waking SWRs may strengthen the synchronised firing of place cells encoding the same location and, consequently, promote synaptic plasticity within these assemblies. Finally, the formation of memory traces might involve SWR as a temporal framework for the coordination of neuronal assemblies between the hippocampus and other brain regions, including the Entorhinal cortex. Altogether, the current data suggest that SWR play critical role in different but complimentary stages of hippocampal dependent memory formation.

S6A.4

HIPPOCAMPAL NEURAL OSCILLATION CORRELATES OF INTACT AND IMPAIRED COGNITION, AND PREVENTION OF COGNITIVE CONTROL DEFICITS IN A NEURODEVELOPMENTAL SCHIZOPHRENIA ANIMAL MODEL

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People selectively interpret and respond to task-relevant stimuli while suppressing the processing of competing irrelevant interpretations and stimuli, an ability called cognitive control that is crucial to organized thought. It is now recognized that cognitive deficits, especially deficits of cognitive control, are a core feature of schizophrenia and that such clinical features are the strongest determinants of functional outcome. Unfortunately, antipsychotic treatments have targeted the positive and negative symptoms, and do little to improve the cognitive deficits. In an effort to understand the basis of the cognitive deficit in schizophrenia, we developed the "discoordination" hypothesis, postulating that neural discoordination underlies the core cognitive deficit in schizophrenia. Here we report studies of cognitive control and neural oscillations in the neonatal ventral hippocampus lesion (NVHL) model, an established neurodevelopmental animal model of schizophrenia. Seven days after birth, male rat pups are injected in the ventral hippocampus with the excitotoxin ibotenic acid to create a lesion and alter development of neural circuitry. Adult NVHL rats were impaired in a two-frame place avoidance task that tested cognitive control, but not in a one-frame control task, indicating impaired cognitive control while spatial memory and basic information processing was spared in adult NVHL rats. Cognitive performance in the two-frame task was associated with increased phase and amplitude synchrony between the two hippocampi. This synchrony was restricted to slower oscillations of local field potentials, especially in the theta range. This interhippocampal neural synchrony was far weaker in adult NVHL rats than sham controls. We examined the possibility of a critical developmental window for early, "prophylactic" cognitive training during the juvenile period of elevated neuroplasticity, in which neural circuits might be tuned in the service of cognition. Indeed, prophylactic cognitive training when the NVHL rats were juveniles prevented both the cognitive and neural synchrony deficits, despite the persistence of the brain lesions. Together these data support the discoordination hypothesis that aberrant cordination of distinct networks of neurons underlies the core cognitive deficit in schizophrenia and that this discoordination can be prevented by early interventions that promote the tuning of brain networks to mediate cognitive functions.

S6B

NEURAL BASES OF COGNITIVE-EMOTIONAL INTERACTIONS IN HUMANS

Although traditionally regarded as two separate and independent aspects of the mind, a growing literature shows that emotional and cognitive processes are intimately related. In particular, studies in neurological patients as well those using neuroimaging techniques have begun to identify the neural substrates of the interactions between emotion and cognitive processes such as perception, attention, memory, motor action and awareness. Furthermore, numerous studies have demonstrated that individual differences exist and that these may underlie the observed differences in vulnerability or resiliency to the development of, or recovery from, psychiatric disorders, such as schizophrenia, depression and PTSD. In this symposium, four speakers will review the existing work on the field of emotion-cognition interactions in humans, present some new findings and highlight the open questions and future directions of this rapidly growing area of research.

S6B.1

HOW EMOTION ENHANCES AND IMPAIRS HUMAN EPISODIC MEMORY

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The apparent memory advantage for emotional events occurs at the expense of memory for the immediately preceding event. A combination of functional neuroimaging, psychopharmacological, human lesion and genetic data will be presented, demonstrating that both emotion-induced memory enhancement and emotion-induced retrograde amnesia are critically dependent on the medial temporal lobe and beta-adrenergic system. I will describe how the principle of emotion-induced retrograde disruption of memory encoding can be applied to evoke a selective impairment in retrieval of target episodic memories following reactivation, *i.e.* an impairment of reconsolidation. Lastly, data will be presented showing that administration of a beta-adrenergic receptor antagonist at retrieval abolishes declarative memory enhancement for emotionally salient items, providing face validity to clinical interventions using □-adrenergic antagonists in conjunction with reactivation of unwanted memories in anxiety-related disorders.

S6B.2

THE AMYGDALA IN CONSCIOUS AND NONCONSCIOUS PERCEPTION OF BODILY EMOTION EXPRESSIONS

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The amygdala is known to be an important structure in brain networks processing emotional signals. But many questions remain concerning its role in different types of emotional signals and the influence of attention or awareness and the influence of amygdala on emotion triggered adaptive action. We have shown previously that using whole body images rather than isolated facial expressions is particularly useful for bringing these aspects to the foreground. This contribution will present new findings obtained in a group of subjects with Urbach-Wiehe disease in whom the basolateral nucleus of the amygdala is selectively damaged. Their performance on a set of body recognition tasks is compared with that of normal controls and we discuss the relevance of these data for a better understanding of the amygdala's role.

S6B.3

INTERACTIONS BETWEEN EMOTIONAL AND MOTOR SYSTEMS

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It is widely agreed that body language is a powerful source of information about emotions and intentions in our daily encounters with people. We will present our recent fMRI studies that aimed at identifying the neural bases involved in processing emotions from body actions and their link with the motor system. We concentrated on two emotions, namely fear and anger, as they both represent potential threats. We assessed the influence of context (in terms of allocation of attentional resources and functional significance for the self) and inter-individual differences in socio-affective skills (Alexithymia and Autism). We hope to show that body expressions of emotions are decoded as interactive social signals (social affordances) in the sense that they require one to automatically adapt or regulate one's own behavior.

S6B.4

INDIVIDUAL DIFFERENCES IN COGNITIVE-EMOTIONAL INTERACTIONS

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Although, as already shown by Darwin and others, some emotional responses (e.g., fear) are highly consistent across species, individuals may react very differently to the same emotional event. Indeed, there is a growing literature supporting the notion that there are substantial individual differences –in terms of sex, personality, development, genotype, etc– in the behavioural and neural processing of emotional information and its interaction with other cognitive mechanisms such as memory and attention. Importantly, these individual differences may underlie, at least to some extent, the observed variability in the vulnerability to the development of psychiatric disorders. In this talk I will present data from our group and others highlighting the influence of sex and personality (particularly anxiety) on emotional processing in healthy individuals, as well as the relation between clinical variables, such as symptom severity, and emotional responses in individuals suffering from post-traumatic stress disorder (PTSD) and schizophrenia.

S7A

IMPULSIVE AND RISK-TAKING BEHAVIOUR: MOLECULAR AND NEURAL BASES

Impulsivity is an important aspect of normal personality. In addition, abnormal impulsive behaviour underlies many psychiatric problems including addiction, pathological gambling and attention deficit hyperactivity disorder (AD/HD). However, impulsive behaviour is not a unitary construct and may be manifest in different ways affecting the ability to with-hold a response, change behavioural tack and make a decision over time or between reward and cost. Research using cutting edge behavioural paradigms, novel animal models and brain imaging techniques in people, is beginning to tease apart the neural and molecular processes underpinning impulsivity. This symposium reflects this, and we will hear talks on different aspects of impulsive behaviour touching upon drug addiction (Dalley), sex differences (Davies), the neural bases of risky decision making (Kalenscher) and epigenetic mechanisms contributing to the evolution of risk-taking (Isles). As such, this symposium will ap peal to a wide range of neuroscientists with a general interest in impulsive behaviour.

S7A.1

NEUROBEHAVIOURAL ENDOPHENOTYPES OF IMPULSIVITY: RELEVANCE TO DRUG ADDICTION

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Impulsivity refers to the tendency to act hastily with little or no foresight. It is generally considered multi-dimensional in nature and to involve distinct yet partially overlapping neural and psychological substrates. It is commonly expressed in clinical syndromes such as attention deficit hyperactivity disorder and is broadly viewed as a behavioural trait that predisposes to alcoholism and stimulant abuse. However, establishing a causal role of impulsivity in human addiction has proven difficult to address. In contrast, research in rats showing naturally high levels of impulsivity has led to the conclusion that poor impulse control predicts several hallmark features of addiction, including escalation of drug self-administration, increased propensity for relapse to drug seeking, and the emergence of compulsive drug self-administration. The neural substrates of impulsivity include the basal ganglia and their limbic cortical inputs, especially top-down inhibitory control of the nucleus accumbens by prefrontal cortical circuitry. Previously, we demonstrated that high impulsive rats show a significantly reduced uptake of the selective dopamine D2/3 receptor antagonist 18F-fallypride in the ventral striatum, including the nucleus accumbens –thereby demonstrating that D2/3 receptor function in this region may be a biomarker for trait-like impulsivity as well as vulnerability for drug addiction. Using structural magnetic resonance imaging and voxel-based morphometry we have since found that high impulsivity in rats is associated with a selective reduction in grey matter in the core sub-region of the nucleus accumbens compared with low impulsive rats. Reduced grey matter was mainly found in the left hemisphere and was associated with significant reductions in glutamic acid decarboxylase (GAD) as well as the dendritic markers MAP2 and spinophillin. These findings provide a putative explanation for the reduction in dopamine D2/3 receptors in the ventral striatum of high impulsive rats in terms of a reduced density of spines on the dendrites of GABA-ergic medium spiny neurons. Collectively, these results indicate that GABA-ergic dysfunction associated with structural abnormalities in the nucleus accumbens core may be a potential biomarker for the high impulsive syndrome in rats. This research was supported by the Wellcome Trust, MRC and European Commission.

S7A.2

HOW SEX-LINKED GENES MIGHT INFLUENCE SEX-BIASED VULNERABILITY TO DISORDERS OF IMPULSIVITY

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Healthy males and females differ with respect to behaviours thought to be related to impulsivity such as sensation-seeking and behavioural risk-taking. Moreover, the sexes are differentially vulnerable to, and affected by, various disorders of impulsivity, notably Attention Deficit Hyperactivity Disorder (ADHD). These behavioural sex differences represent the ultimate manifestation of sex-linked genes (i.e. those on the X or Y chromosomes) being expressed differently in males and females; such genes may act via intermediary mechanisms (such as gonadal hormone production) and/or via direct effects on brain development/function. There are three general genetic mechanisms through which sex-linked genes may theoretically influence sexually dimorphic impulsivity phenotypes: Y-linked gene expression, X-linked gene dosage and X-linked genomic imprinting, and in the first part of the talk these mechanisms will be discussed in detail. In the second part of the talk, I will discuss evidence from our own work that the neurosteroid-modulating enzyme steroid sulfatase (encoded by the sex-linked gene Sts) may modulate aspects of impulsivity and vulnerability to ADHD endophenotypes, and will propose possible neurobiological mechanisms.

S7A.3

BI-DIRECTIONAL EFFECT OF STRESS ON PRESENT BIAS IN INTERTEMPORAL CHOICE

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When making intertemporal choices – decisions between consequences that can only be realized in the future – people often show a strong bias toward the present and consequently find it difficult to act in accordance with their long-term interests. Unlike impatience, which is simply the subject's preference about consumption at different times, present bias refers to the focus on the here and now and is normatively irrational because it leads subjects to fail to execute the future plans that they make today. Intertemporal choices are often made under stress and theoretical considerations as well as cellular evidence from molecular biology hint towards and impact of stress on intertemporal choice. However, it remains unknown how stress really affects intertemporal choice. Here, we show that stress had a bi-directional effect on present-bias, but not impatience, in financial intertemporal decision making: immediately after stress, subjects showed stronger present-bias than controls. In contrast, after some temporal delay, they were less present-biased than controls. This is in line with recent evidence from cellular neuroscience which suggest that stress affects neurobiological processes on different temporal scales: immediately after stress, cortisol and noradrenaline promote rapid neuronal changes, presumably aimed at immediate responses to the stressor, resulting in hypervigilance, automatic responding and focused attention; after some delay, cortisol facilitates restorative processes, putatively aimed at long-term protection and restoration of function. In summary, the finding that stress increases present bias in the short run, but decreases it in the long run suggest a simple behavioral rule: if you want to make future-oriented choices in a stressful environment – wait a while, count 'til 100, then make your decision.

S7A.4

IMPRINTED GENES, IMPULSIVITY AND RISK-TAKING

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Studies in humans and animals indicate that much of decision making is sub-optimal. Underpinning this is a failure to optimise gains and minimise risks. This is apparent by the choice of short-term gains over longer term benefits or offset against longer term risks. In humans this manifests in 'risky' and impulsive behaviours such as failure to diet, unprotected-sex, gambling, and drug usage (1). Naïve evolutionary thinking would predict that natural selection should have eliminated these behaviours. However, natural selection does not necessarily favour traits that benefit individual organisms and may in fact be acting at the level of the gene (2). Imprinted genes, those genes subject to parent of origin specific epigenetic modifications, are an example of 'selfish' genes, in that often different parental copies act antagonistically to promote differing phenotypes, neither of which may be optimal for the individual (3). Genomic imprinting plays an important role in behaviour. This has recently been underlined by the exciting discovery that the number of imprinted genes expressed in the mouse brain has expanded from a small subset, to well in excess of 1000 (4). We are using mice with targeted mutations of brain expressed imprinted genes to examine their contribution to risk-taking and impulsive behaviours. Nesp and Grb10 are maternally and paternally expressed imprinted genes respectively, both showing discrete overlapping expression in the locus coeruleus and dorsal raphe nucleus. Grb10 is also strongly expressed in the VTA and substantia nigra. Both genes are therefore ideally placed to influence monoaminergic function and impulsive behaviours. Mice lacking expression of Nesp and Grb10 show a number of behavioural phenotypes that may be indicative of altered risk-taking, including changes in novelty exploration and social dominance behaviour. I will discuss these findings and present new data systematically examining impulsive and risk-taking behaviours using operant tasks such as delay discounting. Testing these ideas will enable us to gain a broader picture of the functions of genomic imprinting in brain and inform the debate as to why imprinting has evolved. Furthermore, this approach, linking evolutionary genetics and neuroscience, may revolutionise the way we think about the brain processes underlying decision-making.

1. T. Schonberg, C.R. Fox, R.A. Poldrack (2011), Trends Cogn Sci, 15, 11.
2. R. Dawkins, The Selfish Gene (Oxford University Press, Oxford, Ed. Second, 1989).
3. J.F. Wilkins, D. Haig (2003), Nat Rev Genet, 4, 359.
4. C. Gregg et al. (2010), Science, 329, 643.

S7B

NEURAL INTERACTIONS BETWEEN CONSCIOUS AND UNCONSCIOUS VISION

The Symposium will deal with studies showing various kinds of interactions between conscious and unconscious vision. This topic is relevant not only for a better understanding of the neural and cognitive bases of unconscious vision but also to study plastic recovery in the adult brain. Carlo Marzi will deal with the question of whether unconscious or conscious residual vision following damage to the geniculo-striate pathway is subserved by the damaged or the intact hemisphere and which are the possible neural routes. Bob Kentridge will provide behavioural and brain imaging evidence that attention and visual awareness can be dissociated in blindsight patients. Elisabetta Ladavas will report evidence of audio-visual perceptual learning in the hemianopic field, a phenomenon which may represent the neural correlate of the sensory compensation following loss of one modality. Finally, Marco Tamietto will deal with “affective blindsight” and the interactions between unconsciously and consciously detected emotional stimuli.

S7B.1

WHICH HEMISPHERE SUBSERVES CONSCIOUS RESIDUAL VISION OR BLINDSIGHT ?

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It is widely known that patients with hemianopia as a result of unilateral damage to the post-chiasmatic visual pathways and visual cortex can show visually guided behaviour for stimuli presented to the blind field and therefore undetected (blindsight). The aim of the present study was to use a simple behavioural paradigm to test whether unconscious manual responses to stimuli presented to the hemianopic hemifield are triggered by the lesioned or the intact hemisphere. During a rehabilitation procedure, we tested patients with either a unilateral optic tract, optic radiation or visual cortical lesion in a Poffenberger paradigm with visual stimuli briefly presented to the hemianopic or the normal hemifield and a manual response performed with either the ipsilateral or contralateral hand with respect to the stimulated hemifield. As is well known, in healthy participants reaction time is consistently faster with the hand ipsilateral to the stimulated hemifield because in this uncrossed condition there is no need for a callosal interhemispheric transfer (IT) which is instead necessary in the crossed condition in which visual stimulus detection and motor response are subserved by different hemispheres. The crossed-uncrossed difference (CUD) is used as a means to estimate IT which in healthy participants is in the range of 3-5 ms. In the present study we found in all patients a large positive CUD when stimulating the intact hemifield but a negative CUD when stimulating the hemianopic field with the crossed condition faster than the uncrossed condition. This paradoxical result can be explained by the response being triggered by the intact hemisphere even for stimuli presented to the other (lesioned) hemisphere. This possibility was strengthened by the finding that these patients showed an increased activation of the visual cortex in the intact hemisphere following a prolonged visual rehabilitation training with stimuli moving from one extreme to the other of the whole visual field. A kind of procedure that turned out to be effective.

S7B.2

NEURAL AND FUNCTIONAL RELATIONS BETWEEN ATTENTION AND CONSCIOUSNESS IN VISION

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The notion that processes of visual attention and visual awareness are linked has a long history. Even today many philosophers consider attention and awareness to be obligatorily associated. The phenomenon of blindsight, in which visual awareness and visual function dissociate, provides an ideal stage on which to test this assertion. Using modified versions of Posner's spatial cueing paradigm I have shown that a blindsight patient responded more quickly and accurately to targets presented at attended compared to unattended locations. As the patient did not report seeing these targets attention must have been operating without giving rise to awareness. Using the same patient and a slightly modified paradigm Catherine-Tallon Baudry and her colleagues showed that the neural MEG signatures accompanying attention and awareness in this patient also dissociated. By using a meta-contrast masking paradigm we have shown that attention can facilitate processing of unseen targets in normal observers as well as blindsight patients. Again this behavioural dissociation has corresponding dissociated neural correlates. The most recent data I will present shows that masked objects that normal subjects to do not report seeing nevertheless constrain the spread of attention in Egly, Driver & Rafal's object-based attentional cueing paradigm. I will discuss the history of this work, recent criticisms of it, and its relationship to current theories of attention and awareness.

S7B.3

AUDIO-VISUAL PERCEPTUAL LEARNING IN THE HEMIANOPIC FIELD

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The human brain possesses a flexible audio-visual system, which interprets and guides responses to external events according to spatial alignment, temporal synchronization and effectiveness of unisensory signals. Here we explore the possibility that such a system might represent the neural correlate of sensory compensation when a sensory modality has been damaged by a cerebral lesion (patients with hemianopia). We will examine on-line and off-line effects of audio-visual stimulation on the visual and spatial impairments following damage to the geniculo-striate pathway. We will demonstrate that an improvement in spatial orienting can be obtained not only when an on-line response is required, but also after either a brief or a long adaptation to audio-visual stimulation. These findings suggest that the mechanisms subserving audio-visual perceptual learning are still active after a damage to the geniculo-striate pathway; this perceptual learning is probably mediated by the collicular-extrastriate pathway.

S7B.4

AFFECTIVE BLINDSIGHT IN THE INTACT AND DAMAGED BRAIN

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Affective blindsight refers to the uncanny ability of patients with cortical blindness to discriminate reliably the emotional valence of stimuli they cannot consciously perceive. Recent evidence has started to compare conscious and non-conscious emotion perception to reveal: a) which behavioral and neurophysiological aspects are typical of each mode of perception, and b) whether and how conscious and non-conscious emotion perception can coexist and interact. As far as the first issue is concerned, emotional stimuli projected to the blind field of patients with unilateral cortical blindness elicit spontaneous facial expressions and psychophysiological changes that are faster and more pronounced than the reactions triggered by the very same stimuli appearing in the intact visual field. Similar results are also obtained in neurologically intact subjects in whom blindsight-like effects are induced by visual masking. About the second point, non-consciously perceived emotional stimuli can interfere with the ongoing recognition of consciously perceived emotions. In fact, when two emotional stimuli are simultaneously presented in a split-field design, but one of the two cannot be consciously perceived because it is projected in the blind field or because it is masked, reaction times to recognize the normally visible stimulus are faster if the non-consciously perceived stimulus is emotionally congruent. The neuro-functional and neuro-anatomical underpinnings of affective blindsight are discussed are recent fMRI and DTI findings are presented.

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Abstracts Posters

SATURDAY September 10th, 2011

D10-1

DEVELOPMENTAL TRAJECTOY OF SERIAL AND PARALLEL VISUAL SEARCH IN CHILDREN AND ADOLESCENTS

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Present study tries to evaluate the developmental trajectory of the attentional serial visual search and pre-attentional parallel search (pop-out). The central hypothesis of present study is that preattentional selection mechanisms develop before than serial attentional processes. In addition the detailed analysis of errors would provide the different attitudes of experimental subjects of different ages to the task. Sixty-nine subjects between between 6 and 16 years participated in the study. Participants performed a visual search task and a pop-out task in which they had to press a button indicating the hemifield in which the target appeared. Two. four and six items were presented in each single stimulus in order to modulate the complexity of the task. Twenty per cent of the trials were catch trials in which no target were presented. Response times and errors were analyzed as a function of age. Subjects of every age were faster and produced less errors in the pop-out condition than in the visual search condition. In visual search the Rts and the number of errors increased with the number of presented items in each stimulus. The results showed an inverse relationship between the age and the Rts and the different type of errors. The most frequent type of errors were the omissions, that would correspond to a 50% of the trials in children of 6 years old. Incorrect responses, anticipations and responses to catch trials were much more reduced. The results indicate that preattentional search develops much earlier than serial visual search and maturation shows an inverse relationship with age, being faster at early ages than in the adolescent period. In an overcrowded scene the behavioral trend of normal children is to the non-response pattern rather than to impulsive incorrect responses pattern.

D10-2

PSICOENDOCRINOLOGY OF AGGRESSION: USING SOCIAL INTELLIGENCE AS A PREDICTOR

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Objective: The objective of this study was to analyze the potential predictive power of Social Intelligence and hormone levels on aggressive behavior among 7-8-year-old children. Method: Participants were 139 children (79 boys and 60 girls) aged 7-8 from San Sebastian, Spain. Testosterone, androstenedione, estradiol and cortisol levels were analyzed using an enzymoimmunoassay technique in saliva samples. Children's social intelligence was measured using "Peer Estimate Social Intelligence" scale, PESI. Aggressive behavior was assessed using the Direct and Indirect Aggression Scale (DIAS), a peer estimation technique carried out in the classroom. Results: A GLM was conducted to analyze the potential relationship between hormone levels and social intelligence. An interaction between Androstenedione and Social Intelligence was found in girls to explain aggressive behavior but nothing was found in boys. Conclusion: In this study we have found that in girls with low social intelligence, the more androstenedione, the more aggressive behavior. The results of this research project highlight the importance of studying the interactions between biological and psychological variables (biopsychosocial perspective) and their predictive power for behavior. They also underscore the importance of taking gender differences into consideration when studying behavior.

D10-3

CO-MATURATION BETWEEN LATE POSITIVE COMPONENT AND THE DELTA-THETA BANDS ANALYZED BY MULTIVARIATE TECHNIQUES

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The Late Positive Component (LPC), which includes the P3b component, is in the frequency range of the delta and theta bands. It is possible that the maturation of LPC and Low frequency EEG bands could be related. To explore this possibility, the power spectral density (PSD) of the EEG and the P3b component were obtained and analyzed by means of multivariate techniques. Thirty-eight subjects (18 children between 8 and 13 years old and 20 young adults between 18 and 23 years old) participated in the experiment. The P3b amplitudes were obtained in valid and invalid trials of a central cue Posner paradigm in children and young adults. To analyze the relationship between the spontaneous EEG rhythms and the P300 component, Pearson's correlations, Principal Component Analysis (PCA), topographical analysis and clusters analysis were used. The results showed that children presented higher spectral power than young adults in the spontaneous EEG in the lower frequency bands (delta and theta) and in the P3b component. The correlation matrix showed a high correlation between delta band and the posterior region of P300 and high negative correlations in anterior regions. The PCA showed that the loading factors of delta and theta were similar to those of the posterior P3 component. In children, the topographical analysis showed that the P3b and the delta band presented a similar topography in posterior areas. In young adults, the most posterior electrodes (O1 and O2) co-activated in P300 and Delta. Finally, the tree diagram of the cluster analysis revealed that there is a close association (low Euclidean distance in the multivariate space) between the P3b and delta and theta bands during development. The results suggest that there is a co-maturation between delta and theta with the LPC component.

D10-4

UTILITY OF THE CGHA TEST IN NEUROPEDIATRIC PRACTICE

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Introduction: Since few years, the use of the new molecular genetics high resolution tests live CGH array has let us an important increase of molecular abnormalities like microdeletions and the detection of new genetic syndromes. In this situation, there are great advances in the knowledge of the ethiopathogenic mechanisms of theses typo of diseases.
Clinic data : Case 1: Patient 1 and 2. Theses are two sibling girls of three years old that present since 1 year old, an important developmental delay mainly in the language and social areas, behavioral and learning disabilities. These symptoms look like autism-spectrum disorders. There are no specific facial abnormalities. There are no abnormalities at the physical exploration. The result of the studies made, cranial MRI, metabolic and basic genetic tests like karyotype did not showed abnormalities. At the CGH array appear a next alteration "Arr 16p12.1 (21, 744, 793-22, 338, 234) x1" with a high relation with Neuropsychiatric disorders and a high risk factor for neurodevelopmental disease and intellectual disability. Case 2: Patient 3. This patient is a 7 years old that present since 3 years old important problems of learning disabilities, attention deficit and behavioral disorders. There are no specific facial abnormalities. The patient presents a congenital convergent strabismus of right eye. The result of the studies made, cranial MRI, metabolic and basic genetic tests like karyotype did not showed abnormalities. At the CGH array appears a 14q11.2 deletion of 1,2Mb. There are no similar microdeletions reported by now, only a bigger one of 2,7Mb in a patient with mental retardation, autism-spectrum disorder, aggressive behavior and dismorphia.
Conclusions: The use of theses high resolution genetic tests can mean an important change in the usual practices or the beginning of the final of the old genetic tests.

D10-5

SUCKLING, OXYTOCIN AND THE DEVELOPMENT OF ATTACHMENT BEHAVIOUR IN INFANTS

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Oxytocin is known to play a key role in maternal behaviour but its importance in infants still remains to be demonstrated. Because suckling has profound psychodevelopmental effects on the young including mother-young interactions, we investigated in sheep (1) the importance of neonatal suckling on the development of filial attachment and on the release of oxytocin, and (2) whether oxytocin facilitates attachment to the mother. In a first experiment, lambs were deprived of suckling either at 2, 4 or 6 hrs after birth by covering the ewes' udder, while controls had free access to the udder. When tested in a two-choice test at 12hrs of age, only control lambs spent more time near the mother than the alien ewe. During a second test performed at 24hrs, controls and lambs deprived of suckling for 2hrs displayed a preference for their mother while those deprived for 4 or 6hrs were still undecided. We showed that oxytocin was released in the plasma during suckling and that levels were significantly higher than during a non nutritive contact with the mother (33.4 +/- 14 vs. 18.3 +/- 5.0 pg/ml, $p<0.05$). In a second experiment, we used the non-peptide oxytocin antagonist L368,899 (Merck) which is known: 1/ to cross the blood brain barrier, 2/ to affect social attachment in primates and 3/ to be functionally effective in sheep at the peripheral level (uterus). The antagonist was administrated orally through gastric intubations in three groups of animals (control, low dose: 1 mg/kg, and high dose: 10 mg/kg,) at birth, 2 and 4h post-partum, to cover the first 6hrs of life. When tested at 12hrs of age, control lambs showed a clear preference for their mother while lambs receiving the antagonist were slightly (low dose) or severely (high dose) impaired. A mild effect was still observed at 24hrs. These data suggest that oxytocin plays a role in the development of filial attachment in sheep through its release during the neonatal suckling activity.

D10-6

MATURATION OF HUMAN SPONTANEOUS EEG ANALYZED BY POWER SPECTRAL DENSITY, CORRELATIONAL AND PRINCIPAL COMPONENT ANALYSIS

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This report tries to analyze the maturation of the human EEG in the frequency spectrum between 0 and 20 Hz using correlational and Principal Component Analysis (PCA). Forty-eight subjects were recorded during 3 minutes of spontaneous EEG (24 children. 8-13 years old and 24 young adults, 18-23 years old). The comparison of the absolute Power Spectral Density (PSD) among children and young adults showed a higher PSD in children than in adults. The relative PSD showed a more complex pattern including a decrease of delta and theta rhythms and an increase in beta rhythm for adults with respect to children. Both absolute and normalized PSD showed significant correlations with age indicating that these parameters can be considered as predictors of the EEG maturation. Five different regions of the frequency spectrum presented a different rate of maturation measured by the adults/ children ratios of PSD mean and variance. Children and young adults showed the same principal components explaining Delta, Theta, low Alpha, Alpha, high Alpha, Mu and Beta rhythms. A similar but slightly different structure was found in the adults and children. The loading factors of PCA showed that most of the brain rhythms in children presented a lower frequency than adults. PCA found a structure based on latent variables in the EEG relatively stable during development demonstrated by loading factors and factorial scores topographies. A maturational trend of increased PSD and decreased frequency in children with respect to adults was found. These parameters could be relevant to assess the state of maturation of a child or young person and their changes over time.

D10-7

BLOCKAGE OF NORADRENERGIC SYSTEM DURING POSTNATAL DEVELOPMENT AFFECTS ADULT MOTOR REFLEXES AND LEARNING ABILITIES IN MICE

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Functional neuronal properties in the adult are normally determined during the embryonic and the neonatal period. During postnatal development, a critical period for the neuroendocrine and behavioral development, α_2-adrenergic receptors raise their maximum expression values at the level of the brainstem (Happe et al., 1999; Iushkova & Dygalo, 1995), and have been proposed as possible regulators of different processes during development (Dygalo et al., 2000; Happe et al., 2004). Neonatal manipulation of these receptors at the level of the pons in rats has been demonstrated to have consequences in the adult, affecting reflex responses such as startle and pre-pulse inhibition (Shishkina, et al., 2001; Shishkina et al., 2002; Shishkina et al., 2004). Clonidine, an agonist of α_2-adrenergic receptors, applied chronically, reduces neonatal noradrenaline (NA) brain levels and causes hypersensitivity to NA at the CA1 cells in the hippocampus, permanently affecting plasticity and epileptogenic kindling in adults (Gorter et al., 1990). The main objective of the present study has been to reaffirm the importance of the maturation of alpha-adrenergic system, evaluating the behavioural and cognitive effects in the adult. Our study shows that postnatal clonidine treatment in mice affects in the adult, not only reflex responses but also acquisition of conditioned responses.

D10-8

INTACT BRAIN AND MEANINGFUL HAND POSTURE KNOWLEDGE IN TWO AGE COHORTS

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Patients and healthy participants find it more difficult to perform transitive gestures, which involve the use of objects, than intransitive gestures, which do not require the use of objects. This dissociation is considered to be due either to differences in movement complexity (complexity theory), or to activation of different circuits in the brain associated with these two types of gestures (representational theory). The Postural Knowledge Test (PK), which does not require movement (pantomime or gesture production) but demands complex cognitive processes, shows meaningful transitive (PKT) and intransitive (PKI) scenes associated to everyday activities. Research with the PK test has shown that age influences the recognition of postures associated with these types of gestures in AD patients and healthy elderly. If this is due to brain damage or the impact aging has on the brain we might expect differences in adults of different ages. Dissociation between PKT and PKI has been reported in AD patients and healthy elderly (Mozaz et al. 2006), as well in Children (4,1 ±0,7 years old; Hamilton et al.2007). If the differences between PKI and PKT are due to brain pathology, the aging process or brain development, we might also expect age differences between these tasks in healthy younger adult participants. A group of 44 healthy students from the Universidad del Pais Vasco in two age cohorts (Cohort I, M= 21.54, SD = 1.250; Cohort II , M = 31.00, SD= 6.1) performed the PK test under time constraint. The total group of 44 participants showed significant differences between PKT and PKI ($t [43] = 4.35$, $p < .001$). There were no significant differences between Cohort I and Cohort II in PKT ($p > .05$), or in PKI scores ($p > .05$). Cohort II ($p < .001$) but not Cohort I ($p > .05$) showed significant differences between PKT and PKI. Complexity and representational theories are discuss in the light of some relevant cognitive processes required to perform the test and potential changes in brain circuits involved. Results help to better understand the discrimination of meaningful everyday postures.

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D10-9

OVERACTIVATION OF ALPHA-ADRENERGIC SYSTEM DELAYS THE POSTNATAL DEVELOPMENT AND BEHAVIOUR AND ALTERS THE RESPIRATORY ACTIVITY IN MICE

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During the development of the nervous system, the perinatal period, that is the length of time between the end of the gestation and lactation period in mammals, is particularly sensitive. The administration of various drugs, as well as the stress in the mother, can affect connections that are still forming in the brain of the neonate. In many experimental animal models, as in humans, newborns are quite immature, so it is common to use rodents (rats and mice) for these studies in order to see the effects of various actions in the nervous system and then extrapolate them to humans (Mirmiran, 1985). Many of the experimental approaches described can act on brain neurotransmitter systems, endocrine systems and behavioural states, affecting processes such as neurogenesis, trophic factors or relationships with DNA synthesis and also including mild changes when used during the period of rapid brain growth, as the perinatal period is (Mirmiram and Swaab, 1987). Especially important are the neurological consequences resulting from such situations, because at first they may go unnoticed. Alpha2-adrenergic receptors are overexpressed temporarily in proliferative zones in the developing brain. Both stimulation (Gorter et al., 1990) and blocking (Soto-Moyano et al., 1991) during this period alter the development of neural circuits, synaptic connectivity and neuronal responses. They even affect motor and cognitive skills later on in the adult (Shishkina et al., 2001). The main objective of the present study has been to reaffirm the importance of the maturation of alpha-adrenergic system, evaluating the behavioural and cognitive effects in neonates as well as respiratory activity, during early postnatal development, following chronic administration of the drug Clonidine, an alpha2 adrenergic system agonist. Our study shows that mice treated postnatally with clonidine have a general delay in psychomotor development.

D10-10

NEONATAL AND LONG-TERM NEURODEVELOPMENT AND NEUROSTRUCTURE IN A RABBIT MODEL OF FETAL GROWTH RESTRICTION

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Objective: To assess neurodevelopmental and neurostructural changes in a rabbit model of intrauterine growth restriction (IUGR) in neonatal and in the early adulthood period.
Material and Methods: A IUGR model was created in 18 New Zealand pregnant rabbits in which 40-50% of the uteroplacental vessels of one horn were ligated at 25 days of gestation and contralateral horn were considered as control. Caesarean section was performed at 30 days and living and stillborn fetuses were identified. After delivery, neonatal weight was recorded (20 cases and 20 controls). Postnatally, cases and controls were assessed by several neurological tests. At postnatal day +1 (neonatal period), we applied a neurological test that evaluate spontaneous motor activities, limb tone, reflex responses and olfactory sensitivity. After that, brains from 10 cases and 10 controls were collected and diffusion magnetic resonance (MRI) was performed calculating diffusivity and fractional anisotropy were calculated. The rest of the animals were followed until the 70th postnatal day (early adulthood), when they were evaluated by means of Open Field Behavioral test and Object Recognition Task. Results: When compared with controls, case group presented a higher rate of mortality and lower birthweight (g) (35.1% vs. 11.1% and 33.9 ± 9.8 vs. 45.9 ± 8.2, both $p<0.001$), respectively. Regarding neurological test, in neonatal period they presented a reduced locomotion, an increased limb's tone, an impaired reflex responses and olfactory sensitivity. In the early adulthood period, IUGR animals showed a higher degree of anxiety and a problem in short-term memory compared with controls. Regarding diffusion MR, IUGR neonates showed a significantly decreased fractional anisotropy (FA) (0.16±0.01 vs 0.14±0.02, $p= 0.02$) and a trend to higher mean diffusivity (MD) (1.47±0.14 vs 1.53±0.23, $p=0,45$). In addition, both FA and MD correlated with several variables assessed by functional tests. Conclusion: Intrauterine growth restriction by means of selective ligature of uteroplacental vessels in pregnant rabbit presented impairment in neurological performance in neonatal period that also persists in the early adulthood and it is associated with changes in brain structure assessed by diffusion MRI. Thus, it seems a suitable model in which more complex functional tests could be applied in order to describe brain damage in IUGR.

D10-11

HOW DO I FEEL WHEN YOU STROKE ME? ANIMAL/HUMAN RELATIONSHIP: BEHAVIORAL AND NEURONAL STUDIES

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Tactile stimulations are important in positive social interactions. The aims of our work were (1) to characterise the bond between a lamb and its caregiver, (2) to determine if stroking can potentiate the calming effect of the presence of the caregiver, and (3) to study the neuronal activation in the hypothalamus, a structure involved in social behaviour. A female caregiver provided daily care (feeding + stroking) to 24 lambs during 5-6 weeks and attachment to her was assessed in two tests. In a choice test between two humans, lambs preferred their caregiver to the other person (Median [interquartile range 25-75] of contact duration in seconds: 13.5 [1-46.5] vs. 1 [0-3]; P = 0.01). During a Separation-Reunion-Separation test, lambs which were distressed by social separation showed stronger appeasement when reunited with their caregiver than with a familiar human (contact duration: 1 [0-10] vs. 0 [0-1.5]; P = 0.006). In a next experiment, the impact of the presence of the caregiver in association or not with stroking was tested after 90 min of social isolation. Lambs' brains were collected at the end of it and neuronal activation was evaluated using c-fos immunohistochemistry. Following social isolation, lambs were appeased by the presence of their caregiver (decreased vocal activity in comparison to lambs left isolated). However, stroking did not potentiate this calming effect. The neuronal activation in the PVN and SON did not differ between lambs that were in the presence of their caregiver (whether stroked or not) and isolated animals (Neuron number /mm² in PVN: 478 [414-526] vs 487 [278-508] vs 446 [180-494]; in SON : 155 [97-184] vs 120 [94-160] vs 142 [111-227]; P> 0.1). In conclusion, a bonding process between the lamb and its caregiver can establish and the mere presence of the attachment figure is sufficient to appease socially isolated lambs. Stroking does not enhance neuronal activation in the hypothalamus. In future work we will investigate the immuno-chemical characteristics (oxytocin, CRF) of these activated neurons as preliminary results suggest that stroking triggers the release of oxytocin in the plasma.

D10-12

LATERALIZATION IN THE INVERTEBRATE BRAIN: LEFT-RIGHT ASYMMETRY OF OLFACTION IN APOIDEA SPECIES

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Brain and behavioural lateralization at the population level has been recently hypothesized to have evolved under social selective pressures as a strategy to optimize coordination among asymmetrical individuals. We compared olfactory responses of the right and the left antenna in two species of Hymenoptera Apoidea and the results seem to support the hypothesis: eusocial honeybees (Apis mellifera L.) appear to be lateralized at the population level in both behavioural (conditioning of the Proboscis Extension Reflex) and physiological (ElectroAntennoGraphy, EAG) responses (with a dominance of right-sides structures), whereas mason bees (Osmia cornuta L.), a solitary species, appear to be lateralized only at the individual level. In the honeybees, lateralization for short-term memory recalls of PER seems to be correlated with a difference in the number of olfactory sensilla, which is significantly higher on the right than on the left antenna. We also investigated lateralization of odour detection and learning in the bumble bee, Bombus terrestris L., an annual eusocial species of Apoidea. By training bumble bees on the proboscis extension reflex paradigm with only one antenna in use, we found asymmetrical performance favouring the right antenna in responding to learned odours even in this species. Electroantennographic responses did not reveal, however, significant antennal asymmetries in odour detection, whereas morphological counting of olfactory sensilla showed predominance in only one type of receptors, with a higher number of olfactory sensilla trichodea type A in the right antenna. The occurrence of a population level asymmetry in olfactory learning of bumble bee provides new information on the relationship between social behaviour and the evolution of population-level asymmetries in animals.

D10-13

DIFFERENTIAL IMPACT OF ACOUSTIC STARTLE ON SACCADE ONSET AND -DURATION AND ON PSYCHOMOTOR REACTION TIMES

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The Acoustic Startle reflex is known to speed up psychomotor reactions times ('StartReac' effect) and to influence horizontal saccades. Horizontal saccades have also been found to be influenced by the congruency of visual and acoustic stimuli in cross-modal reaction time paradigms. The aim of the current study was to test the influence of lateralized acoustic startle stimuli on important saccadic features such as onset (SOL) and duration (SDT) and on reaction times (RT) in a post-saccadic task.43 participants (12 male) were tested in a cross-modal reaction time paradigm. Their task was to focus visual targets on the left or right side of the screen while acoustic startle stimuli were presented lateralized in half of the trials in a either congruent or incongruent condition relative to the target. In half of the trials participants had to press a button at the side of the target as fast as possible if the target indicated to do so (post-saccadic task). Greenhouse-Geisser corrected within subjects ANOVAs showed that acoustic startle slowed down SOL ($p = 0.03$), but shortened SDT ($p = 0.007$) and speeded up RT in the post-saccadic task ($p < 0.001$). However, all this effects were independent of the congruency between the acoustic startle stimulus and the visual target. Our findings indicate that acoustic startle has differential impacts on SOL and SDT in a cross-modal paradigm and on RT in a post-saccadic task. The speeding up of psychomotor RTs and the decrease of SDT can be explained by the 'StartReac' effect. The slowing down of SOL may be due to shared neuronal circuits between startle, blinks and saccades in such a way, that neuronal resources necessary to process selective saccades are occupied during startle stimulation. The missing impact of the lateralization of the startle suggests that monaurally presented startle noise acts bilaterally on premotor burst neurons and that lateralization does not play an important role in this effect. Taken together our findings indicate that startle may not generally speed up the execution of voluntary movements, but that its influence also depends upon the system investigated.

D10-14

INCREASING SPECIFICITY FOR COMPLEX ACOUSTIC STIMULI TOWARDS THE TEMPORAL POLE OF CAT AUDITORY CORTEX

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Electrophysiological, behavioural, and connectional studies have identified a "what" processing stream within extrastriate visual cortex of the human, monkey, and cat. This pathway arises in occipital cortex and projects anteroventrally across the temporal lobe. Furthermore, studies have shown that visual areas along this pathway become responsive to increasingly complex visual stimuli. Similarly, in auditory cortex, electrophysiological studies suggest that areas beyond primary auditory cortex (A1) become responsive to increasingly complex acoustic stimuli along the sylvian gyrus of the feline temporal lobe. To examine this idea, we tested the hypothesis that ventral, but not dorsal, areas of the cat's temporal lobe have greater specificity for complex acoustic stimuli. We trained four mature cats to discriminate sounds in a two-alternative forced-choice apparatus. The animals concurrently learned to discriminate three classes of sounds: tones, narrow-band bursts, and conspecific vocalizations ("meows"). With criterion performance of 70% correct on three consecutive days, we identified that conspecific vocalizations were learned the fastest, while tonal discriminations often required twice as much time to master. After training, cooling loops were bilaterally placed over primary auditory cortex (A1), second auditory cortex (A2), temporal cortex (area T), and insular cortex (area IN) to permit their temporary and reversible deactivation. The animals were then tested while each of the areas was bilaterally or unilaterally deactivated. Presentation of the three classes of stimuli was randomly presented within each testing session. Bilateral deactivation of A1 resulted in discrimination deficits on all three stimulus classes. Bilateral deactivation of A2 caused deficits only for the narrow-band burst and conspecific vocalization classes. Bilateral deactivation of area T resulted in deficits restricted to the conspecific vocalizations. Unilateral deactivation of left, but not right, area T caused deficits during conspecific vocalization discriminations. Therefore, the present investigation provides evidence for the lateralization of conspecific vocalization discrimination in the left hemisphere. Bilateral deactivation of area IN did not produce deficits on any of the three stimulus classes tested. Overall, specificity for increasingly complex acoustic stimuli was identified along the temporal lobe of the cat. The results of this study indicate a "what" processing pathway in auditory cortex of the cat that arises in primary auditory areas and radiates down the temporal lobe through A2 and into area T.

D10-15

THE ROLE OF TASK ENGAGEMENT IN THE TEMPORAL CODING OF AMPLITUDE MODULATION IN PRIMARY AUDITORY CORTEX

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In the mammalian auditory system, modulations in neural activity related to task engagement have been described across multiple species and paradigms. To date, however, little has been shown regarding the effect of task engagement on the temporal dynamics of single neurons in auditory cortex. In the present study, multi-unit recordings were obtained from primary auditory cortex in awake rhesus macaques in both of two conditions - a passive listening condition and an active engagement condition – while acoustic stimuli were presented. Sounds were either unmodulated or amplitude-modulated broadband noise. The depth of amplitude modulation (AM) was varied from 6% to 100%. The best modulation frequency of isolated units was first determined and all subsequent AM stimuli were presented at this frequency. Initial analyses suggest that task engagement improves neurons' ability to discriminate AM from its unmodualted carrier, using both overall firing rate and phase-locking (vector strength). However, likely due to the limitations of vector strength in analyzing neural responses, only a weak effect of task engagement on phase-locking was found. In the present analysis, multiple robust measures of temporal dynamics of spike trains were used to quantify the effects of engagement on the encoding of AM. Pearson correlation and an entropy analysis (Kajikawa & Hackett 2005) reveal a strong effect of task engagement related to the encoding of AM. Specifically, task engagement disproportionately increases the temporal structure of neurons' responses to AM compared with broadband noise. A main effect of task engagement on the pre-stimulus entropy of multi-unit recordings was found, suggesting that the mechanism of this increase is a shift in the baseline activity of cells. This study provides evidence that behavioral state drives changes in the precision of temporal coding of amplitude modulation. Further, it illustrates the usefulness of measures other than vector strength in measuring temporal dynamics in auditory cortical units. In addition, the present analysis may shed light on the nascent hypothesis that attention can drive global, trans-network changes in the phase of oscillations (e.g. Besle et al 2011).

D10-16

ASPECTS OF MOTOR- AND AUDITORY DISCRIMINATION-LEARNING OF MICE IN THE SHUTTLE-BOX

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Understanding neural mechanisms of brain plasticity due to motor and perceptual learning in mammals requires a reliable training and test apparatus, well controlled procedures for measuring learning progress as well as success in an easily accessible animal model. Here, we present a newly developed behavioral learning paradigm for auditory discrimination learning in mice using a shuttle-box to test the acquisition of perceptual knowledge as discrimination of different auditory stimuli, knowledge transfer from one task to another, the development of sensory-motor associations, the acquisition of procedural knowledge as well as motor and cognitive skills. Also, shuttle-box training is suitable to phenotype mouse mutants and to test effects of agonists and antagonists of neurotransmitter systems of the brain on motor behaviour, auditory perception and auditory-motor association learning. The data presented will show how the shapes of learning curves express the above mentioned parameters measuring the development of motor and cognitive skills. They demonstrate that the shuttle-box discrimination learning paradigm opens up a new window to study brain functions in mice via a behavioural approach.

D10-17

THE RELATION BETWEEN STIMULATION FREQUENCY AND MAGNITUDE OF STEADY STATE VISUAL EVOKED POTENTIALS

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Steady State Visual Evoked Potentials (SSVEP) are neural responses evoked by flickering light. Focussing attention on visual stimulus that oscillate between 5 - 50 Hz, may induce corresponding (i.e., stimulus frequency and higher harmonics) frequencies in the electroencephalogram (EEG). This phenomenon is one of the major paradigms used for construction of Brain Computer Interfaces (BCI). The user may communicate by focussing attention on one stimulus while ignoring other stimuli delivered simultaneously. For the effective SSVEP based BCI the selection of stimuli frequencies is essential. Although it is generally acknowledged that the SSVEP response depends on the frequency of the stimulation, there are relatively few studies investigating this relation. The goal of this study was to investigate the dependence of the magnitude of SSVEP response on simulation frequency. The frequency range from 5 to 30 Hz, with 1Hz resolution, 26 frequencies in total were investigated. Four white squares displayed on LCD were backlighted by LEDs flashing with different frequencies while the subject was supposed to concentrate on an auditory - cued square. For each stimulation frequency, first the Common Spatial Patterns (CSP) method was applied to multichannel EEG data. Next, the statistically significant differences in SSVEP power before and during stimulation were computed for each subject. In this way relations between the average SSVEP strength across trials and the stimulation frequency were obtained. The acquired curves differ markedly between subjects. Besides, in majority of subjects the curve has more than one local maximum. Based on registered data there may be multiple frequencies evoking significant responses in each subject. Among variety of response maxima the range of 13-17 Hz seems to be the most universal.

The “Optimization of stimuli for SSVEP based Brain Computer Interfaces based on psychophysiology of phenomenon” project is realized within the Ventures programme of Foundation for Polish Science, cofinanced from European Union, Regional Development Fund.

D10-18

OPTIMIZATION OF SSVEP-BASED BRAIN COMPUTER INTERFACE - THE INFLUENCE OF VISUAL STIMULI FEATURES ON SSVEP RESPONSE MAGNITUDE

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Common approaches to building an effective BCI system based on Steady State Visual Evoked Potentials (SSVEP) paradigm focus on sophisticated mathematical methods for data analysis. The detailed examination of the role of different stimulus features is still lacking. Therefore, the main goal of this study was to investigate changes of the magnitude of SSVEP response in relation with different-looking stimuli. The five tested paramaters of the stimuli were: size, distance, colour, shape and fixation point. The stimuli were presented on a 4 squares on LCD screen with each square highlighted by LEDs. The tested paremeters were controlled by software and presented on the LCD while the flickering was generated by LEDs, also controlled by software. Four frequencies were chosen on the basis of the pre-test study. Data were obtained from 5 subjects. Each set of stimuli parameters consistently evoked the SSVEP response, but the magnitude depended on the parameters. Significant effect of size and colour was observed. Distance between stimulation fields and presence or absence of the fixation point had no effect on the response. In conclusion, despite of common belief and impressions reported by subjects, preliminary results obtained in this experiment suggest that absence of fixation point does not decrease the magnitude of SSVEP response. However, specific stimulus parameters play an important role in evoking visual response showing that stimuli rendering is an important factor in building effective SSVEP based BCI system.

The “Optimization of stimuli for SSVEP Brain Computer Interfaces based on psychophysiology of phenomenon” project is realized within the Ventures programme of Foundation for Polish Science, cofinanced from European Union, Regional Development Fund.

D10-19

QUALIA AS THE FUNDAMENTAL NATURE OF VISUAL AWARENESS

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It is apparent from much work over the past few decades that primate visual awareness is created through the activation of specific centers of the visual processing system. Research has focused on identifying and mapping the neural circuits and pathways that allow for visual data to be distributed and processed in parallel. Although much work is still required to fully comprehend this complex system, it is clear that the action and interaction of the various centers of the visual system results in our inner visual experience of the outer world. Despite the Herculean effort of the research community, however, it is still not clear how the inner sensation of, for example, a color like red is produced from neural excitation. In part, it is likely that the intimate connection we have with our own visual awareness makes it hard to ask questions about this phenomenon since our subjective experience of the outer world presents a complete picture that does not seem to yield to a reductionistic approach. I propose that awareness is produced in a quantized fashion similar to all other known phenomena. These quanta or qualia[1] of awareness result from the action of hundreds to thousands of neurons acting in concert to produce a specific electromagnetic field (EMF) pattern and all EMFs with the same complex topology will reproduce the same type of awareness. In other words, there is a specific field-topology that corresponds to seeing the color red and another distinct pattern that corresponds to seeing the color blue. A corollary to this hypothesis is that there are a finite number of distinct patterns that are identifiable and can be catalogued in a manner similar to the elements of the periodic table. It is likely that our infinitely varied human experience can be created from this finite set of qualia in the same way that an infinite number of objects in our universe are created from a distinct set of elements. This hypothesis is testable and I believe has much value in reframing the question of awareness and how it can be studied.

D10-20

CAN WHITE MATTER DIFFERENCES INFLUENCE TASK PERFORMANCE IN RHYTHMIC TIMING AND FORCE CONTROL?

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A wide network of brain areas is involved in the control of timing. Imaging and patient studies have recently explored the integration of timing with force control, and identified various cortical and subcortical structures that play a role. Control of force, and co-regulation of timing and force have been primarily associated with basal ganglia structures; while general timing function is believed to be associated with cerebellar structures. These key structures in the brain are connected through white matter tracts or neuronal connections. Our study looks at how the fractional anisotropy (FA) of these specific tracts correlates with behavioural performance. Higher FA values in a particular tract mean more myelination. These measures are collected using diffusion tensor imaging (DTI). The behavioural Expt. 1 & 2 have conditions where time and force are constant or varying. The participant hears a metronome and has to keep pace with the tone (responding with a tap/pulse) in the initial phase (synchronization). Visual feedback is provided in this phase. While in the continuation phase the participant continues to tap /pulse until cued to stop. The continuation phase needs one to keep track of the timing and force required. We expect the FA in tracts connecting the basal ganglia, M1 and the corpus callosum to correlate with better performance where force and time need to be regulated. Conversely, FA of tracts that connect cerebellum and M1 to correlate with performance requiring regulation of timing. We predict that within-subject behavioural variability will correlate with FA in these tracts. The study cohort consists of 15 participants between 20 – 40 years. We would further correlate our anatomical connectivity with functional connectivity using resting state fMRI. The results are discussed in the context of understanding how white matter connectivity of certain tracts influences performance that involves regulating timing and/or force. Future studies are intended to extend this experiment in patients with Parkinson's disease and cerebellar stroke.

D10-21

LATE RECOVERY OF GRAPING MOVEMENT AFTER ISCHEMIC STROKE: CLINICAL AND KINEMATIC ANALYSIS IN A CASE STUDY

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The most common cause of hemiplegia is damage to the corticospinal tract, involved in skilled activities. After stroke motor recovery assumes an exponential shape, with a faster initial recovery followed by a slower asymptotic pattern, with considerable variability in both shape and final outcome. Indeed more than 50% of stroke patients being left with a residual motor deficit, especially affecting the hand. In fully recovered patients, findings have showed an enhanced bilateral activation of motorpathways and recruitment of sensory motor structures. However late recovery of fine grasp hasn't been reported yet. This study assesses upper hand motricity in a case of right hemiplegic patient following ischemic stroke arisen in 2001. The motor performances of a 63years-old patient were assessed through clinical tests (2010), and kinematic analysis of grasping movement (2006 and 2010). Anatomical data (fRMI, DTI tractography) were also collected (2010). In the kinematic analysis of hand movement, the subject was asked to reach and grasp either a glass (2006; 2010), an apple or a cube (2010) Six right-handed healthy subjects performed the same experiment. Right hand movements were recorded in 3D with an optoelectronic system at a sampling rate of 50Hz. For each movement, kinematic parameters (Movement Time, Peak Velocity, Time to Peak Velocity, and Beginning of Finger Aperture) and spatial parameters (elbow and wrist azimuth) were computed and analysed. In 2010, the patient could grasp different objects size in agreement with the fugl-meyer (54/66) and the box and blocks scores (75/150). The patient's hand movement analysis (2006, 2010) revealed a significant reduction of Movement Time, an increase of TPV and BFA close to healthy subjects' values while spatial parameters remain unchanged. The comparison of patient and healthy subjects' performances revealed only a significant increase in patient's MT for all grasping conditions. Moreover in the apple condition the patient's spatial parameters were significantly higher. This first case of late motor recovery for fine grasp could be explain both by an spared cortical representation of the hand involved in motor command and by a partial integrity of the cortcicospinal tract.

D10-22

A POLYMORPHISM OF THE NR2A GENE RELATED TO ALCOHOL DEPENDENCE IS ASSOCIATED WITH AMYGDALAR AND HIPPOCAMPAL ACTIVATION DURING CLASSICAL FEAR CONDITIONING

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Glutamatergic transmission is critical in alcohol drinking behaviors and amygdala-dependent learning. In particular, rodents lacking the subunit NR2A of the NMDA receptor show both impaired associative learning and altered behavioral effects following alcohol administration. Recently in human individuals, a single nucleotide polymorphism of the NR2A encoding gene (rs2072450) has been associated with positive family history, early onset of alcoholism and risky drinking patterns in adolescents. Moreover, previous studies showed that persons at high risk for alcoholism exhibit impaired fear conditioning and amygdala hypo-activation during emotional recognition tasks. In this study we assessed fear conditioning in 102 participants, who were genotyped for the rs2072450 polymorphism. Functional magnetic resonance imaging was used during a classical cued fear conditioning paradigm, in which a conditioned stimulus was paired with a tolerable painful stimulation (CS+, 50% reinforcement), while another one was never followed by pain (CS-). We hypothesized that the group at high-risk for alcoholism, homozygotes for the C-allele (CC), would have shown deficient aversive learning compared to the resilient genotype, carriers of the A-allele (CA/AA), as revealed by decreased amygdala activation. Successful conditioning was proven by skin conductance responses and subjective ratings of valence and arousal. According to our hypotheses, the CC group showed significant bilateral amygdalar and hippocampal hypo-activation during acquisition of fear, compared to the CA/AA group. Additionally, CC displayed significantly reduced bilateral amygdala volume, compared to CA/AA. These results offer a neural base in support of a weak behavioral inhibition system present in individuals at high-risk for developing alcohol disorders. Moreover, as previous studies reported reduced amygdala volume in alcoholic patients, our volumetric data suggest this feature to represent a predisposing factor, rather than a consequence of chronic alcohol intake.

D10-23

BEHAVIORAL CONSEQUENCES OF CHRONIC ADOLESCENT *VS* ADULT CANNABINOID EXPOSURE AFTER PRENATAL STRESS IN FEMALE RATS

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Human epidemiological studies have provided compelling evidence that the risk of developing schizophrenia is significantly enhanced following various environmental insults occurring during the first or second trimester of a pregnancy. They also indicate cannabis exposure during adolescence to be a particular risk factor for schizophrenia. In addition, the “Two hit” model of schizophrenia suggests that an early neurodevelopmental insult sets up a neural predisposition for psychopathology, which may emerge in the presence of a subsequent environmental insult (a second hit) later in life. In the present study, we therefore investigated whether prenatal stress in rats produces a vulnerable state that, when combined to adolescent cannabis exposure, leads to the development of behavioral abnormalities reminiscent of schizophrenic symptoms. Female rats from mothers exposed or not to chronic restraint stress during late gestation (from GD11 to 21) was exposed to the CB1 receptor agonist CP55, 940 (CP) or its solvent, during adolescence (from PND 29 to 50) or adulthood (PND 77 to 98). Their behavior was evaluated later in social interactions and object recognition tests to assess social behavior and short-term memory respectively. The data indicate that adolescence cannabinoid exposure impaired object recognition performance independent of prenatal stress exposure. Social interactions were also significantly impaired in non-stressed rats that were exposed to CP during adolescence. Conversely, deficits in social interaction were also observed in prenatal stressed animals and reversed by CP. No significant effects of prenatal stress or CP were observed in adult exposure experiment. These results demonstrate that adolescence is a critical period for the long term deleterious effect of chronic cannabinoid exposure on both short term memory and social behaviors. The data also suggest that prenatal stress does not combine with cannabinoid exposure to evoke schizophrenic-like symptoms but prenatal stress subjects with social interaction deficits may benefit from pharmacologic manipulation of endocannabinoid signaling.

D10-24

TASTE OR PLACE ASSOCIATION FOR THE AVERSIVE COMPONENT OF LATERAL PARABRACHIAL ELECTRICAL STIMULATION

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The Parabrachial (PB) Complex, among other brain areas, has been frequently involved in emotional-affective processes (Bernard et al., 1991; Seward, 2004). Specifically, this brain area has been related to the aversive processing of noxious substances (i.e. hypertonic NaCl, Lithium Chloride or Copper Sulphate) (Sakai & Yamamoto, 1997; Mediavilla et al., 2000) or even drugs of abuse such as cocaine, methamphetamine or morphine (Bechara et al., 1993; Yamamoto & Sawa, 2000a, b). Thus, lesions of the Lateral PB Complex impair taste aversion learning (TAL) induced by the administration of morphine (Bechara et al., 1993). However, electrical stimulation of the external Lateral PB may develop behavioural preferences or aversions to both place and taste stimuli, a rewarding effect that may involve opioid mechanisms (Simón et al., 2007). In this study, we obtained a group of animals that showed consistent place aversions after electrical brain stimulation in a rectangular maze with three compartments. Subsequently, this "negative" animal group were subjected to a taste discriminative task in which one (of two) flavour, properly balanced and always in the same right/left place, was paired with electrical stimulation of the Parabrachial Complex. However, in this procedure, animals may initially learn the task by relating the aversive stimulation to place or taste sensory stimuli, which are both available at the same time. Therefore, we performed a flavour-placement (right/left) reversal test to examine the relevance of these two alternatives. The results of this study show that, after 8 learning trials, animals apparently developed significant aversions towards the flavour paired with the electrical brain stimulation. During the reversal test, however, the animals maintained their preference for the previous "safe" place and not for the previous "safe" flavour. In other words, the aversive treatment now induced a preference for the taste stimulus previously associated with brain stimulation, i.e., a preference for the place not associated with the stimulation. These data suggest that electrical stimulation of the LPB Nucleus may induce behavioural aversions (of unknown biological nature) that appear to be preferentially related to place (exteroceptive, propioceptive…) rather than taste/olfactory stimuli.

D10-25

ASSOCIATIVE LEARNING IN FEEDING BEHAVIOR AND DEVELOPMENT OF OBESITY

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Overeating results in overweight and obesity, conditions marked by an excessive accumulation of adipose tissue. Obesity is a serious risk factor for physical and mental health; brain pathologies linked to obesity include depression, anxiety and dementia. Eating behavior is a primal behavior and requires learning to associate specific sensory stimuli with different food types. Associative learning can be studied by pavlovian (classical) conditioning. A simple way to study appetitive learning involves paired presentation of a neutral stimulus (e.g. light flash) with an unconditioned stimulus (e.g. food delivery); with time, subjects develop a conditioned response such that the previously neutral stimulus (light) serves as a conditioned stimulus (CS). Using this Pavlovian paradigm, we observed that the majority of male C57Bl6/J develop a conditioned response. Memory for the CS was retained for at least 14 d; the memory was sufficiently strong to prevent metabolic state from influencing the results in subsequent test sessions. Interestingly, although the conditioned response declines over time, it is not extinguished even when the CS is not followed by a reward. Foods that are rich in sugar and fat are highly rewarding and stimulate food intake. Such foods activate limbic brain structures that play an indispensable role in associative learning. We therefore tested whether the fat content of the reward can influence pavlovian conditioning. For this, mice were rewarded with either high-fat (32%) milk or low-fat (5%) milk. Results showed that all mice could associate the visual stimulus with the reward, irrespective of its fat content. On the other hand, scrutiny of the data revealed distinct patterns of response in different individuals: while some developed Sign-directed Conditioned Responses (approached the light CS), others acquired a Goal-directed Conditioned Response (directed toward the location of reward delivery rather than to the CS), or an Intermediate Conditioned Response (combination of Sign- and Goal-directed strategies). When these three subgroups were placed on a high-fat diet for 8 weeks, all animals showed signs of obesity, but weight gains showed the following rank order: Goal-directed and Intermediate groups > than Sign-directed mice. These results suggest a possible correlation between the strategy employed in the pavlovian conditioning paradigm and the propensity to develop obesity.

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D10-26

DEFICIENCY OF LACTATE TRANSPORTER MCT1 IMPAIRS LEARNING AND MEMORY IN MICE

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There is increasing evidence for the neuroprotective effects exerted by lactate following traumatic brain injury, glutamate excitotoxicity and ischemic brain insult. Lactate is transported across the cell membrane, in a proton dependent manner via the Monocarboxylate transporters (MCTs). Several isoforms of MCTs have been described in brain (MCT1, MCT2 and MCT4). MCT1 is expressed by endothelial cells of microvessels, by ependymocytes, by astrocytes and by oligodendrocytes. Recently, consistent with the astrocyte neuron lactate shuttle (ANLS), it has been shown that the transfer of lactate from astrocytes to neurons is essential for long term memory consolidation (Suzuki et al., 2011). In order to better understand the role of lactate in brain energy metabolism, we have developed a mouse model deficient in MCT1 transporter. $MCT1^{+/-}$ heterozygous mice were generated by targeting the MCT1 gene via homologous recombination. In short; coding sequence from the first codon till the end of the exon was replaced by a LacZ reporter gene sequence. The X-gal mapping observed on brain tissue demonstrated the ß-galactosidase (ß-Gal) gene expression in the $MCT1^{+/-}$ mice. A particularly high ß-Gal gene expression was seen in the hippocampus. Furthermore, a 40% decrease in level of MCT1 protein expression was measured in the brain. The purpose of the present study was to investigate behaviors relevant to learning and memory, and motor function in mice deficient for monocarboxylate transporter 1. While mice heterozygous for MCT1, compared with littermate control mice, showed normal muscle strength and motor coordination, they displayed impaired spatial learning in Morris water maze, impaired working memory in an eight arm radial maze and an impaired emotional memory in the inhibitory avoidance task. The learning and memory deficits observed in the MCT1 heterozygous mice suggest that disruption of lactate transport in the brain via the MCT1 transporter results in cognitive impairment, in keeping with the recent evidence of their involvement in long term memory (Suzuki et al, 2011).

D10-27

A NOVEL, NON-MATCHING TO PLACE TASK IN A RADIAL ARM MAZE CONFIRMS EPISODIC MEMORY IMPAIRMENT IN 5XFAD MICE AND REVEALS SPATIAL WORKING MEMORY DEFICITS IN MONOCARBOXYLATE TRANSPORTER MCT2 KNOCKDOWN MICE

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Monocarboxylate transporters have been recently demonstrated to be mandatory for long-term memory storage (Suzuki et al., Cell 2011). However, their role in supporting glial-neuronal metabolic exchanges suggests possible effects also on cognitive abilities not necessarily requiring gene expression and de novo protein synthesis. In an attempt to assess the role of MCT2 in short-term memory, we designed a non-matching to place task on an 8-arm radial maze requiring the animals to focus on the discrimination of more recently vs remotely visited arms (working memory). Briefly, mice introduced in the central platform of the radial arm maze had access to only three baited arms. Once these arms visited, three more arms, intermingled with the first three, were made accessible. Entries in already visited arms were counted as working memory errors. Upon retrieval of all six baits, mice were confined for 2 minutes under a lid in the center of the maze, and a second trial started, where all baited, accessible arms were orthogonal to those of the first trial, thus introducing conflicting information as compared to the spatial references learned in the first trial. We first administered this test to mice carrying human familial Alzheimer's disease transgenes (5xFAD), that made a high number of repeated entries, especially in trial 2, thus showing both working and episodic memory impairments. The test was then administered to mice injected intrahippocampally with a lentivirus expressing a siRNA directed against MCT2 (MCT2 knockdown or KD mice). MCT2 KD mice were severely impaired in their ability to remember already visited arms (spatial working memory), as well as in the ability to benefit of recently acquired elements of salience, showing little or no improvement in working memory between the two consecutive daily trials. In contrast, all control mice invariably decrease working memory errors in the second daily trial. These results strongly support the role of MCT2 in mechanisms of sustained attention that might in turn result in memory deficits on a longer term scale.

D10-28

EARLY EFFECTS OF CHOLINE (CHOL) AND URIDINE-MONOPHOSPHATE (UMP) ON INSTRUMENTAL CONDITIONING AND LONG-TERM POTENTIATION (LTP) IN RAT PUPS

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Objective: To study the influence of oral supplementation with UMP + Chol through the lactation period and infancy on instrumental conditioning and in vivo LTP later in life. Methods: Nine days-old rat pups were paired by body weight and litter and distributed into 2 study groups. The pups were hand-fed a rat milk substitute from postnatal day 9 (PND9) to weaning (PND21) using special bottles and nipples; then an AING-93 powder diet was introduced. The study compounds were prepared in water solution and given to the animal as a daily supplement until PND57. The study groups were: Group 1, water; and Group 2, UMP + Chol. After PND57, the supplements were discontinued and the animals were fed with a regular chow diet. At 12-months, 6 animals per group were trained with instrumental conditioning tasks, using two light on/off protocols: RAND 1 (light on 20 s alternating at random with periods of light off, 20 min every day for 10 days) and RAND 4 (similar to RAND 1 but light was on for 10 s). Pellets were delivered only after pressing the lever during the light period. The animals were also surgically implanted with stimulating and recording electrodes in the hippocampal CA3-CA1 synapse to measure LTP. All the experimental procedures were approved by the corresponding local Ethics Committees, and were carried out in accordance to the Directive 2003/65/CE. Data were analyzed by two-way repeated means ANOVA. Results: Group 2 performed the instrumental conditioning tests better than group 1. Significant differences ($P = 0.022$) were observed for performance during the RAND 4 test. Regarding LTP, there were significant differences ($P < 0.05$) between the amplitudes of field excitatory postsynaptic potentials (fEPSPs) evoked in the two groups of animals by the 1st and the 2nd stimulus. In both cases, animals in group 2 presented fEPSP values higher than those evoked in group 1. Conclusion: Oral supplementation with UMP + Chol during the postnatal period resulted in a long lasting effect on cognitive performance (instrumental learning and experimentally evoked synaptic potentiation) measured in adult life. This points to an early programming effect of brain functionality by these dietary ingredients.

D10-29

EFFECTS OF VITAMIN A STATUS ON STRESS REACTIVITY, EMOTIONAL BEHAVIOUR AND SPATIAL MEMORY

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Vitamin A and its derivatives, all-trans retinoic acid (RA), are involved in the control of hippocampal synaptic plasticity and in cognitive functions. RA treatment can counteract the effects of vitamin A deficiency (VAD) on spatial memory deficits and on adult hippocampal neurogenesis disruption (Bonnet et al. PloS ONE, 2008). Furthermore, recent data have revealed interaction between retinoid and glucocorticoid signalling pathways. Particularly, an inhibitory effect of RA has been observed on the 11 _HSD1 expression, enzyme which regenerates active glucocorticoids. This modulation might contribute to the beneficial effects of retinoids on memory since it has been recently shown that hippocampal 11_HSD1 expression increases by ~30% with aging and correlates with spatial memory deficits. The present study aimed to elucidate the effects of vitamin A status on hippoccampal glucocorticoid activity and the consequences on emotional behaviour, spatial memory and cerebral plasticity. Thus, in order to characterize HPA axis function we firstly examined the effects of VAD (10 weeks) on plasma corticosterone levels in basal conditions and in stimulated conditions after open field test. To address the role of vitamin A status on stress reactivity, half of the vitamin A deficient rats and controls were supplemented with a vitamin A enriched diet during the 4 last weeks. Then, we examined the effects of long term VAD (14 weeks) and the preventive effects of 4 weeks of nutritional vitamin A supplementation on exploratory activity, anxiety-like behaviour and memory. Finally, we studied the different steps of hippoccampal neurogenesis by immunohistochemistry and the expression of retinoid and glucocorticoid target genes in the hippoccampus by quantitative RT-PCR. Our results showed that VAD induced a significant increase in corticosterone levels compared to controls after open field test, indicating HPA axis dysfunctions. Moreover, VAD rats exhibited anxiety-like behaviour evaluated in the plus-maze test and vitamin A supplementation prevented anxiogenic effect. Furthermore, VAD rats showed spatial memory deficits in the Morris water-maze restored by vitamin A supplementation. Finally, these cognitive changes were associated to modulation of hippocampal neurogenesis and expression of genes involved in glucocorticoid and retinoid signalling pathways.

D10-30

SEXUALLY DIMORPHIC SHORT AND LONG-TERM EFFECT OF EARLY STRESS IN EMOTIONAL AND COGNITIVE PROCESSES: POSSIBLE IMPLICATION OF AMINOACIDERGIC SYSTEMS

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It is well documented that stress during the brain development can induce long-term modifications in several neurotransmitter systems, but changes at different stages in life related with early and late behaviour are not well known. The aim of this study was to determine the sexually dimorphic effect of early stress (as maternal separation during the SHRP) in emotionally behaviour and spatial memory in early and late adolescence and in adulthood. In addition, we have study the possibility of alterations of aminoacidergic systems development as a consequence of maternal separation: focusing on the implication of these systems in behavioural processes, we assayed the tissue glutamate, GABA and taurine content of PN15, PN35, PN55 and PN175 in dorsal and ventral hippocampus. According to our results, maternal separation induces a different modification of aminoacidergic system of the hippocampus depending on sex. The concentration of glutamate and GABA is modified in the hippocampus of PN15 and PN35 males. Taurine levels are altered in the hippocampus of PN15 and adolescence maternal separated males and of adult females. We have notice that the ratio of internal ambulation in the open field is affected by maternal separation in early and late adolescence as well as in adulthood. There could be a relation between the variation in taurine content in the hippocampus and the emotionally response. Taurine modulates the aminoacidergic neurotransmission by the activation of GABA receptors and by an enhancement of both synaptic efficacy and axon excitability in glutamate neurotransmission. It is reported that neonatal brain contains high levels of taurine, and that the concentration of this aminoacid increases under stressful conditions. Spatial memory of males is modified by maternal separation: it is impaired in late adolescents but improved in adults. Considering the neurochemical changes, it seems that alterations in aminoacidergic systems due to maternal separation have behavioural effects and could be reversed during the adolescent period. In short, this study shows a sexual dimorphism in short and long-term responses to postnatal stress, and suggests that taurine has an anxiolytic effect and that could play a long-term neuroprotective role by modulating glutamate and GABAergic systems along the postnatal brain development.

D10-31

ENHANCED MEMORY CONSOLIDATION BY POST-LEARNING AUTONOMIC ACTIVATION IN RESPONSE TO STRESS

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Emotional material tends to be better remembered than neutral one, an effect that has been partly attributed to enhanced memory consolidation following arousal. In this study we investigated whether autonomic activation in response to stress might enhance consolidation for emotional pictures of different valence. 206 subjects saw a picture-set of 52 different faces (50% happy, 50% angry). Directly after the acquisition 2/3 of the subjects were exposed to a socially evaluated cold pressor test (immerse right hand into ice water for 3 min while being videotaped) the remaining subjects underwent a control procedure (warm water). Heart rate was recorded at baseline and during stress exposure. Recognition memory was tested two times at 30 min and 24 h after acquisition, using different pictures for each test. Subjects were divided into 3 groups of equal size according to their heart rate reactivity in response to the stressor: controls, non-responders and responders (Mean Delta HR +/-SEM: -.5 +/-.5 , -1.2 +/-.4 , 10 +/-.7 bpm, respectively). Analysis of variance revealed a significant interaction between group and time of memory testing (p=.001) but no interactions including valence: Responders outperformed controls (p=.003) and non-responders (p=.04) on the second test (but not on the first), irrespective of stimulus valence. These results show that consolidation of emotional material can be modulated by autonomic activation shortly after acquisition, and furthermore provide evidence that the stress induced heart rate response may be an adequate predictor of this effect.

D10-32

ACUTE RESTRAINT STRESS IMPAIRS CONTEXTUAL FEAR MEMORY CONSOLIDATION BY ALTERING HIPPOCAMPAL ERK1/2 ACTIVATION

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Although numerous studies have been devoted to stress-mediated disorders since 2001, such as posttraumatic stress disorder (PTSD), the understanding of stress-induced changes on memory consolidation and related cellular mechanisms is still fragmentary. Here we used two versions of Pavlovian fear conditioning that differentially involve the hippocampus to examine the specific effects of acute restrained stress on hippocampus-dependent fear memory. Contextual conditioning (tone-footshock unpairing) in contrast to elemental conditioning (tone-footshock pairing) requires essential hippocampal contribution. Exposure to acute restrained stress immediately before fear did not affect the acquisition but impaired the retention of contextual fear memory, an effect that was not observed in elemental condition. We have previously reported a differential activation of the ERK1/2 pathway in CA1, which was monophasic in paired conditioning (0–15 min post-conditioning), but biphasic (0–1 h and 9–12 h post-conditioning) in unpaired conditioning as revealed by immunocytochemistry. Interestingly, stress-induced deficits in contextual fear were associated to a reduction of the duration of the first ERK1/2 activation phase and blocked completely the occurrence of the second phase. Additionally, the monophasic activation of ERK1/2 observed after elemental conditioning was not affected by the stress. Because acetylation of hippocampal histone H3 is increased following ERK activation or contextual fear conditioning *(Levenson et al., J. Biol. Chem. 2004, 279: 40545–)*, we also examined the effect of acetylated H3 in CA1. We observed that contextual conditioning-induced histone H3-K9 acetylation was slightly reduced by stress, the first hour after contextual conditioning but had recovered towards control levels at 9 h suggesting a weak cross-talk interaction between ERK1/2 and histone H3 acetylation in this paradigm. In order to examine the effect of stress during the delayed consolidation phase, mice were submitted to a restrained stress either 3h or 7h30mn after contextual condition and tested to the context 24h later. None of these conditions was shown to alter the retention of contextual fear memory suggesting the absence of proactive effect of stress on the testing to the context. Therefore, stress impact on psychobiological processes involved in memory consolidation depends on temporal relationships between the stress event and the acquisition of the hippocampal-dependent information.

D10-33

ALTITUDE ACCLIMATIZATION IMPROVES SUBMAXIMAL COGNITIVE PERFORMANCE IN RODENTS

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The potential benefits of altitude acclimatization on submaximal cognitive performance (understood as the expected dependence on the complexity of the proposed task) were evaluated in rodents with electrophysiological and behavioral techniques. We used four groups of mice, separated according to whether they had been acclimated or not, to a simulated altitude of 5000 m and were tested at a height of 35 or 5000 m. The simulated altitude acclimatization necessary for the animals was achieved in a hypobaric/hyperbaric chamber prepared for the development of cognitive tests and conventional electrophysiological studies. First, we performed classical eyeblink conditioning. To achieve a submaximal performance, we presented a tone (20 ms, 70 dB, 6 KHz) as a conditioned stimulus, followed 250 ms later by an unconditioned stimulus, consisting of an electric shock applied to the supraorbitary nerve (50 μs in duration and 2 _ threshold). With the repeated exposure to this pair of stimuli we collected a learning curve, expressed as a percentage of conditioned responses. Another behavioral test was object recognition. This test is related to declarative memory and shows the preference of the mouse for a novel object compared to another object family, after this identification and discrimination. In this case, the novel object was designed from the same family, increasing its complexity. The animal that best remembers the familiar object explore longer the novel one. We also performed an operant conditioning test, using a Skinner box. The animal gets a reward (food) after pressing a lever, assuming an 1:1 fixed ratio paradigm, and increasing complexity in successive paradigms. Finally, we assessed spatial memory and orientation ability using a 8-arms maze, three of which have a key indicating the presence of food at its end. Taken together, the collected results indicate that simulated altitude in the hypobaric chamber decreased cognitive abilities and that, in contrast to data obtained when maximum performance is expected, the altitude acclimatization improves cognitive performance, even surpassing those of control animals, when the complexity of tests do expect a submaximal performance.

D10-34

BEHAVIOURAL ALTERATIONS IN ADULT RATS THAT HAD UNDERGONE GLOBAL HYPOXIA AT BIRTH

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Perinatal asphyxia remains as one of the most important causes of death and disability in children, without an effective treatment. Moreover, little is known about the long-lasting behavioral consequences of asphyxia at birth. Therefore, the main aim of the present study was to investigate the motor, emotional and cognitive functions of adult asphyctic rats. Therefore, the main aim of the present study was to investigate the general activity/motor exploration, anxiety-like behaviors, and learning and memory processes of adult asphyctic rats. Experimental subjects consisted of rats born vaginally (CTL), by cesarean section (C+), or by cesarean section following 19 min of asphyxia (PA). At three months of age, animals were examined in a behavioral test battery including elevated plus maze, open-field, Morris water maze, and an incentive-downshift procedure. Results indicated that groups did not differ in anxiety-related behaviors, although a large variability was observed in the asphyctic group and therefore, the results are not completely conclusive. In addition, PA and C+ rats showed a deficit in exploration of new environments, but to a much lesser extent in the latter group. Spatial reference and working memory impairments were also found in PA rats. Finally, when animals were downshifted from a 32% to a 4% sucrose solution, an attenuated suppression of consummatory behavior were observed in PA rats. In summary, PA rats showed reduced exploration in a novel environment, spatial reference/working memory deficits and an attenuated behavioral response to incentive-downshift. These results confirmed and extended those reported previously about the behavioral alterations associated with acute asphyxia around birth.

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D10-35

ANTIHYPERTENSIVE TREATMENT DECREASES COGNITIVE LOSS IN TG HYPERTENSIVE/AD MODEL MICE

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Midlife hypertension is a risk factor for stroke and vascular dementia, and the incidence of these diseases grows with increasing blood pressure. Recent studies have shown that hypertension is also a risk factor for Alzheimer's disease (AD). In our previous studies we have demonstrated that long-term midlife untreated hypertension leads to perturbed vascular function in AD model mice. Together this, in turn, leads to increased cognitive dysfunction and pathology in these mice. Therefore we hypothesized that hypertensive AD model mice that are treated with an antihypertensive drug Losartan would show less AD pathology and cognitive deficits compared to untreated (and thus hypertensive) mice.

Blood pressure, cerebral blood flow, cognitive performance and A□ deposition and inflammation were quantitatively assessed in Tg AD model mice that were infused with Angiotensin II to make them hypertensive and in Tg Hypertensive/AD model mice (LZM line mated with APPswDI) at 8 months of age, after being implanted with an Alzet minipump containing Losartan (30mg/kg/day) at 5 months of age. At 8 months of age the animals (n=10/group) were tested in an array of behavioral tests to determine their emotional and cognitive status. Following the cognitive analysis, the animals were anesthetized, and sacrificed for biochemical and histopathological analysis. The treatment with Losartan significantly decreased blood pressure, which in turn improved functional hyperemia ("the neurovascular unit"). The non-treated Hypertension/AD mice were cognitively impaired compared to treated Hypertensive/AD mice, and they showed a significantly higher A□ load and increased inflammation in the brain. In conclusion, sustained midlife hypertension leads to decreased cerebral blood flow, cognitive deficits and increased Alzheimer's pathology, and treating this hypertension prevents these changes, indicating that early treatment of hypertension is important for preventing Alzheimer's dementia.

D10-36

COGNITIVE DEFICIENCIES ASSOCIATED WITH ARTHRITIC PAIN ARE RESCUED BY DREAM DELETION

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It is well known for long time that chronic pain impairs memory and learning in humans. Transgenic mice overexpressing the Tnf-alpha human gene is an excellent model of chronic pain caused by arthritis. In this project we have extensively characterized Tnf-alpha transgenic mice with respect to learning and memory and show clear deficiencies in object recognition memory compared to wild type mice. Interesting, treatment with indometacin, a non-sterioidal anti-inflamatory drug, over two days before and during cognitive tests partially rescued cognitive impairment caused by arthritis. On the other hand, DREAM protein is involved in cognitive processes as well as in pain modulation. In fact dream knock out mice show marked analgesia as well as facilitation in learning and memory processes compared with non-mutant mice. We have characterized cognitive properties of the double mutant mice lacking dream and overexpressing TNF (Tnftg/dream-/- mice). Interesting, Tnftg/dream-/- mice still show arthritis, they do not suffer from pain. On the other hand, the double mutant mice show similar cognitive properties as the non-arthritic wild-type mice. All this data suggest that DREAM could be a missing link between pain responses and cognition. Thus, DREAM could be a potential new target to reduce pain but also to increase cognition in patients affected by arthritis.

D10-37

THE ROLE OF SLEEP IN THE PROCESSING OF EMOTIONAL MEMORIES- EVIDENCE FROM BEHAVIOUR AND EVENT-RELATED POTENTIALS

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Recent studies proposed that rapid eye movement (REM) sleep is crucially involved in the consolidation of emotional over neutral memories. In this context, it was argued that emotional affect and the content of emotional memories are decoupled during periods of REM sleep which results in enhanced retention of the emotional contents and in a down-regulation of the emotional tone. Empirical evidence on this concept is still lacking. In the present study, we investigated the effects of sleep intervals rich in slow wave sleep (SWS) vs. REM sleep on the consolidation of emotional pictures using event-related potentials (ERPs) as well as on subjective ratings of valence and arousal. On the background of previous studies showing that correctly remembered stimuli elicit more positive slow potentials (slow wave) we hypothesized that REM sleep after learning results in increased positivity of the slow wave during successful recollection of emotional pictures. In parallel, we expected the subjectively rated emotional arousal to be decreased after REM-rich periods of sleep. Sixteen healthy, young men learned 50 negative and 50 neutral IAPS pictures. After subsequent 3-hrs retention sleep interval filled with SWS-rich early sleep or REM sleep-rich late sleep recognition memory as well as subjective arousal and valence ratings were assessed. Event-related potentials were recorded during learning and retrieval of the pictures. In accordance with our hypothesis, emotional pictures were remembered better than neutral pictures after REM- compared to SWS-rich sleep. Moreover, enhanced positive-going ERP activity in an early interval of the slow wave (300-500ms after picture onset) was selectively detected after REM-rich sleep when comparing emotional old vs. new and neutral pictures. Valence and arousal ratings of emotional pictures were not particularly affected by periods of REM or SWS after learning. Our results confirm previous findings of REM sleep supporting emotional memory retention thereby uncovering ERPs as a sensitive measure for the beneficial effects of sleep on emotional memory consolidation. Nevertheless, the emotional tone was not modulated by REM-rich sleep.

D10-38

SLEEP SELECTIVELY ENHANCES CONSOLIDATION OF EPISODIC-LIKE MEMORY

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Episodic memory refers to the conscious recollection of a unique past experience in terms of "what" happened, "where" and "when" (Clayton, Griffiths, Emery and Dickinson, Philos. Trans. R. Soc. Lond., Biol.Sci, 2001, 356, 1483–1491). Sleep has been identified as a state that optimizes the consolidation of newly acquired information in memory, depending on the specific conditions of learning and the timing of sleep (Diekelman and Born, Nat Rev Neurosci, 2010, 11, 114-126). To determine if sleep is important for the consolidation of episodic-like memory, we tested in rats retention of and episodic-like memory requiring the binding of an object memory into a spatio-temporal context, as well as retention of its individual components using separate tests of novel object recognition, place object recognition and of temporal memory, respectively. The 90-min retention interval between encoding of the task (learning) and retrieval testing covered either a period of normal morning sleep or sleep deprivation or a period of evening wakefulness. Sleep during the retention interval, in comparison with the other two retention conditions significantly enhanced retrieval in the episodic-like memory task as well as in the place object recognition and temporal memory tasks. In fact, when the rats stayed awake during the retention interval, there was no significant memory left at retrieval testing for the learnt object place and temporal memory. Sleep did not benefit object recognition memory which unlike the other components of episodic memory is not dependent on hippocampal function. Further experiments revealed that episodic memory in rats which had stayed awake during the first 90-min interval after learning, was not recovered when they were allowed to sleep during the second 90-min interval after learning. The pattern of findings indicates that sleep specifically supports the consolidation of hippocampus-dependent (episodic-like) memories, in particular when it occurs shortly (i.e., within 90 min) after the learning phase.

D10-39

FEELING YOUNGER: IMPACT OF VOLUNTARY EXERCISE ON BEHAVIOURAL FUNCTION IN SAM MICE

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Evidence is accumulating that an active lifestyle and physical activity might prevent the decline in the age-related cognitive function, best defined in aged animals and elderly populations. We therefore analyzed the effects of voluntary exercise in the senescence accelerated prone mouse 8 (SAMP8) showing impaired learning and memory and its control line (SAMR1), also assessing gender differences. A battery of behavioral tasks (sensorimotor task, hole-board, elevated plus maze, home cage activity, and visual discrimination task) was used to determine the long-term benefits. Voluntary exercise was assessed during 24 hours, 3 alternate days every week, for 25 weeks. The results indicated that female and P8 mice reflected higher number of wheel revolutions. SAMR1 mice had better performance in the sensorimotor task, increased exploration in the hole board and better performance in the visual discrimination task than SAMP8; whereas SAMP8 and male mice showed decreased anxiety-like in the elevated plus maze. Home cage activity was higher in females than males and females showed better cognitive performance than males; whereas exercise overall increased home cage activity and performance over the acquisition in the visual discrimination task, although no differential effects and significant interactions between exercise and SAMR1/SAMP8 or exercise and males/females were detected. Thus, the voluntary exercise protocol used in this study improved sensorimotor ability, increased overall activity, learning acquisition and memory performance, resulting in a beneficial and not stressful treatment to palliate the detrimental cognitive effects seen in the aging process.

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D10-40

SLEEP ENHANCES MEMORY CONSOLIDATION IN THE HIPPOCAMPUS-DEPENDENT OBJECT-PLACE RECOGNITION TASK IN RATS

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The positive impact of sleep on memory consolidation has been shown for human subjects in numerous studies, but there is still sparse knowledge on this topic in rats, one of the most prominent model species among neuroscience. Here, we examined a possible role of sleep in the object-place recognition task, a task closely comparable to declarative tasks typically applied when testing human subjects. It is a one trial task, doesn't involve stressful procedures, is hippocampus-dependent and can be repeated within the same animal. In a first experiment animals underwent the task twice. In, a Morning condition the retention delay was in the natural inactive phase and in the Evening condition the delay was placed in the active phase. As hypothesized, the task could only be successfully completed after the inactive Morning delay, during which the animals presumably slept. To control for an effect of putative circadian factors, a second experiment was conducted involving continuous EEG recordings and two sleep deprivation conditions, during which animals were kept awake within the 2 hour retention delays. Again, animals performed well only in the Morning condition ($p < .05$). Sleep deprived animals of both conditions failed to complete the task. FFT analyses during the non rapid eye movement (NREM) sleep periods revealed increased power in the EEG slow oscillation (0.85 – 2.0 Hz) and delta (1.0 – 4.0 Hz) bands in the Morning as compared to the Evening condition. EEG power in the spindle band (12.0 -15.0 Hz) was increased in the Morning delay as compared to a baseline recording. We conclude that memory consolidation in the object-place recognition task is sleep dependent, and requires NREM sleep rich in both slow wave and spindle activity.

D10-41

AGE, LEARNING AND MEMORY SPECIFIC REGULATION OF HIPPOCAMPAL ESTROGEN RECEPTOR α IN MALE RATS

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Estrogen and estrogenic functions are well known to be involved in the modulation of learning, memory and mood in female humans and animals. However, possible similar effects in males have been largely underestimated. The ligand of estrogen receptors in the male hippocampus can be locally synthesized by enzymatic (aromatase) conversion of testosterone to estradiol. The functions of different steroid receptors are closely interconnected and undergo developmental changes. Therefore we investigated the expression of estrogen receptors α and ß, androgen and glucocorticoid receptors and the concentrations of 17-ß-estradiol, testosterone and corticosterone in the hippocampus of pubertal (8 weeks), young adult (12 weeks) and adult (24 weeks) male rats. Within each age class, one group of rats was treated with testosterone (i.c.v.), a second group received vehicle during spatial training; untrained rats served as additional controls. We found differences in learning and memory formation in an age dependent manner with the best performance in pubertal rats. These differences could not be reduced to age dependent differences in general activity and exploration that were also observed. Testosterone and vehicle treated adult rats showed reduced expression of estrogen receptor α and the androgen receptor and increased expression of the glucocorticoid receptor as compared to untrained animals. The concentrations of estradiol in both experimental groups were lower than in controls. The concentration of testosterone was increased in the testosterone treated group. We found no difference in the behavioral performance of the two experimental groups. Pubertal rats showed no difference in the concentrations of any hormones. In contrast to adult rats, the expression of estrogen receptor α was massively increased in both experimental groups as compared to controls and adult trained rats. The behavioral performance again was unaffected by the application of testosterone. The results suggest a specific role of estrogen receptor α not only in age class related differences in impulsivity, increased risk and novelty seeking, reflected in general activity and exploration, but also in cognitive abilities. In addition, these differences seem to be more related to estrogen and estrogenic functions rather than to testosterone.

D10-42

ENVIRONMENTAL ENRICHMENT IMPROVES RECENT BUT NOT REMOTE LONG-TERM MEMORY IN ASSOCIATION WITH A MODIFIED BRAIN METABOLIC ACTIVATION PROFILE IN ADULT MICE

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Many reports have shown that environmental enrichment constitutes an interesting model to elicit brain plasticity in laboratory animals. Indeed, it enhances learning and memory performances in rodents and is able to reduce several memory deficits, such as those occurring during aging. Whereas the morphological changes underlying these beneficial effects are well documented, few studies have addressed the influence of this housing condition on the neuronal networks underlying memory processes. We assessed the effects of environmental enrichment on behavioural performances and brain metabolic activation during a long-term memory task in mice. Adult mice were housed in standard or enriched conditions for three weeks. Then, recent (24 hours) and remote (8 weeks) long-term memory performances were measured in the passive avoidance test. After testing, brain metabolic activation was assessed through cytochrome oxidase histochemistry. Enriched condition significantly improved recent long-term memory performances in the passive avoidance test in association with an increased metabolic activation in the frontal and prefrontal cortices and a decreased activation in the baso-lateral amygdala and the hippocampus. By contrast, enriched condition did not improve remote long-term memory performances, but globally decreased cytochrome oxidase activity. Our findings suggest the involvement of regions of pivotal importance during recent long-term memory, such as the frontal cortex, in the beneficial effects of environmental enrichment.

D10-43

THE EFFECTS OF LONG TERM ENVIRONMENTAL ENRICHMENT ON THE HIPPOCAMPAL METABOLIC ACTIVITY OF AGED RATS

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Aging is associated with deterioration of the retention process and learning impairment, being spatial learning the most affected. Environmental enrichment could have beneficial and protective effects against aging. Therefore, we aimed to determine whether long-term environmental enrichment has effects on neural metabolic activity of middle old rats (18 months-old) and whether this enrichment has a positive effect on age-related spatial memory impairment. The following groups of Wistar rats were used: G1 aged rats that were maintained in a prolonged (7 weeks) environmental enrichment (n=8); G2 aged rats that were submitted to an allocentric spatial memory task (n=10); G3 aged rats that were maintained in a prolonged (7 weeks) environmental enrichment and trained in the spatial task. A control group (n=10) G4 composed by 18 month-old rats was included. The rats that were maintained in the environmental enrichment were submitted to it at the age of 16 months. During this condition, the rats were housed during four hours each day in a group of eight in a cage contained wood houses and sound colored toys. G2 and G3 were submitted to a spatial reference memory task in a four-arm radial water maze during four consecutive days. Six trials were performed each day. The animals were released from different arms whereas the platform remained submerged in a fixed position. For each animal, the latency to reach the platform, distance covered and velocity were recorded. All groups were decapitated, 90 min. after the last trial in the case of trained groups. Brains were removed and frozen in isopentane. Coronal sections (30 µm) were submitted to cytochrome oxidase (COx) histochemistry. Staining intensity of the hippocampal CA1, CA3 and dentate gyrus (DG) regions was quantified by densitometric analysis. The results show better spatial reference memory in G3 than in G2. This better learning could be related with a decreased COx activity in CA1 region of G3 compared to G2. Nonetheless, there are not differences between these groups in CA3 and DG regions. The environmental enrichment could help spatial reference memory learning causing a decrease in energy consumption of CA1. This could be related to a reduction of typical aging synapse loss.

D10-44

BEHAVIORAL FLEXIBILITY DURING PHYSIOLOGICAL AGING AND IN THE ANIMAL MODEL OF NEURODEGENERATIVE DISEASES

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Aging is a long lasting and irreversible physiological process during life of all organisms. Two main groups of factors leading to aging could be distinguish – factors determining and factors modifying aging. The outcome of actions of these factors determine successful or pathological aging. Experimental data suggest that, in central nervous system, differences between successful and pathological aging apply not only to plastic changes but also to the rate of decline in behavioral flexibility. The present study was undertaken to determine the influence of aging on behavioral flexibility in physiologically aging rats and TgL1 mice which overexpress truncated human tau. We used three age-groups of Wistar rats: 3, 12 and 24 months old and six groups of mice: 1.5, 3, 6, 9, 12 and 15 months old. The cognitive behavior of animals was assessed in tests: Object Re-location Test and Object Recognition Test both in rats and mice, as well as Non-matching to Position Test - acquisition and reversal in rats, and Open Field Water Maze (Chen protocol) in mice, which measure different aspects of behavioral flexibility. In rats we observed that the decline in behavioral flexibility is mild and appears at a late age and not in all forms of memory. In contrast, TgL1 mice present with early onset and long lasting impairment of behavioral flexibility. Additional immunohistochemical analysis of brain tissue revealed significant increase in phosphorylated tau expression and changes in tau compartmentalisation in neurons of only aged rats, whereas those abnormalities were present both in young and aged transgenic mice. In physiologically aging rats we observed age-dependent, changes in functional (beta-tubulin) but not structural defects in the cytoskeleton (MAP2). In TgL1 mice, both functional and structural breakdown of the cytoskeleton (beta-tubulin and MAP2) was present and this was accompanied by the degeneration of neurons in both age groups. Our data indicate that the time course of behavioral flexibility and pathomorphological changes is different in both models. Rat model of physiological aging and the model provided by TgL1 mice represent different types of aging. Thus both models could be used to examine mechanisms of successful and pathological aging and to test therapeutic strategies in age-related neurodegenerative diseases.

D10-45

PRIMING EFFECT MODULATION IN PATIENTS WITH ALZHEIMER'S DISEASE

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There are many studies to see how changing the mode of presentation of stimuli can do to influence more or less on the effect of priming. Our study aims to find if you change the mode of presentation of a stimulus can occur in an increase or decrease in response time (RT) in AD patients in a phase of priming. We present a computerized task SuperLab 4.0 software with which subjects had to categorize stimuli presented to him on the screen (pictures or words) as "living" or "be not alive". These two categories were divided into four: animal, vegetable (living), utensils and clothing (not live). There were two control conditions (without change of form in the presentation of stimuli in the priming phase) and two experimental conditions (change in the mode of presentation) to 3-stage AD subjects and 3 subjects with mild to moderate stage AD. This experiment controlled for age of acquisition, frequency and typicality and the dependent variable was the RT of those responses answered correctly by the subjects. The results supported the data obtained in other studies with subjects without brain damage and that patients with AD respond faster priming phase when the mode change occurred verbally drawing drawing by word and faster when stimuli were "alive" to "not live". Looking at the results in terms of semantic categories in which the stimuli were grouped, we can see how it meets the pattern found in control groups, except for the clothing category since subjects sometimes confused with the clothing body covering. This caused the subjects hesitate to whether they should be categorized as living or nonliving. All these results lead us to believe that the variable "mode of presentation of items" is the priming effect by modulating the increase or decrease the RT.

D10-46

MEMORY IMPAIRMENT AND NEUROPHYSIOLOGICAL ABNORMALITIES IN ACROMEGALY

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Introduction: De novo acromegalic patients show neurocognitive impairment associated to high GH and IGF-I levels1. It has been suggested that this impairment might be a consequence of lasting exposure to GH and IGF-I excess on the central nervous system. Nevertheless, it remains undetermined whether neurocognitive problems are still present when the disease is cured or controlled with drugs. Aims: To study the neurocognitive state of acromegalic patients after cure and patients with successful pharmacological control of acromegaly. Methods: Cognitive functions, emotional status and quality of life (QoL) were assessed in fifteen patients cured of acromegaly (10 women, median age = 50.93) and 15 patients with pharmacologically control of acromegaly (somatostin analogs) (10 women, median age = 48.19). The criteria established for cure after pituitary surgery were normal IGF-I levels for age and gender and a GH nadir < 1 ng/mL after an oral glucose tolerance test. The criteria established for good control of acromegaly were normal IGF-I levels for age and gender and a basal GH < 2 ng/ml. These patients' data were compared to two age- and gender-matched additional groups, comprised of 15 patients with non-treated active acromegaly and 15 healthy controls. Results: No difference was observed in tests assessing attention, verbal skills and executive functions among the different groups. However, significant differences were found in memory tests (all Ps < 0.01). Concretely, patients with active non-treated acromegaly and patients with good pharmacologically control performed worse in working memory and long-term memory than healthy subjects and cured patients. Further analyses showed a significant correlation between emotional/QoL and severity of memory impairment in pharmacologically controlled patients. In the active non-treated group, no correlation between QoL, depression and severity of memory impairment was observed. Patients with cured acromegaly did not differ from healthy subjects in cognitive functions and emotional/QoL status. Conclusion: Our results confirm memory impairment in active acromegaly that could be due to GH and IGF-I excess. In addition, our findings suggest a good recovery of cognitive impairment after cure of acromegaly while patients with good pharmacological control of the disease show similar memory impairment than that observed in de novo patients.

D10-47

EFFICIENT STRATEGIC PROCESSING IN WORKING MEMORY IMPLEMENTED BY A FRONTO-TEMPORAL NEURAL NETWORK, PROMOTES EPISODIC MEMORY FORMATION

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Introduction: Two subtypes of memory have been shown to engage partially overlapping neural networks: working memory (WM) as a type of short-term memory and episodic memory (EM) as a subtype of long-term memory (Ranganath et al., 2003). To explore the relation between WM and EM we examined neural activity during WM tasks that differentially promote strategic processing, assuming that MTL and prefrontal regions should contribute to successful EM formation by relieving WM resources in conditions that help to implement the strategic organisation among items. Methods:16 adults were scanned using fMRI as they studied pictures in a delayed match-to-sample (WM) task using 4 conditions: items belonging to the same semantic category (semantic chunking), items differently associated with each other (associative chunking), items not associated with each other (random) and a control condition with one item in the WM set (control). To examine EM performance, participants assign confidence ratings to old vs. new pictures on a 6-point scale. Results and Discussion: In the EM test, subjects recognized items from the semantic chunking condition significantly better than random items. A trend to significance was found that associative items were better recognized than random items. fMRI results show neural activity during WM retention for all conditions evoking activity in several areas including frontal and temporal regions. Supporting EM formation, neural activity was found for chunking conditions in frontal and temporal regions. An overlap in neural activity was found during WM retention and successful EM formation in frontal and parahippocampal areas. In the random condition, neural activity in frontal and temporal regions during WM correlated negatively with EM performance, suggesting that increased neural activity during WM is not beneficial for successful EM formation. Our results confirm that EM performance is promoted by neural activity in frontal and temporal areas during WM retention, which implements efficient strategic processes that are critical for correct subsequent EM recognition.

D10-48

SEMANTIC ENCODING IMPROVES MEMORY CONSOLIDATION

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Evidence suggests that sleep facilitates memory consolidation, which can, however, itself occur in wake states. According to the synaptic homeostasis hypothesis, the role of sleep is to downscale synaptic strength to a baseline level that is energetically sustainable, makes efficient use of gray matter space, and is beneficial for encoding new memories in long-term memory. Here we evaluate the effects of direct and indirect manipulations of memory encoding on subsequent consolidation processes. One of these manipulations occurs during the study phase and aims to improve recognition in an associative memory task; the second one, introduced after the study phase, evaluates the effects of the previous treatment on early consolidation processes; and the third one occurs in the night preceding the study phase with the aim of interfering subsequent encoding and consolidation processes. In order to facilitate the formation of new associative memories, we manipulated the semantic context where the to-be-remembered associations were encoded. For this, participants were trained to memorize pairs of celebrities who either have an equal (semantically congruent context) or different profession (semantically incongruent context). The beneficial effects of semantic congruence are expected to be more resistant to factors interfering with encoding and subsequent consolidation processes. To test this hypothesis, one group of subjects was sleep deprived during the night immediately preceding the study phase; whereas the other group performed an interference task one hour just after the study phase. Recognition for semantically congruent associations not only was better than recognition for semantically incongruent associations, but also was more resilient to sleep deprivation and interference following the encoding task. However, these two forms of interference affected in a different way recognition judgments either based on the recollection of details about previous events or on the assessment of stimulus familiarity. In particular, we found that recollection was reduced after sleep deprivation regardless of whether the semantic context was congruent or incongruent, whereas interference following encoding only affected familiarity of semantically incongruent associations. Our results revealed that providing subjects with supplementary semantic knowledge during encoding (i) enhances the memory trace, (ii) accelerates stabilization processes, which makes this trace more resistant to external interferences, and (iii) makes encoding processes less dependent on the synaptic homeostasis' processes operating during sleep.

D10-49

MULTIPLE REACTIVATIONS AS BOUNDARY CONDITION FOR MEMORY RECONSOLIDATION IN HUMANS

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The reactivation of apparently robust memories can render them unstable, thus requiring a period of stabilization known as reconsolidation. During reconsolidation, amnesic manipulations such as interference by new learning may alter reactivated memories. Human and rodent studies show that repeated reactivations create strong memories and that stronger memories are less vulnerable to reconsolidation effects than weaker ones. These findings raise the question whether multiple reactivations make memories less susceptible to reconsolidation effects. We addressed this question in a series of three experiments. In the first experiment, healthy participants learned a set of negative and neutral pictures and reactivated it one week later. Immediately after reactivation, they learned a second set of pictures. On the subsequent day, memory for the initially learned pictures was measured in a recognition test. New learning after reactivation reduced memory performance, whereas new learning without reactivation or reactivation without new learning had no effect. Thus, new learning after reactivation seemed to alter the reconsolidation of the original memories. In order to assess whether multiple reactivations make memories less sensitive to reconsolidation effects, we gave either three additional reactivations (experiment II) or one additional reactivation (experiment III) between initial learning and the experimental manipulation (new learning after reactivation). The impact of new learning after reactivation disappeared after three additional reactivations as well as after a single additional reactivation. Instead, new learning without reactivation reduced memory performance after three additional reactivations. These findings show that the number of reactivations is a potential boundary condition for reconsolidation in human episodic memory and may have important implications for anxiety disorders such as post-traumatic stress disorder (PTSD) for which treatments after fear memory reactivation (i.e., during reconsolidation) appear to be a promising therapeutic avenue.

D10-50

EFFECTS OF GOAL-RELEVANCE PROCESSING ON MEMORY FOR NEUTRAL FACES: AN fMRI STUDY

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The affective dimensions responsible for the modulation of memory by emotion are subject to debate, several hypotheses having been suggested for the cause of such an emotional effect. The arousal hypothesis of memory facilitation suggests the arousal dimension as the key determinant in whether emotional events are more likely to be recognized or recalled than neutral, less arousing, events. The valence hypothesis suggests preferential status for intrinsically unpleasant as compared with intrinsically pleasant or neutral stimuli in memory. An alternative explanation is that events that are better recalled are those that are relevant to the current concerns of the individual. Such concern-relevant stimuli typically also elicit emotional processes. In this present study, we report results from a functional magnetic resonance imaging (fMRI) designed to test for goal-relevance effects on brain activity during a memory recognition task. The experiment consisted of an incidental memory task and a delayed recognition phase (20 minutes of delay). Neutral faces were presented either in a goal-relevant context (goal-relevant faces) or in a goal-irrelevant context (goal-irrelevant faces) during the encoding phase. In the recognition phase, old and new neutral faces were presented while participants had to indicate whether each face had been previously presented or not. Behavioral results showed that neutral faces related to the goal-relevant context (i.e. goal-obstructive or goal-conducive) were better recognized than those related to the goal-irrelevant context (i.e. not related to goals of the individual). The fMRI results showed that medial frontal gyrus, a region known to be critical for the processing of self-relevant information, was more activated by the processing of faces related to relevant compared to irrelevant context, although the faces did not display any emotional expression. We also found activation located in the amygdala, critical region for the relevance detection, associated with successful retrieval of faces related to goal-obstructive context. Finally, a stronger responses in the fusiform gyrus, known to be involved in the identification of faces, were occurred during the presentation of faces related to goal-relevant compared with faces related to goal-irrelevant context.

D10-51

EFFECTS OF EXPOSITION TO BENZENE, TOLUENE AND XYLENE (BTX) IN NEUROCOGNITIVE PROCESS IN WORKERS OF OIL COMPANIES

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BTX exposures have proven to be neurotoxic and it affect in neurocognitive processes. From the age of 90, different studied show its effects on attention and memory (especially visual) and increase fatigue and deficits in learning (Adams & Victor, 1993; Bleecker, 1994; Feldman, White & Albers, 1998). Castillo, Mayor & Almirall (2003) have demonstrated, in a study similar to ours, that occupational exposure to BTX does not have a specific profile and describe it as a picture asymptomatic in other aspects of health (these symptoms may not be evident by worker). Instead, they showed affectation in Attention, Perception, Memory and, weakly, in Psychomotor Coordination. Also, they demonstrated predictive associations for the years of exposure. The aim of the present study was to detect possible effects in: Sustained Attention, Non-Verbal Learning, Memory Span, Neurocognitive Interference and Space Capacity due to long-term neurotoxic exposition (BTX) in 939 employees in three refineries from Andean Region (South America). Two parallel, double-blinded studies were carried out. One study focused in the Analytic Hygiene Area (Direct and Atmospheric Reading devices in the workplace, and Personal Monitoring devices with suction pumps); other study focused on Neurotoxicity using the computerized Vienna Test System, scaled by age and educational level in this neurocognitive process. In order to study the prevalence of Cognitive process deficits a screening task was conducted using a case-control study. Effects were measured by source refinery, seniority labored and homogeneous exposition group (HEG). The results indicate that one of the three refineries has an incidence rate higher than the other two (proving a high rate of neurotoxicity for toxicity exposition employment). The number of errors is higher as laboured seniority increases. Groups with daily overexposure showed higher prevalence of cases (X^2=0,05). Some HEG (Non-Catalytic and Catalytic, Setria and Laboratories) had a higher incidence of cases, coinciding with higher concentrations of BTX as measure by Analytical Hygiene indicators. In conclusion, the increased incidence of Neurocognitive Process deficits coincided with a higher level of exposure to BTX in the factor work area and in the factor time of exposure.

D10-52

URINARY LEVELS OF ARSENIC, LEAD AND MERCURY AMONG CHILDREN AND NEUROBEHAVIOURAL TOXICITY: AN EXPLORATORY STUDY

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Background: Diet and living near to chemical/metal industries are a potential source of environmental exposure to metals such as lead, mercury and arsenic, which are recognized causes of neurological disorders in children. Our objective was to explore the relationship between urinary levels of arsenic, lead and mercury, and neurobehavioral performance (subclinical effect) in children aged 9-11.
Methods: Spot urine samples were obtained from 79 children recruited from cities representative of five different environmental scenarios in Andalusia (Spain): 14 from urban/residential, 34 from urban/industrialized, 7 from mining, 14 from rural, and 10 from rural/industrialized. Neurobehavioral performance was satisfactorily assessed in 37 boys and 36 girls by the Behavioral Assessment and Research System (BARS) using Spanish instructions. Multielemental ICP-MS was used to quantify urinary levels of arsenic, lead and mercury. General linear models were used including age, gender, social class, global physical activity, and shore fish consumption as covariates, plus the exposure variable (log transformed urinary levels of each metal separately) to predict each of 14 neurobehavioral outcome variables.
Results: Higher levels of mercury were associated with a worse performance of the Alternate Hand Finger Tapping (AHFT) test (measures “coordination”) (p=0.03), of the Digit Span Forward test (measuring “attention”) (p=0.08) and of the Errors on Simple Reaction test (measures “response speed”) (p=0.02); and with better performance of the Continuous Performance Hit Latency test (measures “attention”) (p=0.001). Children with higher arsenic levels scored better on the Continuous Performance False Alarm Latency test (p=0.08), and tended to score worse on the AHFT test (p=0.10). No statistically significant associations were observed for urinary lead, although children with higher levels tended to perform better with the AHFT test (p=0.09), and worse with the Continuous Performance Correct Rejections test (p=0.15).
Conclusions: Our results suggest that urinary levels of mercury are related with poorer neurobehavioral performance among children.

D10-53

WHAT DOES "WELL MAKING ENVIRONMENT" MEAN FOR THE BRAIN? AN fMRI STUDY

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There is a growing body of evidence indicating the impact of environment on restoration from stress and illness, as well as on the tempo of return to health after injuries and surgeries (Ulrich, 1984). To maximize and adapt the healing qualities of environment, we should better understand its salutary effects embracing psychological, emotional, physical and neural components. In the present study we wanted to go beyond existing behavioral and physiological measures, creating a link between optimal healing environment (OHE) studies and brain research involving functional MRI technology. 16 healthy right-handed volunteers (9 females; mean age 23.1 years) were pretested for imagery ability (QMI, Sheehan, 1967; mean score 54.4) participated. Previous to the study, all participants took part in a training in which they imagined and described in writing the phenomenological characteristics of a (1) well-making and a (2) non-well-making environments being a part of their episodic memory. A block design was used with 8 blocks per each condition. The order of blocks was pseudo-randomized. The study was conducted with a 3T system (Philips ACHIEVA). The fMRI data was analyzed with SPM8. Subtraction analyses revealed common activations in the visual cortex and in the supplementary motor area for both conditions. An additional activation of the left prefrontal cortex was observed for the "non well-making" condition. Activations in the visual cortex probably correspond to imagination processes. We suggest that the imagination of a "non-well-making" scenario requires an additional semantic monitoring. Since the left prefrontal cortex may play a role in inhibiting negative emotions, the observed activation in the "non-well-making" condition may be also an indicator of emotion regulation strategy. Lack of the left PFC activation in the "well-making" condition could be understood as a cortical relief, suggesting that human beings may find some environments more health promoting than others because the former place fewer psychological and energetic demands on the cortex.

-Sheehan P (1967). Journal of Clinical Psychology, 23(3), 386-389.
-Urlich R.S. (1984). Science, 224(4647), 420-421.

D10-54

ANXIETY-TRAIT MODULATES THE IMMUNE RESPONSE TO ACUTE PSYCHOSOCIAL STRESS IN CAREGIVERS OF AUTISM SPECTRUM DISORDER

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Introduction: A down regulation in salivary immunoglobulin A (IgA) levels has been observed during psychological chronic stress periods in a healthy population. Taking care of a member of the family who suffers a long-term pathology can be considered a chronic stress situation with potentially negative influences on health, mood-related disturbance of the immune response to stress, and high scores for depression and anxiety. However, few studies have focused on the effect of an anxious personality on immune activity in this population. The objective of the present study is to evaluate the effect of the anxiety-trait on the IgA response to psychosocial stressor in caregivers of autism spectrum disorder (ASD) compared to a control group. Methods: Participants were classified into three groups: 26 caregivers of ASD offspring with high scores in anxiety-traits (higher than percentile 50th, HA-T); 15 caregivers of ASD offspring with low scores in anxiety-traits (lower than percentile 50th, LA-T); and 37 non-caregivers (all LA-T). Participants were exposed to a psychosocial stressor and salivary samples were collected for IgA levels before, during, immediately after; and at 10, and 20 minutes after the stressor. Anxiety state, anger, and mood were evaluated before and after the stressor and the stimuli appraisal was assessed afterwards. Results: The HA-T caregivers perceived the task as more stressful than the other two groups and showed significantly lower IgA levels than the controls. No significant effects were found on mood scores. For the stress response, the HA-T caregivers showed an immunological stability that contrasts with the decreases of the LA-T caregivers and increases in the controls. Conclusions: Higher levels of anxiety-trait in caregivers could favor stability in immune activity in response to acute stress without changes in mood. Further investigation is needed to elucidate the role of this lack of responsivity to acute stress on the health of caregivers. Results suggest that psychosocial intervention focused on appraisal of stressful events and anxiety could modulate the mucosal defense system in this risk population.

D10-55

SOCIAL DEPRIVATION IS A RISK FACTOR FOR THE EMERGENCE OF BEHAVIOURAL AND NEUROBIOLOGICAL ENDOPHENOTYPES OF DEPRESSION

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Stress is a main risk factor for the emergence and the precipitation of psychiatric disorders, including major depression. Neurotrophins, such as Brain-Derived Neurotrophic Factor (BDNF), are neuroendocrine effectors involved in the response to stress and in the neurobehavioural changes associated with psychiatric disorders, in particular with depression. Aim of this study was to investigate the relationship between neuroendocrine activation (circulating corticosterone and brain BDNF levels) and a wide array of behavioural responses referred to as endophenotypes of depression (anhedonia, behavioural despair, generalized and social anxiety) resulting from exposure to chronic stress. To this end, 3-month-old C57BL/6J male mice were exposed to either chronic disruption of the social hierarchy (SS), to a stable hierarchy (SG) or to individual housing (IC), a condition lacking social stimuli. Results show that, despite not developing anhedonia (decreased preference for a sucrose solution), IC mice were characterized by behavioural despair and increased hypothalamic-pituitary-adrenal axis activity and anxiety-like behaviour, in addition to reduced BDNF levels. By contrast, SG and SS mice showed increased anhedonia accompanied by no alterations in behavioural and neuroendocrine profiles. These results suggest that isolation, rather than social stress, is a stressful condition able to induce selective endophenotypes of depression and clearly indicate BDNF as a main neurobiological variable involved in these events.

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D10-56

EVOKED RELATED POTENTIALS CORRELATES OF EMPATHY FOR PAIN FROM ADOLESCENCE THROUGH ADULTHOOD

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Empathy is a complex emotion that continually develops from infancy through adulthood. Affective and cognitive empathy are traditionally dissociated, the affective component being concerned with resonating with another's emotional state and the cognitive component focusing on regulating the resulting distress and on understanding of another's mental state (Decety, 2004). Considering that adolescence is a critical period for the development of the cognitive control necessary to regulate affective processes (Steinberg, 2005), one should expect adolescents to show greater automatic empathy than young adults. The present study aimed at exploring the neural correlates of affective (automatic) and cognitive empathy for pain from adolescence to young adulthood. With this aim, 32 participants (aged from 11 to 39) watched stimuli depicting hands in painful or non painful situations. They performed a pain judgment task that required attention to pain cues in the stimuli (controlled empathy for pain) or a counting task that withdrew their attention from these cues (automatic empathy for pain). ERPs results showed an early automatic frontocentral response to pain (that was not modulated by task demand) and a late parietal response to painful stimuli modulated by attention to pain cues. As expected, results showed that adolescents had stronger automatic responses to painful situations than young adults do. Adolescents also showed greater activity in the late component even when viewing neutral stimuli, suggesting a lack of regulatory abilities in pain evaluation processes. Taken together, results provide additional evidence for the maturation of regulatory competences in adolescence, sustained by a better coordination of affective and cognitive aspects of emotional processing.

D10-57

STRESS INFLUENCE ON THE STARTLE EYE BLINK REFLEX

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The magnitude of the eye blink response to startle probes is modulated by affective states. Negative affective states will increase, positive states decrease the startle reflex. The influence of stress on the startle response is less clear. On the one hand, the negative affective dimension of stress might have an enhancing influence on the startle response. On the other hand stress might shift the attentional focus away from the stimulus modality and thereby decrease startle responsiveness. We assessed the influence of a physiological stressor on the startle response in a study with 20 participants (within subjects design). Participants were startled with acoustic startle probes (105 dB, white noise, binaural, instantaneous rise time) via headphones. In the stress condition, participants had to immerse their right hand in cold water (Cold Pressor Test, CPT), in the control condition the water was warm (body temperature). Startle probes were presented in three blocks: during the experimental intervention and in resting phases before and after the intervention. The startle response was measured with electromyographical recording (EMG) of the obicularis oculi muscle as well as video based assessment of the actual eye blink via an eye tracker (SMI iView X Hi-Speed, 500 fps). We found a significant reduction of the EMG-response in the post-stress condition when comparing the pre-intervention with the post-intervention resting phase in contrast to the control condition ($F=7.79$, $p<0.05$). The reduced startle magnitude after stress might be attributed to opponent processes after stress or a reduced sensitivity to sensory information input.

D10-58

REM SLEEP EEG THETA ACTIVITY IS A NEGATIVE CORRELATE OF ATTACHMENT ANXIETY

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Introduction: Several behavioural correlates of EEG theta activity were reported previously. Some of these correlates were shown to be trait-like in nature belonging to the affective domain. Frontal theta activity measured during wakeful resting conditions was found to be a negative correlate of anxiety-related measures mainly. However, knowledge on the trait-like affective correlates of REM sleep theta activity is sparse. Based on the intimate relationship between REM sleep and attachment, as well as on the neurobiology of this sleep state we hypothesize that REM sleep frontal theta activity is negatively correlated with measures of attachment anxiety (AAn). As Heart Rate Variability (HRV) as an indicator of the sympatovagal balance was shown to be related to theta activity, we also hypothesized that REM sleep HRV is related to both theta activity and AAn.
Methods: 35 subjects (20 men, M_{age}=31.6 years) slept two consecutive nights in the sleep laboratory. Polysomnography covered EEG, EOG, and ECG. Power spectra of whole second night NREM and REM sleep EEG as well as spectral HRV measures of the ECG in NREM and REM sleep were calculated. Subjects filled the Relationship Scales Questionnaire measuring adult attachment along the dimensions of AA and attachment avoidance (AAv). Pearson correlations between log-normalized 0.25 Hz wide EEG power bins and attachment, between log-normalized EEG power and HRV, as well as between HRV and attachment were calculated.
Results: Significant negative correlations between REM sleep EEG power and AAn were observed at frequencies pertaining to the theta range (4.75-7.5 Hz) in the fronto-central and temporal regions. These correlations were specific to REM sleep as NREM sleep theta EEG power was found to be uncorrelated with AAn. The hypothesized correlations between REM sleep theta EEG power and HRV, or AAn and HRV were not supported by our data. Unpredicted correlations were negative between AAn and REM sleep frontal beta (12.25-20.25 Hz) power, and positive between AAv and NREM sleep alpha/sigma (8-13 Hz) power.
Discussion: Frontal theta activity and HRV are unrelated, perhaps physiologically uncoupled during REM sleep. REM sleep theta EEG, but not HRV is negatively associated with questionnaire measures of AAn.

D10-59

EMG ACTIVITY IN RESPONSE TO DYNAMIC AND STATIC NATURAL FACES

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Several studies have shown that artificially prepared dynamic facial emotional expression (avatar, morphs) evoked stronger facial muscle activity (EMG) than static ones. In our recent study we found that in response to morphed stimuli subjects reacted spontaneously and rapidly to happy faces with increased zygomaticus major EMG activity and decrease corrugator supercilii EMG activity - showing greater changes in response to dynamic than to static stimuli in both muscles. In the present study, we compared facial muscle response to natural static (picture) and dynamic (video movie) stimuli. We hypothesized that as in our previous study dynamic stimuli would cause stronger muscle activity than static ones. Thirty subjects were exposed to dynamic and static stimuli of happy, feared, surprised and angry facial expression while electromyographic (EMG) activity from the zygomatic major and the corrugator supercilii muscle regions was recorded from the left side of the face. The analysis of data showed that presentations of angry expressions induced stronger EMG activity in the corrugator supercilii and presentation of happy expressions induced stronger EMG activity in the zygomatic major. Moreover happy faces evoked decreased corrugator activity. Unexpectedly angry expression elicited decreased zygomaticus EMG activity. Two other expressions of emotion (fear and surprise) did not evoke significant changes in EMG activity of none of two muscles. As expected, the dynamic stimuli induced stronger facial muscle activity in comparisons to static stimuli. Presentation of dynamic facial expressions evoked greater changes in zygomaticus m, in responses to happy; while in corrugator m. greater changes were observed for happy and angry faces. Comparison between male and female participants revealed that women comparing to men responded with decreased zygomaticus m. activity in response to fear, surprise and anger as well as with decreased corrugator m. activity in response to happy faces and with increased activity in response to angry faces. Our results suggest that women were less facially expressive, since their muscle activity was decreased in comparison to men but only in response to dynamic stimuli. The modality (static vs. dynamic) of natural stimuli evokes the differences in the level of facial muscle activity. Further study should evaluate if such a difference also exists in response to authentic “everyday” facial expressions.

D10-60

THE AUTOMATIC EFFECT OF SOCIAL APPRAISAL ON THE RECOGNITION OF EMOTIONS

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The notion of social appraisal emphasizes the importance of a social dimension in appraisal theories of emotion by proposing that the way an individual appraises an event is influenced by the way other individuals appraise the same event. We recently found that the social appraisal plays a significant role on the recognition of emotion. The purpose of this study was to directly investigate the automatic nature of this effect. Furthermore, studies revealed that socially anxious individuals show an attentional bias to threatening facial expressions even when they were presented under conditions of restricted awareness. One might therefore predict that high social anxiety would be associated with a selective attention to negative facial expressions and indirectly to the negative appraisal made by other individuals. In this study, high and low socially anxious individuals were asked to recognize dynamic facial expressions of emotion (fear or anger) in a target face presented at the center of a screen while a contextual face, which appeared for 30 ms in the periphery of the screen and was immediately masked, expressed an emotion (fear, anger) or not (neutral) and either looked at the target face or not. Manipulation of the gaze direction of the contextual face—either towards the target face or away from both the target face and the participant—allowed us to verify that a putative specific social appraisal effect does not reflect a more general contextual effect. Results provided evidence of an automatic effect of social appraisal on the recognition of an emotion of fear. Therefore, the recognition of the target emotion of fear was improved, in low and high socially anxious individuals, only when the contextual face expressed anger and a gaze directed towards the target face (social appraisal condition). Moreover, when the contextual face was not expressing any emotion, the same target emotion of fear was recognized differently between the two groups: low socially anxious participants perceived as much as fear as surprise in this expression whereas the high socially anxious individuals perceived only fear, without any ambiguity.

D10-61

REAPPRAISAL FRAMES OF POSITIVE AND NEGATIVE PICTURES ALTER EMOTIONAL RESPONSES AS REFLECTED IN SELF-REPORT AND FACIAL ELECTROMYOGRAPHIC ACTIVITY

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Cognitive reappraisal is an emotion regulation strategy that was shown to effectively modulate self-reported emotions, ERP activity and autonomic responses triggered by emotional stimuli. However, the effects of reappraisal on expressive responses (i.e. facial expressions) have not been well studied so far. This seems surprising because of the important social function of facial expressions and their well-known effect on emotional experience. The present study investigated the effects of reappraisal on both emotional experience and emotional facial expressions triggered by positive and negative picture stimuli. Twenty four participants were exposed to 125 pairs of auditory narratives and scenery pictures reflecting negative-up, negative-down, positive-up, positive-down and neutral conditions. Results indicate that up-regulation compared to down-regulation in the context of negative stimuli led to greater self-reported unpleasantness and arousal, as well as greater corrugator activity; while in the context of positive stimuli, up-regulation caused greater self-reported pleasantness and greater zygomatic activity. These results suggest that reappraisal effectively alters both emotional experience and facial expressions. Moreover, temporal dynamic analyses indicate that reappraisal rapidly affected facial EMG activity within 1 s after picture onset which is corresponding to the modulation role of facial expression in emotional experience as assumed by the facial feedback hypothesis.

D10-62

ELECTRODERMAL ACTIVITY RESPONSE TO STRESS AND EMOTIONAL INTELLIGENCE IN CAREGIVERS OF AUTISM SPECTRUM DISORDERS

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Introduction: Electrodermal activity response (EDA) is a reliable indicator of mood states and arousal and enables an objective measurement to be obtained of the activation of the autonomic nervous system. Emotional intelligence (EI) is the ability to perceive, express, understand, and think about emotions appropriately. Higher levels of EI involve a great emotional regulation and this has a direct influence on environmental adaptation and relationships. Aims: To our knowledge, no studies have analyzed EDA reactivity to stress in caregivers of autism spectrum disorders (ASD) and the relationship with emotional intelligence. This is the main aim of this work. Methods: The sample is composed of 40 caregivers (26 women and 14 men) of people diagnosed with ASD. EDA was continuously recorded before, during, and after a set of mental tasks. Participants then completed the Trait Meta-Mood Scale (TMMS-24) which evaluates EI across three scales: attention, clarity, and repair.
Results: There is a significant effect of the attention subscale of TMMS-24. Caregivers with higher attention showed less number of EDA responses during the tasks when considering the rest period than those with lower attention. These effects were not found for the clarity and repair subscales of TMMS-24. Conclusion: EI can be a good indicator for predicting the ability of someone to adapt to stressful and adverse situations of quotidian life. In the case of caregivers, this could help implement programs for developing EI and providing mechanisms for practicing.
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D10-63

DISCOVERING MITOCHONDRIAL BIOMARKERS FOR ANXIETY DISORDERS

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To date, no molecular biomarker exists that can aid premorbid diagnosis, accurate patient subcategorization, prediction of treatment efficacy and drug development for anxiety disorders. In our efforts to discover candidate biomarkers and unravel the neurobiological underpinnings of anxiety-related behavior, we investigated a mouse model of trait anxiety. To achieve an accurate quantitative comparison, we established a comprehensive and sensitive proteomics and metabolomics platform based on in vivo ^{15}N metabolic labeling and quantitative mass spectrometry. We applied this platform to compare the cingulate cortex synaptic proteomes and metabolomes of high and low anxiety-related behavior mice and identified affected pathways by in silico analyses. We found up to 300 differentially expressed proteins and metabolites involved in energy metabolism, mitochondrial import and transport, oxidative stress and neurotransmission pathways, strongly suggesting mitochondria as a common denominator of these alterations. We then performed follow up studies assessing relevant mitochondrial pathways and proteins that indicate a previously non-highlighted role of mitochondria in modulation of anxiety-related behavior. This work underlines the value of animal models and emerging –omics technologies toward the establishment of a biomarker panel for anxiety disorders and provides evidence for a mitochondrial implication in anxiety-related behavior, advancing our systemic understanding of anxiety pathophysiology

D10-64

THE INVOLVEMENT OF FKBP51 AND FKBP52 IN THE BEHAVIOURAL AND NEUROENDOCRINE EFFECTS OF ACUTE AND CHRONIC STRESS

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Chronic stress is increasingly considered to be a key risk factor in the development of a variety of human diseases, including depression. This is further supported by an impaired negative feedback of the hypothalamic-pituitary-adrenal (HPA) axis, which has been observed in the majority of depressed patients. The effects of glucocorticoids, the main hormonal endpoint of the HPA axis, are mediated via the glucocorticoid receptor (GR) and the mineralocorticoid receptor. In mammals, the co-chaperones FKBP51 and FKBP52 of the hsp90-corticoid receptor complex differentially regulate the GR at two levels: hormone binding and nuclear translocation. FKBP51 has been shown to regulate ligand binding sensitivity of the GR. When it is attached to the hsp90-complex, glucocorticoids bind with decreased affinity to the GR and the nuclear translocation of the receptor is less efficient. Upon ligand binding, FKBP51 is replaced by FKBP52. In contrast to FKBP51, FKBP52 triggers the translocation of the GR-complex into the nucleus and promotes subsequent DNA-binding. Polymorphisms in the human FKBP51 gene predispose individuals to increased sensitivity to social stress and have been associated with an enhanced recurrence of depressive episodes. Thus, FKBP51 and FKBP52 represent interesting therapeutic targets for the prevention and treatment of stress-related psychiatric disorders. This study aimed to investigate the function of FKBP51 and FKBP52 as possible mediators of the stress response system and their potential role in the development of stress-related disorders. Therefore, we assessed the effects of three weeks of chronic social stress (CSDS) in mice either lacking the gene encoding FKBP51 (51KO mice) or mice heterozygous for the gene encoding FKBP52 (52HET mice). Both mouse lines were subsequently analysed with regards to physiological, neuroendocrine, behavioural and mRNA expression alterations and demonstrated an altered physiological and neuroendocrine response to CSDS. These results suggest a modulation of the negative glucocorticoid feedback within the HPA axis, possibly modulated by an influence on GR sensitivity. Taken together, our results emphasize the important role of these co-chaperones in regulating stress vulnerability or resilience.

D10-65

EFFECTS OF STRESS IN EPISODIC MEMORY UPDATING

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Episodic memory updating occurs when a previously acquired memory is reactivated before another episode of learning similar information. Without reactivation, such updating does not occur, and new learning is kept separate from old learning. The present study explored the effects of stress on episodic memory updating. Participants learned a set of 20 objects (Set 1) on Experimental Day 1. Two days later on Experimental Day 2, participants were either stressed or not stressed, using the Trier Social Stress manipulation. They were then reminded of their learning experience on Day 1, after which they learned another set of 20 objects (Set 2). Two days later, on Experimental Day 3, participants were instructed to recall all objects they had learned in the two prior sessions (i.e. Set 1 and Set 2 objects), either in the same context as Day 1 or in a new context. Recall of Set 2 objects was higher than recall of Set 1 objects across all groups, reflecting a recency effect. While there were no overall differences in recall of Set 1 and Set 2 objects between the stress and no-stress groups, participants who were not stressed showed more memory updating, manifested as a higher number of objects from Set 2 being attributed to Set 1 (intrusions). Those participants who were stressed before the reminder showed less updating, i.e. fewer intrusions. These results suggest that stress may reduce episodic memory updating by dampening the magnitude of reactivation. Updating, as shown by intrusions, was also affected by the recall context. Recall in a new context led to a bimodal distribution of intrusion rates in our participants, as was observed in a previous study (Hupbach et al., 2008). Our results show that episodic memory updating can be influenced by conditions at both encoding and retrieval; in both instances working through effects on context. These results may have implications for memory integration under stress and may also shed light on problem solving that involves integrating information across contexts.

D10-66

THE ROLE OF DIFFERENT Homer1 ISOFORMS IN ACUTE AND CHRONIC SOCIAL STRESS

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Homer proteins are scaffolds that interact with metabotrobic glutamate receptors and bind to Ca^{2+} signaling proteins at synapses. Homer1, a subtype of the Homer protein family, has been implicated in the processing of novel experiences and memory formation in animal studies, whereas clinical studies suggest an association of SNPs in the Homer1 gene with major depression. Two major isoforms of Homer1 have been described: Homer1b/c, consisting of a conserved amino-terminal target-binding domain and a coiled-coil structure including two leucine zipper motifs, is predominantly expressed in the nervous system. Homer1a, a short form which is missing the coiled-coil structure, has been shown to act as a dominant negative for long Homer1 isoforms at the metabotrobe glutamate receptor binding site. Our study aims to unravel the role of Homer1 isoforms in the mediation of responses to chronic and acute social stress. We therefore investigated the regulation of Homer1 on both mRNA and protein level and its interaction with stress-associated behavioral phenotypes. Our results show that chronic social defeat stress has a pronounced impact on both the animals' neuroendocrine profile and their behavior. Accompanying these findings, Homer1b/c mRNA levels are increased following chronic social defeat stress, while Homer1a gene expression did not change. On the other hand, Homer1a transcription was induced 1 hour after a single defeat and was followed by a decline in Homer1b/c mRNA expression 4 hours after the stressor. These findings suggest an important role of Homer1 modulating the effects of social stress. Future investigations will be directed towards the manipulation of the glutamate system in conjunction with social stress to further elucidate the role of Homer1 in the stress response.

D10-67

GENDER DIFFERENCES IN HEALTH IN INFORMAL CAREGIVERS OF CHILDREN WITH ASPERGER SYNDROME

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Introduction: Caregiving of offspring with a chronic illness increases health complaints and alters the cortisol awakening response (CAR). Women show worse health than men when giving care to people with several alterations. Nevertheless, no studies have analyzed this aspect in parents of offspring with Asperger syndrome (AS). Objectives: The main purpose of this study is to evaluate whether there are gender differences in health of informal caregivers of children with AS. Furthermore, the study aims to analyze the role of time spent in caring and CAR in the health of caregivers. Method: The sample is composed of 44 caregivers of both genders (19 men and 25 women) of people diagnosed with AS. The number of consumed drugs (ad-hoc questionnaire), general health (standardized tests: general health questionnaire) and ESS-R (somatic symptom scale)) and the cortisol awakening response of caregivers are assessed. Results: There are significant differences in health between men and women. Women take a higher number of drugs and report more somatic symptoms such as anxiety, insomnia, and depression than men. Women also show more gastrointestinal, neurosensorial, muscular, and skin-allergic symptoms than men. Additionally, only for women there is a positive correlation between the time spent in caring and immunological, respiratory, gastrointestinal, neurosensorial, muscular, and depressive symptoms. In men, a negative correlation between immunological and neurosensorial symptoms and CAR was found. Discussion: Gender moderates the effects of caring for offspring with AS on the health of caregivers – with women being more affected than men. Different patterns of relationships by gender were found, since the time spent in caring is related to health in women, while symptoms are associated with CAR in men. Although the greater implication of women in caring and their styles of socialization could explain these results, there may also be a higher biological sensibility. Future studies should analyze these effects in order to prevent illnesses and offer appropriate treatment to caregivers.

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D10-68

IMAGING THE STRESS RESPONSE - DEVELOPMENT OF THE Scan*Stress* PARADIGM

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Central nervous processes play a major role in the regulation of the stress response and of one of its main components, the hypothalamus-pituitary-adrenal (HPA) axis. To study the neuronal mechanisms underlying the acute stress response, we sought to design a paradigm that would be (a) feasible to serve as a psycho-social stressor inducing robust HPA axis responses and (b) suitable for scanner environments. Based on the psychological characteristics uncontrollability and social-evaluative-threat our paradigm consists of two tasks with adaptively varied speed and difficulty that have to be solved under time pressure. A scientist panel that is presented by live video stream monitors the subject's responses and gives continuous visual feedback during the tasks and social-evaluative verbal feedback between both sequences. The paradigm is presented as block design with four stress and four control blocks. The ScanStress paradigm was evaluated in an fMRI study with 32 healthy adults (15 females). For measurement of HPA axis hormones saliva and blood samples were collected prior to, during and after the fMRI session. Additionally, heart rate was continuously recorded and mood ratings were assessed. ACTH levels showed an increase in 55% of the subjects. Under stress a significant increase of neural activation was observed in areas related to completion of cognitive tasks and in stress relevant regions as the thalamus, hypothalamus and limbic structures. Significant deactivation was observed in the perigenual anterior cingular cortex, a region involved in emotion regulation. Currently we analyse sex differences in the neuronal activation patterns under stress as well as the association of HPA axis reactivity, subjective ratings and heart rate responses with the neuronal activation. Results of these analyses will be reported at the conference. Our data suggest that we developed a stress paradigm that is capable of inducing stress related changes on the endocrine and neuronal level. We propose that the ScanStress paradigm can be applied to address questions considering the neuronal basis of the human stress response.

D10-69

WORSENING OF HEALTH RELATED TO BUFFERED CORTISOL AWAKENING RESPONSE AND NEGATIVE EMOTIONAL PERSONALITY TRAITS

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The cortisol awakening response (CAR) is an index of the activity of hipothalamic-pituary-adrenal axis and is frequently associated with poor health. However, few studies have focused on this relationship while also considering the role of personality traits. The aim of the present study is to evaluate the interactions among CAR, personality, and health in 103 healthy young participants (83 women and 20 men). The total sample was distributed into two groups according their scores in the Goldberg General Health Questionnaire. For all participants, salivary cortisol was measured at awakening and 30, 45, and 60 minutes afterwards; and coping styles, temperament and character, trait anxiety, anger expression, and life stressful events were assessed. Results show that lower CAR levels are related to poorer levels of health. Participants with worse health also reported higher emotional intensity in their stressful life events, higher scores in cognitive avoidance as a preferred coping style, higher trait anxiety, greater external expression of anger, and lower levels of social tolerance, empathy, compassion, and altruism. In sum, a worsening in the health of the non-pathological population is related to a buffered CAR and a profile of personality characterized by negative affectivity. Further research is needed about the link between personality and health in order to design therapeutic programs from a preventive perspective.

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D10-70

SEXUAL DIMORPHISM AND ANXIOLYTIC RESPONSE TO AN ACUTE STRESS AFTER MATERNAL SEPARATION

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There is evidence that stressful events during the neonatal stress hyporesponsive period may influence both emotional behavior and brain neurochemical development. It is known too that later in life acute stress could modify several neurotransmitter systems and behavioural tasks. In the present study we have analyzed the effects of acute stress on brain dopaminergic system and anxiety-like behavior in male and female adolescent rats that were previously subjected to maternal separation. The pups were separated from the dam 5 hour daily during the first two weeks of life. At 25 days of age they were submitted to 10 minutes of white light stress, and then their anxiety-like behaviour was tested in elevated plus-maze. Septal and striatal samples were assayed to determine possible dopaminergic levels alterations. We have seen a sexually dimorphic response to maternal separation that seems to affects the anxiety-like behaviour of males and the motor activity of females. In terms of anxiety, it seems that males have no response to acute stress if they were maternal separated, tough the acute stress affects the same way to control and separated females. Surprisingly both types of stress induce a decline of anxiety-like behaviour. A possible interaction between the effects of the two types of stress induces only in females a disappearance of the increase of motor activity due to maternal separation. Results show that the dopaminergic system is affected by acute stress and that dopamine content is lower in double stressed animals than in only acute stressed animals both in septum as in striatum of both males and females. We have seen that the exposure to a double stress causes sexually dimorphic responses in terms of anxiety-like behaviour and motor activity. Indeed the dopaminergic system appears differently affected by acute or double stress Taking into consideration our results all together, it seems that both maternal separation and white light stress could have anxiolitic effects, at least in early adolescence.

D10-71

METABOLIC STATE EFFECTS ON THE STARTLE EYE BLINK MAGNITUDE

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Acoustic startle eye blink reflex (ASR) magnitude is highly sensitive to the emotional, motivational and attentional states of the individual, constituting an excellent physiological measure of affective and cognitive processes. Previous research suggested higher ASR magnitude as a response to food cues during food restriction, suggesting that food deprived might enter in an aversive motivational state. Furthermore, it is known that ASR is sensitive to endocrine modulation and that the characteristic hormonal fluctuation of the female menstrual cycle influences appetite and eating behavior. We conducted two studies to test how the metabolic state would affect the general startle eye blink magnitude and habituation in different gender and menstrual cycle phase. In the first study, 28 healthy participants (14 males) were assessed. All the women were taking oral contraceptives. In the second study, 20 healthy women were divided by menstrual phase with 10 being tested in the follicular phase (FP) and 10 other in the luteal phase (LP). In both studies, we assessed the ASR (via EMG) to six brief (50 ms) and intense (105 dB) binaural acoustic white noise startle stimuli with a variable inter-stimulus-interval, tested on 2 days, either after a period of normal-food-intake (NFI) or after an 18h period of food-restriction (RFI). We found a higher ASR magnitude for the participants in the RFI condition in both studies (ps<.05). Habituation of the startle reflex occurred in the normal fashion for both conditions (ps<.01) and no interaction between condition and time was seen in the data. No gender differences were found in the first study for general startle reactivity or habituation of the startle response. In the second study, women in the FP showed a higher ASR magnitude than the ones during LP (p <.05), however no interaction with condition was found. These results indicate that both food deprivation and the hormonal fluctuations during the menstrual cycle can influence the ASR. However, those effects seem to occur in an independent fashion. Gender seems not to play a role in this effect, based on the comparison of men with women taking oral contraceptives. These findings implicate that metabolic factors have the potential to modulate early information processing in humans.

D10-72

REORIENTATION BY GEOMETRY IN BUMBLEBEES

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Human and non-human animals are capable to make use of geometric information (metric and sense) specified by the macroscopic layout of surfaces to reorient in an environment. It is debated, however, whether geometric information is encoded by explicitly computing the layout of surface geometry of by matching images of the environment. View-based spatial encoding is generally thought to hold for insect navigation and, very recently, evidence for navigation by geometry in ants has been reported. Here we tested bumblebees (Bombus terrestris) abilities for spatial reorientation. After spatial disorientation, bumblebees had to find one of the four exit holes located in the corners of a rectangular enclosure. Bumblebees systematically confused geometrically equivalent exit corners. When one wall of the enclosure was made of a different colour, bumblebees conjoined this featural information with geometric information to find the uniquely correct exit corner. When after training geometric and featural information were set in conflict by displacing the feature from one wall to another, bumblebees appeared to rely on both geometric and non-geometric information depending on whether the feature was located near or far from the goal during training, and whether the change in the location of the feature was associated with an increase or a decrease in its size from training to test. Results are discussed in relation to the hypothesis that bumblebees reorient by matching images at different spatial scales.

D10-73

EFFECTS OF REARING IN ENVIRONMENTS OF DIFFERENT GEOMETRY ON SPATIAL REORIENTATION IN REDTAIL SPLITFINS FISH (Xenotoca eiseni)

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Following spatial disorientation in a rectangular enclosure, a variety of animal species have been proved to be capable to reorient themselves using geometric (sense and metric) or nongeometric (featural) information. Here we investigated the effect of rearing redtail splitfins fish (Xenotoca eiseni) in environments of different shapes on their ability to reorient themselves. After rearing fish singly in a rectangular or circular enclosure, they were trained in a rectangular enclosure with a wall of a different colour (so-called Blue-Wall test) and then tested at different ages (7-10 days or 30-40 days) with an affine transformation (moving the wall from a small to a large wall) that produced a conflict between geometric and nongeometric information. During training no effect of rearing was observed in animals tested at 7-10 days of age. In contrast fish reared in a rectangular environment were faster to learn when tested at 30-40 days of age. This suggests that although experience in environments with different shapes may affect spatial orientation, it is not necessary to encode geometric information in itself (in fish tested at 7-10 days of age learning was accomplished with identical velocity irrespective of the rearing conditions). At test, with the affine transformation, fish chose the geometrically correct corner far from the feature (the Blue Wall) more than its rotationally equivalent near it. The reason for this paradoxical avoidance of the feature following the affine transformation could be related to stress effects induced by rearing in social isolation, that are known to exacerbate fear responses in these animals (also revealed by reduced level of responding). Further research with socially-reared animals kept in environments of different shapes are needed to clarify this issue.

D10-74

USE OF PROPERTY/KIND INFORMATION FOR OBJECT INDIVIDUATION IN YOUNG CHICKS (*Gallus gallus*)

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Object individuation is the process by which organisms establish the number of distinct objects present in an event. Previous research demonstrated that chicks are able to use spatiotemporal and property information for object individuation. The ability to use property/kind information is assessed employing imprinting objects and food items (i.e. mealworms). Newborn chicks were reared with 5 identical imprinting objects. On day 2 each chick underwent a free choice test in which 2 groups of events were shown: a group comprised two stimuli i.e. an imprinting object and a food item; the second group was composed by a single stimulus (i.e. either imprinting object or food item) presented twice (Exp.1). Each stimulus in each group of events was sequentially presented and concealed in the same spatial location; each group of events took place in a different spatial location and the number of events was equalized. Chicks (N=24) spontaneously approached the two different stimuli rather than the single stimulus seen twice. A possible preference for the more varied set of stimuli was excluded by testing chicks (N=12) in a simultaneous presentation of two imprinting objects vs two food items (Exp.2).

D10-75

ASYMMETRICAL NUMBER-SPACE MAPPING IN THE AVIAN BRAIN

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Young chicks (Gallus gallus) are able to use ordinal information to identify the 3rd, the 4th or the 6th target element in a series of 10 identical, fixed and equally spaced elements, sagittaly oriented with respect to the chicks' body. Interestingly, whenever, during a subsequent generalisation test, the target had to be identified on a series identical to the training one but oriented from left to right, chicks would refer the correct position starting from the left end of the series (Rugani et al., 2007; 2010). This asymmetry could be due to a right hemispheric dominance for the spatial processing required by the test. Though in those experiments numerical and spatial information were intertwined. We therefore devised a series of experiments to disentangle the information coded by the two hemispheres. In Experiment 1, birds were trained to identify a target element solely on the basis of ordinal information. To avoid any possible use of spatial information, the inter-elements distances were changed from trial to trial, throughout training and testing. When solely the ordinal information was available, chicks identified as correct both the target positions from the left ($t(11)=4.532$; $p<0.001$) and from the right $t(11)=4.504$; $p<0.001$) ends. In Experiment 2, subjects were trained to peck the 4th position in a series of 10 identical fixed and equally spaced positions, sagittaly aligned with respect to the chicks' starting point. All subjects then underwent two generalization tests (one with a series of 10 and the other of 16 elements). All subjects manifested the leftward bias when 10 ($t(11)=10.169$; $p<0.001$), but not when 16 elements (left: $t(11)=3.220$; $p=0.008$; right $t(11)=3.373$; $p=0.006$) were employed. Data demonstrated that purely ordinal representation seems to be bilaterally represented in the chick brain and activation of this representation would not produce any imbalance in the activity of the two hemispheres. As a result, allocation of attention would be identically directed towards both the left and the right visual hemifields. In contrast, the purely spatial representation would be unilaterally represented in the right hemisphere.

D10-76

PARADOXICAL EFFECTS OF ENVIRONMENTAL ENRICHMENT AND FOOD ENTRAINMENT IN THE R6/2 MOUSE MODEL OF HUNTINGTON'S DISEASE

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Huntington's disease (HD) is a neurodegenerative disorder caused by an expanded CAG repeat in the HD gene. It has been shown previously that motor and cognitive performance, and ultimately survival, can be improved in transgenic mouse models of HD mice by providing environmental enrichment. In addition to their cognitive and motor deficits, R6/2 mice show a progressive disintegration in circadian rhythms, which mirrors the problems associated with sleep-wake disturbances experienced by HD patients. Here we have shown that a food entrainment schedule, where food availability is limited to a specific time of day, can restore daily behavioural cycles in R6/2 mice. We investigated the effect of overnight (the natural active period for mice) food entrainment and environmental enrichment (exposure to a Perspex playground containing running wheels, tunnels, climbing frame, chew blocks etc), both separately and in combination, on cognitive performance in the touchscreen and two-choice swim tank. We report that while there were no obvious differences between groups in performance in the touchscreen, enriched R6/2 groups performed better in the 2-choice swim tank, irrespective of feeding regime. Furthermore, different combinations of environmental enrichment, food entrainment and behavioural testing delayed the onset of phenotype, improved survival and revealed differences in locomotor and exploratory behaviour in the open field. While the precise mechanism by which environmental enrichment affects disease progression in R6/2 mice is unknown, unlike food entrainment, it produced no obvious deleterious effects and results suggest that it could be used therapeutically, to enhance the quality of life of HD patients.

D10-77

VISUAL DISCRIMINATION AND REVERSAL LEARNING IN A NOVEL TOUCH SCREEN TASK IS DIFFERENTIALLY MODULATED BY 5-HT(2A) AND 5-HT(2C) ANTAGONISTS IN RATS

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Cognitive flexibility is impaired in psychiatric conditions such as obsessive-compulsive disorder (OCD) and schizophrenia, but current treatments for these conditions are mostly ineffectual in improving such impairment. Serotonin signalling has been implicated in cognitive flexibility through a number of tasks including spatial reversal learning. However, the influence of serotonin 2A and 2C antagonism on reversal of visual discrimination, an animal model with high face validity, remains unexplored. We developed a three-choice paradigm for visual discrimination reversal learning to assess cognitive flexibility in rats. Lister Hooded rats were tested for visual discrimination, reversal learning and strategy shifting (ie., switching from visual to spatial discrimination), under the influence of a 5-HT2A antagonist (M100907; 0.1 mg/kg i.p.) or a 5-HT2C antagonist (SB242084; 1.0 mg/kg i.p.). SB242084 increased the number of trials required to reach criterion on both reversal learning and strategy shift, compared to M100907, whereas no significant effect on discrimination was noted. Further, M100907 transiently reduced the number of trials completed during reversal but not during discrimination sessions; in contrast, SB242084 transiently increased the number of trials completed during reversal. Our results corroborate the notion that 5-HT2A and 5-HT2C antagonism have opposing effects on behaviour, in the present experiment pertaining to the reversal but not to the acquisition of visual discrimination. These differential effects on cognitive flexibility may be relevant for the understanding, and future treatment, of OCD and schizophrenia.

D10-78

DISSOCIATION BETWEEN DECISION-MAKING AND GAMBLING PRONENESS BY REDUCED BRAIN SEROTONIN SYNTHESIS IN THE RAT

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Impulsive decision-making and exaggerated risk-taking are associated with sensation-seeking and pathological-gambling, both influenced by the brain serotonergic system. We assessed if manipulation of brain serotonin levels affected decision-making and risk-proneness in adult male rats, subjected to an L-tryptophan deficient diet (T–) or control diet (T+; 2.8g/kg). They were tested for decision-making with the rodent Iowa Gambling Task (r-IGT) using home-cage operant-panels. Successively, the same rats were tested for risk-proneness with a probabilistic-delivery (PD) task in operant-chambers. After sacrifice, serotonin and its metabolite were evaluated in selected brain areas. As expected, T+ rats tended to choose the option with best long-term payoff in the r-IGT. They also shifted from large-unlikely to small-sure reinforcers in the PD task. In contrast, T– animals showed a weaker improvement of performance in the r-IGT and maintained a sub-optimal attraction for the large-unlikely reinforcer in the PD task. HPLC demonstrated drastically reduced brain serotonin synthesis in T- rats. Comparing individual performances in both tests, we found significant correlations within T+ but not T- rats. This may indicate a dissociation between decision-making and risk-proneness, due to an altered function of the serotonergic system. Further studies will focus on neuropsychiatric conditions characterized by gambling and/or disturbed cognitive skills.

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D10-79

HIPPOCAMPAL CODING OF SPATIAL INFORMATION ABOUT DYNAMIC CUES

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Since the discovery of the place cells, pyramidal neurons that fire for a specific location in the environment by John O’Keefe (O’Keefe, J. Exp Neurol, 1976), numerous studies have been done to better understand spatial coding. These studies have mostly studied the relation of place fields with the environmental static cues as the basis to locate the subject position in the space (O’Keefe, J. and N. Burgess. Nature, 1996 and Mehta, M.R., et al. PNAS, 1997). However, in the real world often referential cues are dynamic. Tracking of dynamic cues while escaping from predators, foraging or mating, is critical for survival. The present study try to, assess the role played by the hippocampus in the tracking and localization of dynamic cues. Lister-Hooded rats were trained to discriminate movements of a robot as a dynamic cue and once they reached a high and stable level of performance were chronically implanted with tetrodes (McNaughton, B.L., et al. J Neurosci Methods, 1983) in the CA1 area of hippocampus. After the isolation of single units during the protocol, data was analyzed looking for correlates between neuronal firing and the movement and position of the dynamic cue. Some of the identified place cells showed neuronal firing that was modulated by the position of the robot. In order to quantify this spatial specificity, the Skaggs index (SI) was calculated, as a value of the spatial information content (Markus, E.J., et al. Hippocampus, 1994), and then compared to a shuffled data constructed with the spike trains of the neurons shifted randomly in time. This analysis revealed a significant modulation of neuronal firing by the position of the robot. Out of 129 neurons isolated in three different subjects we observed a significant SI regarding the dynamic cue in 28 of them ($p<0.05$, 21.7 %) and 34 neurons regarding the animal position ($p<0.05$, 26.3%). The modulation of firing rate by other parameters of the dynamic cue, such as velocity, sense or direction, was also analyzed.

D10-80

THE ROLE OF HIPPOCAMPUS IN POSITION AND OBJECT DISCRIMINATION

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The role of hippocampus in cognition is intensively studied. It is unclear whether hippocampus is necessary for discriminating position of a distant object and what is its role in object discrimination. To study these questions we have developed two novel operant-conditioning tasks: a) a task in which rats discriminate different objects presented on a computer screen (object discrimination task) and b) a task in which rats discriminate different positions of the same object presented on the computer screen (position discrimination task). Operant responses (lever presses) were reinforced when one particular object was displayed (object discrimination task) or when the object was displayed in one particular position (position discrimination task). After the rats reached an asymptotic performance, we have studied the role of hippocampus in these tasks by injecting a $GABA_A$-receptor agonist (muscimol 0.3 µg) into both hippocampi. The results showed that hippocampal inactivation impaired performance in both tasks without affecting motor activity. In the object discrimination task the rats were evaluating visual similarity between the rewarded object and a currently presented object. The hippocampal blockage affected specifically this process. The same rats were subsequently tested in a brightness discrimination task which is considered as hippomcapal independent. As expected the hippocampal inactivation had no effect on behavior in this control task. We conclude that a) the ability to discriminate position of a distant object requires hippocampus and b) the perception of visual similarity of different objects depends on hippocampus.

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D10-81

DIFFERENTIAL ROLE OF LATERAL ENTORHINAL CORTEX AND DORSAL HIPPOCAMPUS IN ACQUISITION AND FLEXIBILITY OF CROSS-MODAL ASSOCIATIONS IN RATS

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Most rodent models devoted to the study of neural basis of learning and memory are based on tasks in which the conditioned stimulus is processes by one sensory modality (a tone, an odor…). Here we developed a new behavioral paradigm allowing investigating on neural basis supporting cross-modal olfacto-tactile associations. In rat this two modalities are of prime behavioral importance for object exploration. The task consists in finding among 3 cups which one is baited (+) according to a specific odor (0) texture (T) combination. For task 1 the 3 cups were configurated as following: O1T1 +, O2T1, O1T2. Interestingly, most rats learned this task within 3 to 6 training sessions (20 trials/session). Task 2 consisted in a new set of stimuli (O3T3+, O4T3, O3T4) and we observed that rats managed the task within 1 to 3 training sessions only. Finally, task 3 consisted in a flexibility test based in a recombination of previously learned items (ex: O2T3+, O2T4, O2T3). To solve this task rats had to neglect previously reinforced items and learn the new specific reinforced combination. Surprisingly, most rat solved the flexibility task within 1 or 2 training sessions. We tested for the importance of lateral entorhinal cortex (LEC) and dorsal hippocampus (DH) for the 3 phases of the testt. This was done using transient inactivation with lidocaine (4%) injected bilaterally (0,4 µL) just before the test session. We found that inactivation of either structure did not impair recall of the previously learned task 1. Interestingly, LEC inactivation severely impaired acquisition of a new set of combinations (task 2). In contrast, DH inactivation produced no affect on acquisition of task 2 but selectively impaired performance during the flexibility test. As a whole the experiment suggests a role of LEC for the formation of new olfacto-tactile associations, while DH is important for flexibility of this cross-modal associations.

D10-82

MODULATION OF SPATIAL PROCESSING BY SOMATOSENSORY INPUTS IN THE RAT

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It has been demonstrated that the generation of the spatial cognitive map encoded in the hippocampus is modulated by different senses (vision, audition or smell). Recently it was showed that the hippocampus also process tactile information (Pereira et al., PNAS, 2007 and Itskov et al, PLoS One, 2011). However, the role of somatosensory (tactile) information on spatial representation remains unknown. Tactile information processed by whiskers is a relevant sensory stream for rats that devote a large area of cortex (barrel cortex) to its processing. Our hypothesis was that tactile information is as well relevant for the cognitive map generation in rats. Consequently, the loss of tactile information in the absence of other sensory cues should affect the spatial representation. The absence of other sensory cues was achieved in darkness, clean maze and white noise playing as auditory background. Under these conditions, we carried out early experiments where place cells were recorded before and after rotation of tactile cues. These experiments revealed a large influence of tactile cues on the location of place fields, and so we proceeded to use deprivation techniques. To test our hypothesis, three types of experiments were carried out. First, we developed a paradigm to carry out temporary deprivation of tactile inputs using a local anaesthetic (lidocaine) applied to the base of the whiskers (Gener et al., J Neurosci Methods, 2009). Second, to assure that the tactile deprivation by local application of lidocaine was effective in the awake animal, we carried out a tactile discrimination task with and without lidocaine application. Our results were that, after lidocaine, the percentage of successful discriminative responses decayed from 88% to 48%. We thus demonstrated that tactile deprivation by lidocaine worsened performance in tactile discrimination tasks. Finally, once the technique of somatosensory deprivation was developed and validated in the behaving animal, it was applied to characterize the properties of place cells' firing fields. Place cells properties such as firing rate, location and/or extension of firing fields were quantified. Our results showed that place cells recorded in a controlled environment were sensible to tactile cues. This study suggests that whisker-mediated somatosensory input is relevant for the cognitive map creation.

D10-83

SHORT-TERM HIGH FAT FEEDING TEMPORARILY IMPAIRS BEHAVIOURAL FLEXIBILITY IN A DELAYED MATCHING AND NON-MATCHING TO POSITION TASK IN RATS

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Epidemiological evidence suggests that people with type 2 diabetes or insulin resistance exhibit deficits in cognitive function relative to age matched controls. Similarly, rats fed a high fat (HF) diet for 10 weeks exhibit impaired behavioural flexibility and task accuracy that correlated negatively with insulin resistance. Metabolic changes were evident after 2-3 weeks of HF feeding. The current study tested the hypothesis that short term HF feeding was sufficient to elicit a cognitive deficit in this task. Male Wistar rats (150-175g) were trained to perform a delayed matching to position (DMTP) task in operant chambers reinforced with sucrose pellets. They were then fed either a HF diet (45% kcal lard) or standard chow (SC). Task retention was assessed during week 3 and behavioural flexibility during week 4 by switching from DMTP to a delayed non-matching to position (DNMTP) task. All animals were then fed standard rat chow for the remainder of the study and performance re-tested during weeks 9 and 10. Body weight, plasma glucose, insulin and leptin were monitored throughout the study. Fasting insulin resistance index (FIRI) was calculated to assess whole body insulin sensitivity. After 4 weeks on the HF diet animals were significantly heavier, had higher levels of leptin and reduced insulin sensitivity as measured by the FIRI index ($p<0.05$ for all). HF diet had no significant effect on accuracy in the DMTP task but HF animals were significantly impaired when the task was changed to DNMTP. Task accuracy was negatively correlated with body weight, plasma leptin and insulin levels. Following the switch to standard chow the HF animals continued to exhibit a deficit in behavioural flexibility when compared to SC animals. However, in contrast to the results obtained in week 4 this deficit was not sustained to the final day of testing. In addition body weight, leptin and insulin sensitivity were the same as SC controls. This study has shown that 4 weeks of HF feeding is sufficient to elicit deficits in cognitive flexibility which can be attenuated by reverting to a standard diet.

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D10-84

EFFECTS OF NEONATAL T-MAZE LEARNING UNDER CONDITIONS OF REWARD OR DENIAL OF EXPECTED REWARD ON PREFRONTAL CORTEX FUNCTION

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Early life experiences are considered as major determinants of adult behavior and brain function. Adverse events have a profound impact on the development of brain areas such as the prefrontal cortex and predispose individuals for maladaptive reactions and even psychopathology. We utilized the animal model of neonatal training in a T-maze under conditions of reward or denial of expected reward to investigate its long-term effects on prefrontal cortex function in the Attention Set Shift Task (ASST), a rat analogue of the Wisconsin Card Shorting Test for humans. In ASST, animals have to learn to predict the presence of hidden food based on a specific type of environmental cue (i.e. the type of texture of the material covering the food) while ignoring other types of cues (i.e. the odor of the material covering the food) and then learn by trial-and-error to reverse the predictive rule either intradimensionally (i.e. one type of texture over another) or extradimensionally (i.e. odor over texture). Most interestingly, adult rats denied expected reward as neonates were deficient in the intra-dimensional rule reversal trials of the ASST, compared to both rewarded as neonates and control animals, indicating a prefrontal cortex malfunction. This behavioral deficit was accompanied by lower activation during ASST, as assessed by Fos immunoreactivity, of the medial orbitofrontal cortex, an area necessary for inhibiting learned reactions and impulses. Moreover, as determined by HPLC, dopamine levels in the prefrontal cortex were lower in adult animals denied expected reward as neonates. Our findings that the neonatal experience of learning under conditions of denial of expected reward had long-term effects on prefrontal cortex activity both at the neurochemical and the behavioral level, support the concept that early-life experiences can program in an experience-specific way, adult brain function and thus behavior.

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D10-85

FACILITATION OF AMPA RECEPTOR SYNAPTIC DELIVERY AS A MOLECULAR MECHANISM FOR COGNITIVE ENHANCEMENT

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Cell adhesion molecules and downstream growth factor-dependent signaling are critical for brain development and synaptic plasticity, and they have been linked to cognitive function in adult animals. We have previously developed a mimetic peptide (FGL) from the neural cell adhesion molecule (NCAM) that enhances spatial learning in rats. We have now investigated the cellular and molecular basis of this cognitive enhancement, using biochemical, morphological, electrophysiological and behavioral analyses. We have found that FGL triggers a long-lasting enhancement of synaptic transmission in hippocampal CA1 neurons. This effect is mediated by a facilitated synaptic delivery of AMPA receptors, which is accompanied by enhanced NMDA receptor-dependent long-term potentiation (LTP). Both LTP and cognitive enhancement are mediated by an initial PKC activation, which is then followed by a persistent CaMKII activation. These results provide a mechanistic link between facilitation of AMPA receptor synaptic delivery and improved hippocampal-dependent learning, induced by a pharmacological cognitive enhancer.

D10-86

DEVELOPMENT OF AN ATLANTIS RAT WATER MAZE SYSTEM: KEY FACTORS FOR CONSIDERATIO

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The Morris water maze was first described over thirty years ago and is still one of the most commonly used cognition paradigms to measure spatial learning and memory in rodents. More recently, a modified version using an on-demand rising platform, also known as the "Atlantis" platform, has been developed to increase task difficulty thus overcoming the confounding ceiling effects associated with the fixed platform protocol. The aim of the present studies was to develop a robust Atlantis water maze protocol amenable for detecting pharmacological enhancement whilst determining the impact of key variables on performance. The water maze comprised of a polypropylene pool (d: 2.0 m, h: 0.5 m) surrounded by a variety of spatial cues. The maze was daily filled with clean water and warmed up to 25 ºC ± 1 ºC. The water was made opaque by adding two litres of opacifier (Opulyn®, Dow). An on-demand platform (diameter: 20cm) was situated in the centre of one of the four quadrants. When the platform was fully raised, it was covered by 2 cm of water and therefore invisible to the rat. A video camera was positioned directly above the tank to record the rats swim trajectory and this was connected to a personal computer in which all of the parameters (latencies, path length, swim speed etc) was acquired using Noldus® Ethovision (XT v7). As the primary aim of these studies was to define the most appropriate parameters for the Atlantis component, the first series of studies focused on defining the optimal fixed platform habituation training protocol. Analysis of all parameters including latencies, path length, time in periphery and qualitative characterization of tracking plots, revealed that a minimum of seven trials were required to establish robust spatial locating performance. The next series of studies aim to define the optimal trigger zone dwell times and their respective day-2-day increases to ensure a window for potential pharmacological improvement. Several studies revealed subtle, yet significant performance effects of minor alterations in dwell times highlighting the need for critical determination of these parameters. Other important parameters such as the impact of platform rise speed and mechanical-induced variations of rise speed across trials will also be discussed.

D10-87

EXPERIMENTAL DESIGN FOR THE STUDY OF ACTIVITY-DEPENDENT CORTICAL AND SUBCORTICAL SYNAPTIC FUNCTIONS DURING INSTRUMENTAL CONDITIONING OF BEHAVING RATS

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It is well known that different brain regions are related to different kind of memories. We recorded in freely moving rats the activity-dependent changes in synaptic activity of several cortical and subcortical structures related with working and procedural memories. For this, we implanted chronic recording and stimulating electrodes in up to three selected synapses, which were mono-synaptically activated during the acquisition and performance of different instrumental conditioning tasks. Specifically, with the help of implanted tetrods, we recorded field excitatory postsynaptic potentials (fEPSP) in the hippocampal formation (dentate gyrus, CA3, CA1, subiculum), medial prefrontal cortex (mPFC), and thalamic reuniens nucleus (REUn) evoked by the electrical stimulation of the perforant pathway, pyramidal CA1 area, and mPFC. The selected synapses were activated during performance of different behaviors (lever approaching, lever press, eating pellets, grooming, etc.). We checked the changes in synaptic activity in a series of learning task performed by the rats. Firstly the rats were trained to press a lever to obtain a pellet (FR 1:1), and then the animal were confronted with increasing levels of difficulty. In one of the tasks, rats were trained to press the lever when an internal light was on, using a time-random paradigm (RP). In a different test, we checked animal's expectancy or frustration modifying the rate of reward or removing the lever in absence of any previous signal. Preliminary results indicate that the strength (determined in changes in evoked fEPSPs) of several recorded synaptic sites changes during the performance of the selected behaviors (mainly during lever presses and food intake). Interestingly enough, the activity-dependent synaptic strength (determined in fEPSP slope, in mV/s) in the CA1-mPFC synapse decreased both when the lever is removed unexpectedly (expectancy) and when no pellet was rewarded after a correct lever press (frustration) as compared with when the lever was present (no change in expectancy) and when the pellet was delivered appropriately (no frustration). On the other hand, the synaptic activity at the CA1-reunniens and CA1-subiculum synapses were not modified during performance of these complex behaviors.

D10-88

MENTAL ROTATION IN MONKEYS: REAL VERSUS VIRTUAL SPACE

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The ability to perceive space and to create inner representation of this space is one of the key functions for most of animal species, including humans. We study the ability of monkeys to perceive information from one spatial frame and to choose particular position according to these stimuli in another spatial frame. Originally, the monkeys were trained to respond by choosing one position from the pattern presented on a touch screen ("response space") according to stimuli presented on the second screen ("stimulus screen"). The response space consisted from the rectangle with four circles at its corners. In previous experiments we used as a stimuli similar rectangle but only with one circle of which position indicates the rewarded position on the complementary response space. We demonstrated that monkeys were able to choose correct position according to such stimuli. However, when the stimuli were rotated in frontal plane it seems that monkeys do not use for orientation only the position of the circle in the stimulus itself, but also another cues from the real space (for example the monitor itself and others cues in the room). Therefore in this experiment we study whether the monkeys prefer the information from the stimulus itself or the "extra-stimulus" information from the surrounding environment; and how they would orient when the rotation of stimulus (virtual space) and monitor (real space) became conflicting. This allows us to study in more details how the monkeys perceive abstract visual stimuli and whether they are able of mental rotation in this task.

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D10-89

EXTENDING THE FIVE-CHOICE SERIAL REACTION TIME TASK PARADIGM: DEVELOPMENT OF NOVEL ANALYTIC AND METHODOLOGICAL TOOLS TO ENHANCE SENSITIVITY FOR COGNITIVE CHANGE

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Disruptions in attentional processing and response inhibition are prominent features of numerous psychiatric disorders such as schizophrenia and attention-deficit/hyperactivity disorder, and there is growing interest in improving detection of potential treatments targetting these disruptions. Such cognitive disruptions are typically assessed using tests of frontal lobe function including measures of continuous performance which tax behavioural control and sustained attention. The five-choice serial reaction time task (5-CSRTT) in rodents was developed as an analogue of human continuous performance tasks, and large body of research highlight the task's translational properties. Here we report on our development and application of signal detection theory to 5-CSRTT performance variables, as well as a novel touchscreen version of the 5-CSRTT, to enhance sensitivity for detecting cognitive change. We illustrate the utility of these tools in experiments investigating the cognitive effects of modafinil (diphenylmethyl sulphinyl-2-acetamide), a novel wake-promoting agent with putative cognitive-enhancing properties. Male, Lister Hooded rats received modafinil (0, 10, 30, 100 mg/kg/ip) and 5-CSRTT performance was assessed following training under either variable (VITI 3-7s) or fixed (FITI 5s) delays to stimulus presentation (believed to exert differential attentional demands). We replicated several previous studies showing increased premature responding at the highest (100 mg/kg) dose of modafinil, and no statistical effects on other standard task parameters (e.g., accuracy, omissions). However, we detected significant enhancements of lower-dose modafinil (10 mg/kg) using a novel sensitivity index based on signal detection analysis. Moreover, as expected, these enhancements were observed primarily under VITI conditions and in subjects with poor-accuracy baselines. Indices of response bias were significantly increased after higher doses of modafinil. To corroborate and extend these findings, rats were further assessed on novel touchscreen version of the 5-CSRTT affording presentation of distinct "go" and "no-go" stimuli, more similar to human continuous performance tasks. Overall, our results demonstrate that analytic and methodological modifications of the standard 5-CSRTT paradigm in rodents may offer improved sensitivity for detecting changes in cognitive performance, and add further preclinical translational potential to the 5-CSRTT.

D10-90

VASOTOCIN INFLUENCES ZEBRAFISH SHOALING BEHAVIOUR

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Social behaviour such as group formation is adaptive in many species, for example providing anti-predator benefits. Group formation can also potentially affect other processes, such as the transmission of information between individuals. The oxytocin-vasopressin nonapeptide family has been shown to influence a wide range of social behaviour patterns, including mate choice and aggression in mammals, and, more recently, flocking in birds. In addition, this nonapeptide family appears evolutionary conserved in function and structure across vertebrates. Considered together, this suggests that these nonapeptides could play a conserved role in group formation. To gain insight into such a mechanism mediating social behaviours, we studied shoaling behaviour in female zebrafish (Danio rerio), investigating the influence of isotocin and vasotocin (the teleost homologues of the mammalian oxytocin and vasopressin). Zebrafish are a schooling species and while their development and genetics are well studied, their behaviour is less well explored. We investigated the effects of single peripheral injections of vasotocin, isotocin and their antagonists on shoaling preferences. After administration, subjects were tested in a two-choice-paradigm, being offered a choice between a shoal of conspecifics or an empty compartment for a 10 minute period. We predicted that vasotocin would decrease and isotocin would increase shoaling tendencies. Vasotocin administration indeed significantly decreased the time subjects spent interacting with the shoal compared to control treatments. In addition, vasotocin increased the latency to start shoaling and interacting with the shoal. However, administration of the vasotocin antagonist (an arginine vasopressin receptor 1A antagonist) also reduced the time spent interacting and shoaling, contrary to expectations. Isotocin administrations did not show clear effects compared to control treatments, although isotocin-administered subjects were faster to shoal and interact with the shoal than vasotocin-administered subjects. The isotocin antagonist (an oxytocin receptor antagonist) had no significant effects on the measured behaviours. Our results show that administration of nonapeptides, specifically vasotocin, decreases shoaling tendency in a teleost fish. This raises the possibility that this family of peptides plays a conserved role across vertebrates in the neural mechanisms underlying sociality.

D10-91

FROM ATTRACTION TO AGGRESSION: THE EMOTIONAL VALUE OF MALE PHEROMONES CHANGES DURING LACTATION IN FEMALE MICE

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Female mice are innately attracted by male pheromones (which are rewarding), detected through the vomeronasal organ. On the other hand, females are generally not aggressive towards intruders, whatever their sex. However, lactating dams show a high level of aggressiveness towards intruders, which gradually decreases during the second week after parturition (maternal aggression). Mutant females lacking vomeronasal function (trpc2$^{-/-}$) show impaired maternal aggression, thus suggesting that this behaviour is promoted or elicited by vomeronasal stimuli. This work explores the hypothesis that pheromones of the intruder elicit aggression in lactating females. If so, maternal aggression to castrated males would be reduced. Moreover, it is likely that the same male pheromones that attract to virgin females, would elicit aggression in dams, for which they might be non-attractive, or even aversive. To test these hypotheses we performed aggression test towards male intruders in three groups of FEMALES: dams, maternalized females (sisters of the dams sharing pup care) and virgins. Each female was tested against two MALE intruders: intact and castrated (order counterbalanced). There was a significant effect of FEMALES (log rank test, $p< 0.01$) on the latency to attack, with dams showing shorter latency. Moreover, attack time to intact males differs significantly among females (randomization test, $p=0.002$), dams attacking more and in longer bouts. In contrast, aggression to castrated males is low and similar among females ($p=0.256$). Maternalized and virgin females showed no apparent differences. The lack of aggressiveness of maternalized females suggests that continuous interaction with the pups from parturition (at least three days), is not enough to promote aggression, which would be dependent on endocrine/physiological changes related to parturition and lactation. To test whether dams had lost attraction to male pheromones, we performed preference water vs male urine test, following Kobayakawa et al (2007, Nature 450:22). Preliminary results indicate that urine investigation is reduced in dams and maternalized females as compared to virgins, thus suggesting a change of emotional value of male pheromones during lactation.

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D10-92

EFFECTS OF A FRUSTRATED EXPECTED REWARD IN C57BL/6J AND MU-OPIOID RECEPTOR KNOCKOUT MICE

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Consequences of frustration occurring when the reward is no longer available represent one aspect of the addictive process that has received reduced attention. Therefore, animal models of frustrated expected reward can be of relevance to study the behavioural and neurobiological consequences related to the emotional states generated during frustration in the addictive process. C57BL/6 and mu-opioid receptor knockout mice were trained for 10 consecutive days to lever-press for obtaining palatable food (chocolate-flavoured pellets), paired with a cue light, on a fixed-ratio (FR) 1 schedule of reinforcement followed by 10 sessions under FR5, FR10 and 10 additional sessions under progressive ratio (PR) schedule where the response requirement to earn a reinforcer escalated according to the following series: 1-2-3-5-12-18-27-40-85-115-150-300. After this period of intense training, animals were then tested on an additional PR session. In the frustration group, no reward was delivered at the breaking point 150 whereas the cue light was presented. In another group, neither chocolate pellet nor light were presented at the breaking point (despair group). A positive control group receiving the reward plus the light at the breaking point was included as well as a negative control group that did not receive the reinforcer nor the light during the whole experiment. After reaching the breaking point animals remained in the training box and their operant responding was registered. The aggressiveness was measured using the resident-intruder test after this last session. Our results reveal that mice of both genotypes exposed to the frustration event perseverated in the operant responses. Interestingly, the frustrated knockout mice show a higher number of responses after the breaking point than the wild-type group. This mouse model of frustration provides a new tool to evaluate the genetic factors involved in frustrated food consumption.

D10-93

KAR-MEDIATED GLUTAMATE RELEASE FACILITATION AT THALAMO-CORTICAL SYNAPSES INVOLVES CALCIUM-CALMODULINE AND A HIGH CALCIUM THRESHOLD

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Kainate-type glutamate receptors (KAR) participate in conventional neuronal transmission and processes like Long-Term Potentiation (LTP) and Long-Term Depression (LTD) that are believed to be responsible of the plastic changes that occur in the CNS during development, learning and memory and recovery after CNS lesions. The inadequate activation of KARs has detrimental effects that have been related to excitotoxicity, epilepsy and other disorders. At thalamo-cortical synapses presynaptic activation of KARs modulates glutamate release but the mechanisms involved in this modulation are not known. The aim of this work was to establish the mechanisms involved in glutamate release facilitation mediated by KAR-activation at thalamo-cortical synapses in mice. We used whole-cell patch-clamp recordings for this purpose. We found that activation of presynaptic KARs facilitated glutamate release via activation of adenylate cyclase (AC) by the Ca^{2+}- calmodulin complex. This effect was highly-dependent on the intracellular Ca^{2+} levels and involves: i) Entry of Ca^{2+} trough L-type voltage-gated calcium channels; ii) Ca^{2+} entry trough GluK1-containing KARs; and iii) and Ca^{2+}-induced Ca^{2+} release from intracellular stores.

D10-94

MODULATION OF THE ENDOCANNABINOID SYSTEM IN DIFFERENT STAGES OF PROCESSING OF AVERSIVE MEMORIES IN RATS: INTERACTIONS AND SYNAPTIC PLASTICITY HIPPOCAMPAL STUDIED WITH THE AGONIST CP55,940

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Introduction: The CB1 receptors modulate synaptic plasticity in the hippocampus, as well as consolidation and retrieval of memory. This study investigate the roles of the metabotropic CB1 receptors infusing the agonist CP55,940 into the dorsal hippocampus of rats.
Methods and Results: Male Wistar rats were cannulated bilaterally in the dorsal hippocampus and trained in the context fear conditioning task. Animals received vehicle or CP 55,940 pre and post training. The test was performed 24 hours after training. Immediately after training, the animals were bilaterally infused into the dorsal hippocampus with CP55,940 (0,01µg/µl, 0,1µg/µl, 1µg/µl, 5µg/µl e 10µg/µl). The post hoc Tukey test showed significant difference only in the concentration of 5µg/µl compared with the control group. Posttraining infusion of CP55, 940 (5µg/µl, or CP55,940 5µg/µl + 0.2 mM of CB1 antagonist AM251) caused a significant difference between groups. Infusion before of the test, with CP55,940 (0.1 g / ul, and 1µg/µl 5µg/µl): there was a significant difference between groups, were amnestic upon memory retrieval. Pretest infusion of CP55,940 5µg/µl, or CP55,940 5µg/µl concomitant with a higher concentration (1,0µM) of the CB1 antagonist AM251 reverted the effect of CP. The electrophysiological procedure was performed by long-term potentiation(LTP) protocol with theta-like frequency stimulation. Hippocampal slices were perfused with artificial cerebrospinal fluid or CP55,940. The CP55,940 at concentrations equivalent to 5µg/µl intra-hippocampal infusions of 10 mM was prepared in 20 ml of buffer solution and used to perfuse slices during recording. After LTP induction, we can see a reductionin the magnitude of the potentiation. In conclusion, the intrahippocampal administration of CP 55,940 impaired both the consolidation and the retrieval of memory in concentrations that were similar to those capable of LTP induction inhibition. The quite selective CB1 receptor agonist CP 55,940 exhibited a very particular profile in terms of behavioral effects. This variability of effects may be attributed to the diffreent selectivities, afinities and even target aimed by each drug.

D10-95

DIFFERENTIAL NORADRENERGIC MODULATION IN THE RAT SOMATOSENSORY AND PREFRONTAL CORTEX

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Noradrenaline (NE) is known to modulate sensory processing by increasing the signal-to-noise ratio (SNR). Pre- and postsynaptic mechanisms acting on cortical adrenoreceptors have been implicated. The noradrenergic nucleus Locus Coeruleus (LC) is activated by sensory stimulation. However, the contribution of the sensory-evoked discharge in LC to modulation of cortical sensory responses is not well understood. We compared the effects of systemic or local (in LC) application of clonidine, an alpha2-receptor agonist, which is known to inhibit LC-NE neurons, on sensory responses in two cortical targets of LC. Simultaneous recordings in LC, primary Somatosensory (S1) and medial Prefrontal Cortex (mPFC) were performed in the urethane-anesthetized rat. Electrical foot shocks (FS) of the contralateral hind paw served as somatosensory stimuli (0.5ms, 5mA). The LC responses to FS differed dramatically after local and systemic clonidine administration. Iontophoretic application of clonidine (50nA, 50µl/ml, 20min) into LC resulted in complete cessation of both spontaneous and evoked activity of LC-NE neurons. Systemic clonidine (50 µl/ml, i.p.) produced a decrease in LC firing (less than 50% baseline for 30 min), however the LC responses to FS were preserved. Both local and systemic clonidine administration increased spontaneous activity in S1 and mPFC. The evoked responses in S1 were unchanged under condition of complete inhibition of the ipsilateral LC by local application of clonidine (n=13) and decreased during systemic clonidine condition (n=13). In mPFC, 8 units (40%) increased and 9 units (45%) decreased the response amplitude following local inhibition of LC. Four out of 24 mPFC neurons showed increased responses after systemic clonidine injection. Strikingly, 20% of initially non-responsive mPFC neurons became responsive (n=7) in case of local inhibition of LC. The same phenomenon was observed during systemic clonidine in 58% of cases (n=14). Thus, blocking the LC sensory-evoked discharge differentially affected signal processing in S1 and mPFC. The responses in S1 were preserved, while responses of a large proportion of mPFC neurons (~50%) were affected. We observed the opposite effects in S1 (decrease SNR) and mPFC (increased signaling) after blocking the alpha2 receptors in the entire brain. Overall, we conclude that alpha2 receptors are involved in sensory signal processing in both cortical regions, but mPFC receives a stronger NE neuromodulatory input.

D10-96

ANTI-INFLAMMATORY DRUGS ATTENUATES THE EARLY ANTIDEPRESSANT RESPONSE OF DEEP BRAIN STIMULATION FOR DEPRESSION TREATMENT: A TRANSLATIONAL STUDY

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Background: Deep Brain Stimulation (DBS) in the subgenual cingulate (Cg25) is a new and promising non-pharmacological therapeutic alternative to treat severe and resistant depression. In a seminal study, the patients displayed clinical benefits from DBS accompanied by a normalization of the metabolism in this region that is frequently overactive in depressed patients. Strikingly, the first clinical series have reported an initial large effect followed by a decay in the first month of treatment. This phenomenon attributed to a possible placebo or to an "insertional effect", remains to be resolved. Methods: We evaluated the effect of surgery and DBS in the rat infralimbic cortex (rodent Cg25 correlate) in the forced swimming test, an animal model of antidepressant activity. Furthermore, we characterized the early antidepressant effect in patients with major depression treated with DBS in the Cg25 involved in a clinical trial. Results: The results demonstrated that animals with the electrodes just implanted showed a similar antidepressant-like effect than those which in addition received electrical brain stimulation. This antidepressant effect was via a main action on 5-HT transmission because was blocked by the pre-treatment with an inhibitor of serotonin synthesis. Additionally, the "insertional effect" may be due to a regional neuroinflammation because the antidepressant-like effect was temporally correlated with an increase of GFAP immunoreactivity and was prevented by anti-inflammatory treatment. This is in agreement with the clinical study, where the earlier response in patients was poorer when they took anti-inflammatory drugs. Conclusions: Our study shows that electrode implantation is sufficient to produces an early antidepressant-like effect. Moreover, both preclinical and clinical findings suggest that the use of anti-inflammatory drugs after electrode implantation may attenuate the early antidepressant response.

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D10-97

THE STRESS IN CHRONIC PAIN SITUATION LEADS TO AN INCREASE OF NEGATIVE PAIN EXPERIENCE BY IMPAIRMENT OF NORADRENERGIC LOCUS COERULEUS NEURONS

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The brain noradrenergic system is susceptible to changes by stress exposure. The Locus Coeruleus (LC), the main source of noradrenaline in CNS, is involved in intrinsic control of pain. Due to the possible association between pain and stress via LC neurons, our study evaluates if the presence of stress in a situation of chronic pain may contribute to a worsening the emotional/sensory component of pain by changes in LC noradrenergic neurons. Thus, the chronic constriction injury (CCI) was used as a model of chronic neuropathic pain and the isolation as a model of stress. We compared the affective/sensory component of pain such as anxiety-like behaviour in four experimental groups: Sham, Sham-stress, CCI and CCI-stress. Subsequently, the expression of tyrosine hydroxylase (TH) and the electrophysiological properties of LC neurons were evaluated in all groups. The results revealed that CCI-stress showed the most negative pain experience in the affective test without changes in sensory dimension of pain or anxiety behaviour. Chronic pain or stress did not show effect on TH expression or LC spontaneous activity. Interestingly, the group with chronic pain and stress increased the TH expression while a decrease in the firing rate spontaneous activity in the LC neurons was observed. However, no differences were found in doses-response curves of UK14,304 (α2-AR agonist) or desipramine (noradrenaline reuptake inhibitor) in LC neurons. In conclusion, we report that when chronic pain and stress coexist it is required high levels of noradrenaline and, in consequence, it is produced a dysregulation of LC neurons which affect negatively on the emotional pain experience.

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D10-98

EFFECT OF PUERARIN AND DAIDZIN ON GHRELIN BLOOD LEVEL IN ALCOHOL PREFERRING AND NON-PREFERRING RATS

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Recent evidence has suggested that ghrelin, insulin and leptin and the volume-regulating hormones could play a role in the alcohol-seeking behavior (Addolorato et al. 2009). It is known, that ghrelin serum levels were found to be altered in alcohol-dependent patients and central ghrelin administration (to brain ventricles or to tegmental areas involved in reward) increased alcohol intake in a 2-bottle (alcohol/water) paradigm in mice (Jerlhag et al. 2009). There are some suggestions that isoflavonoids (i.e. puerarin - PUE, daidzin - DAI) present in Pueraria lobata are responsible for antialcoholic effect of this herb (Keung 2003, Abenavoli et al. 2008). The aim of this study was to assess the effect of PUE and DAI on ghrelin plasma level in the model of alcoholism. The experiments were performed on ethanol high preferring (PR) and low preferring (NP) of male rats received 10% ethanol using voluntary intake procedure for 8 weeks with two 2-week withdrawal periods. Next the animals were treated with PUE (150 mg/kg, p.o.) or DAI (40 mg/kg, p.o.) for 28 consecutive days and both total and acylated ghrelin (active form) levels in plasma of rats were measured using ELISA method. It was found out that PR rats differ from their counterparts NP in alcohol intake. With respect to drinking pattern in the investigated rats, it was noticed that there were no statistically significant differences in daily total fluid intake or body mass after the experiment. Both total and active ghrelin levels were significantly decreased in PR rats when compared with NP animals. DAI or PUE treatment lowered alcohol intake in PR animals, but not that of NP rats. It corresponded with significant increasing of both active and total ghrelin levels in DAI- and PUE-treated PR rats, whereas the two isoflavonoids did not change the levels of ghrelin in NP animals. In conclusion, it was found out that the increased ghrelin level after both DAI and PUE administration in PR rats is negatively coupled with alcohol intake.

D10-99

VASOPRESSINERGIC INNERVATION OF THE VENTRAL STRIATOPALLIDUM: POSSIBLE ORIGIN AND HINTS ON ITS ROLE

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Besides its role as a neurohormone, arginine-vasopressin (AVP) is found in neurons of the medial extended amygdala giving rise to central, sexually dimorphic, steroid-dependent pathways that terminate in key brain centres for socio-sexual behaviour. Our group is investigating the neural basis of a neglected aspect of sexual behavior: intersexual attraction through pheromones. In mice, vomeronasal-detected male pheromones are reinforcing to females. We have previously shown that pheromones' reward is independent of the dopaminergic tegmento-striatal pathway, but apparently depends on projections of the vomeronasal cortical amygdala to the ventral striatum (medial olfactory tubercle and islands of Calleja, and adjoining striatal cell bridges). This work explores whether AVP might modulate pheromones' reward at the level of the above-mentioned amygdalo-ventrostriatal system. In fact, patches of AVP-immunoreactive fibres densely innervate a nowhere area of the medio-ventral striatopallidum located just medial to the olfactory tubercle and lateral to the diagonal band nucleus. AVP-fibres apparently concentrate onto the medial islands of Calleja (including the major one). Assessment of the density of AVP-fibres in intact and castrated males, and in female mice indicates that this vasopressinergic innervation is sexually dimorphic and testosterone-dependent. The number of AVP-cells in the medial bed nucleus of the stria terminalis (BSTM) is also dimorphic and testosterone-dependent. AVP-fibre density in the ventral striatopallidum (and septum) correlates with the number of AVP-cells in the BSTM. The origin of the AVP-positive innervation of the ventral striatopallidum in the BSTM was confirmed by combining Fluorogold retrograde tracing with AVP immunohistochemistry: double-labelled neurons were found in the posteromedial and posterolateral BSTM. Lesions of the BSTM are being applied to further confirm this issue. The posteromedial BSTM receives direct vomeronasal inputs from the accessory olfactory bulb. Evidence presented in this work suggests the existence of an AVP-rich sexually dimorphic pathway from the BSTM to the ventromedial striato-pallidum. This pathway provides an anatomical substrate for a possible role of the AVP system in the control of sexual attraction/aggression induced by vomeronasal cues.

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D10-100

EFFECTS OF ADENOSINE A_{2A} RECEPTOR BLOCKADE OR KNOCKOUT ON CHOLINOMIMETIC-INDUCED ORAL TREMOR: STUDIES WITH A MOUSE MODEL OF DRUG-INDUCED PARKINSONISM

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Parkinson's Disease is characterized for a series of motor and non-motor symptoms. The primary motor symptoms of parkinsonism include akinesia, bradikinesia, rigidity, postural instability, and resting tremor. Tremor can be modeled in rats using the tremulous jaw movement (TJM) model. TJMs are defined as a "rapid vertical deflection of the lower jaw that resembles chewing but is not directed at any particular stimulus" (Salamone et al. 1998, 2005). In rats, TJMs can be induced by a number of neurochemical conditions that parallel those seen in human parkinsonism, including DA depletion, DA antagonism, and cholinomimetic administration. The TJMs induced by these manipulations generally occur in bursts, with the peak frequency in the 3-7 Hz range, which is similar to the frequency characteristics of parkinsonian tremor. Additionally, TJMs in rats can be attenuated using antiparkinsonian agents, including adenosine A_{2A} antagonists. In the present studies, a mouse model of TJMs was established. The focus of these studies was to investigate the effects of adenosine A_{2A} antagonism, and knockout (KO) of adenosine A_{2A} receptors, on cholinomimetic-induced TJMs in mice. The muscarinic agonist pilocarpine induced TJMs in a dose-dependent manner (0.025, 0.05, 0.075, 0.1 mg/kg IP). Systemic administration of the adenosine A_{2A} antagonist MSX-3 (2.5, 5.0, 10.0 mg/kg) significantly attenuated pilocarpine-induced TJMs. Additionally, adenosine A_{2A} receptor knockout mice showed a significant reduction in pilocarpine-induced TJM's compared to wild-type controls. A_{2A} KO mice were also more resistant to pilocarpine-induced reduction in horizontal and vertical locomotor activity, parameters related to bradykinsia and postural instability. These results indicate that adenosine A_{2A} antagonism and A_{2A} KO are capable of reducing cholinomimetic-induced TJMs in mice. Future studies should continue this extension of the TJM model to mice, and seek to characterize the pharmacology of drug-induced TJMs in mice using agents such as anticholinesterases and dopamine D2 antagonists.

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D10-101

mGlu2/3 AGONIST MODULATION OF KETAMINE-INDUCED OXYGEN AMPEROMETRY SIGNALS IN AWAKE RATS – A TRANSLATIONAL NEUROPHARMACOLOGICAL BIOMARKER

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Human functional imaging has had a major impact on cognitive neuroscience since its introduction, linking brain structure to function. The technique is translatable since rodent functional magnetic resonance imaging (fMRI) is possible but is limited to anaesthetised or restrained animals. In-vivo oxygen amperometry is an alternative approach that can measure oxygen changes related to behaviour since it allows real time monitoring of extracellular tissue oxygen in freely-moving animals. Neuroimaging techniques have previously been used to determine the effects of NMDA receptor antagonists on brain activation in humans and animals; these compounds have been shown to be psychotropic and to induce cognitive disturbances. Pharmacological reversal of the NMDA antagonist-induced imaging response may represent antipsychotic activity, as previously seen with mGlu2/3 agonists. Here, we compared the effect of i.v. ketamine challenge on neuroimaging signals in healthy volunteers and anaesthetised rats to the oxygen response in the medial prefrontal cortex (mPFC) and dorsal hippocampus (dHPC) of freely-moving rats using in vivo oxygen amperometry. The modulation of the oxygen amperometric ketamine response by the mGlu2/3 agonist LY379268 was also assessed. For the oxygen amperometry, rats were implanted with oxygen sensors in the mPFC and dHPC and were given a 1mg/kg i.v. infusion of ketamine over 2 minutes. For the mGlu2/3 agonist modulation studies, LY379268 (1, 3, and 10mg/kg) was dosed i.p. 30 minutes before ketamine was administered. Our results show a translational response to i.v. ketamine challenge, with the human fMRI, anaesthetised rat CBV imaging, and freely-moving rat oxygen amperometry showing similar increases in activation in the cingulate/mPFC. Pretreatment with LY379268 caused a dose-dependent reversal of the ketamine response in the oxygen signal in freely moving rats. We show that oxygen amperometry may be a good translational surrogate for imaging studies in freely-moving animals, and modulation of the oxygen ketamine response may provide a translational neuropharmacological biomarker of antipsychotic activity.

D10-102

PERINATAL HYPOTHYROIDISM: AN ANIMAL MODEL OF ATTENTION DEFICIT HYPERACTIVITY DISORDER?

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The Attention Deficit Hyperactivity Disorder (ADHD) is the most prevalent childhood disorder. Due to the high impact on our society, we think that it is necessary to have some instrument, an animal model in this case, in order to study the disorder in deep. The current ADHD animal models are based on the face validity. However, most of them only prove this validity partially. On the other hand, previous results from our laboratory showed that perinatal thyroid hormone deficiency causes long term behavioural alterations which resemble the hyperactivity and impulsivity seen in children with ADHD, in spite of a large period of rehabilitation. These effects have been proposed as animal model for ADHD. The aim of the current investigation was to assess if perinatal hypothyroidism is a good animal model of ADHD by studying face and construct validity in juvenile and adult period. We also analysed if the alterations seen in perinatal hypothyroid animals were reverted with methylphenidate treatment. Pups bred from female Wistar rats were used in this study. Treatment was administrated via the drinking water containing 20mgr/100ml Methimazole. Pregnant animals were exposed to methimazole from gestation day (GD) 7 to postnatal day (PD) 20. All male subjects were evaluated during neonatal period. Moreover, two male from each litter was randomly selected to be evaluated either during juvenility or adulthood. One of each pair received methylphenidate (1 mgr/Kg weight), whereas the other one received saline serum before experimental procedures. In the present study differences were found between control and treated rats at the neonatal period. Perinatal methimazole-treatment reduces body weight and impairs neuromotor development, mainly inducing retardation in neuromuscular abilities. Juvenile and adult behavioural analyses showed that perinatal methimazole treatment provokes a significant increase in activity and emotionality in both periods. A significant increase in impulsive behaviour was also seen in adult period; nevertheless this increase did not reach the significance in juvenile period. No significant differences appeared in attention measures. The methylphenidate administered did not revert behavioural effects.

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D10-103

ANALYSIS OF THE SUBCELLULAR DISTRIBUTION OF MELATONIN IN RAT BRAIN

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Melatonin (N-acetil-5-metthoxitriptamine), an hormone synthesized by the pineal gland, is also produced in many other tissues of the body. Although the biosynthetic route of melatonin synthesis is the same in these tissues than in the pineal, the regulation of extrapineal melatonin is yet unknown. The aims of the present study were to analyze the daily melatonin variations and its subcellular distribution in rat brain under several experimental conditions, including pinealectomy (Px), continuous light exposure (CL), luzindole-treated, and melatonin-injected animals. Male Wistar rats were maintained in a 12:12 h light/dark cycle or under continuous light for 7 days before the experiments. For the determination of the melatonin content in brain subcellular fractions, the brains were quickly removed after the sacrifice, and nuclei, membranes, mitochondria and cytosol pure fractions were obtained by differential centrifugation under Percoll gradient. Melatonin concentration in these cellular compartments was fluorometrically measured by HPLC. Our results showed a daily variation in the melatonin content in cell membranes, cytosol, nuclei and mitochondria, although these variations did not adjust to a circadian rhythm. Cell membranes have the highest content of melatonin, followed by mitochondria, nuclei and cytosol. Pinealectomy significantly increased the content of melatonin in all subcellular compartments, whereas luzindole treatment had little effect on melatonin distribution. Administration of 10 mg/kg b.w. melatonin to sham pinealectomized, Px, or CL rats increased the content of melatonin in the subcellular compartments studied. Doses of melatonin from 10 to 200 mg/kg b.w. increased in a dose-dependent manner the accumulation of melatonin in cell membranes and cytosol, although the former accumulated 10 times more melatonin than the latter. In contrast, melatonin content in nuclei and mitochondria was saturated at 40 mg/kg b.w. These data suggest that, although biological membranes are permeable to melatonin, the indoleamine cannot fully equilibrate through them, and specific mechanisms regulate the subcellular distribution of the indoleamine. Together, our results modify the current view of the physiology and pharmacology of melatonin.

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D10-104

REAL-TIME OXYGEN AMPEROMETRY CONFIRMS HUMAN NEUROIMAGING EVIDENCE FOR A ROLE OF THE NUCLEUS ACCUMBENS IN THE CODING OF REWARD ANTICIPATION AND MAGNITUDE

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According to human fMRI studies, reward prediction relies on fronto-striatal interactions involving the nucleus accumbens. As reward pathways are well conserved across species, they are an amenable substrate for translational research. However, no techniques at present allow the measurement of brain activation in freely moving animals in a manner homologous to human fMRI. In-vivo oxygen amperometry may help to bridge this gap by allowing real time monitoring of tissue oxygen changes in freely-moving animals. To demonstrate this, we investigated oxygen amperometric responses in the nucleus accumbens in rats performing a discriminative cue rewarded task. Rats were trained to discriminate between a discriminative cue (DS) which signalled the availability of a reward and a cue (NS) that led to no reward. Oxygen amperometric (O_2) responses were measured in the nucleus accumbens via carbon paste electrodes (i) after the acquisition of the task, (ii) during a reversal of cue contingencies and (iii) under different conditions of reward value and after prefeeding. During initial acquisition, animals learn to respond to the DS as they associate it with reward, while omitting responses to the NS. At this stage, an increase in the O_2 signal was only observed following correct responses to the DS. On the first day of cue reversal, animals pressed for both cues and the O_2 signal increased following both the current and previously rewarded cues. After the reversal was fully acquired, the O_2 signal increased again only in response to the DS cue. Under conditions of different reward values, Animals learn to discriminate between cues associated with small and large reward and the O2 signal increased only to the cue associated with larger reward. Prefeeding animals resulted in a decrease in lever response rate and no O_2 signal increase to any of the cues presented. Overall, these data suggest a role of the nucleus accumbens in both anticipation and magnitude coding of reward. Our data bear striking similarity to results obtained in human neuroimaging studies, suggesting that oxygen amperometry may be a valid surrogate for human fMRI, allowing novel avenues of translational research in the study of reward in disease states.

D10-105

SPATIAL LEARNING AND FEAR CONDITIONING IN gtf2ird1 KNOCKOUT MOUSE

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Williams-Beuren syndrome (WBS) is an autosomal dominant disorder, caused by a hemizygous deletion of 1.55 Mb on chromosome 7q11.23 spanning 28 genes. These candidate genes include a novel, three-member family of general transcription factors, one of which, GTF2IRD1 has been suggested to be linked to mild mental retardation and seriously deficient visuo-spatial abilities in WBS. Here we present data showing that neither homozygous (hom) nor heterozygous (het) gtf2ird1 gene deletion causes visuo-spatial learning and memory deficits in mice. Separate groups of gtf2ird1-manipulated mice were evaluated in tests measuring spatial learning and memory, a paddling Y maze and a swimming Y maze, and in a fear conditioning test measuring both contextual (hippocampus-dependent) and cued (amygdala-dependent) fear memory. There was no between-group difference in the number of correct arm choices in the paddling Y maze test. All groups improved their performance during six daily, 5-trial sessions; however, latency to escape from the water was shorter and speed was higher in wild-type animals (wt) compared to the mutant mice, and immobility was higher in hom animals compared to both the wt and het group. In the swimming Y maze there were no between group differences in the number of correct arm choices in three daily, 5-trial sessions, either during acquisition or reversal learning. Probe tests conducted 24 and 72 hours after the last reversal session showed no between-group differences in spatial memory. Neither latency to escape nor speed differed between the mutants and wt animals. In the contextual fear conditioning test, het animals displayed less freezing in the environment paired 24h earlier with electric stimulation (0.5 mA, 1s) compared to the wt group. In the cued condition, sound previously paired with the shock significantly increased freezing duration in all paired groups. There was no between group difference in the duration of freezing in the cued condition. Our results suggest that neither homozygosity nor heterozygosity for the gtf2ird1 has a major impact on spatial learning and memory, but may decrease hippocampus-dependent contextual fear conditioning in mice.

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D10-106

EARLY MATERNAL DEPRIVATION MODULATES DISTRIBUTION OF INTERLEUKIN-1 AND NMDA RECEPTORS AT THE SYNAPTIC MEMBRANE IN A SEX DEPENDENT MANNER

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Severe stress early in life induces changes in neuronal function, determining a different setting in synaptic organization, which could be implicated in promoting an adaptive response under physiological conditions and/or in stress-related disorders later in life. The pro-inflammatory cytokine Interleukin-1_ (IL-1_) has been recognised as a central regulator of stress responses. IL-1_ signal transduction in neurons occurs through the IL-1 receptor type I (IL-1-RI). We recently demonstrated in primary hippocampal neurons that IL-1RI is enriched at synaptic sites, where it co-localizes with, and binds to the GluN2B subunit of NMDA receptor (NMDAR) suggesting a functional interaction. In a model of maternal deprivation (MD), we investigated the expression and distribution at the post-synaptic site of IL-1RI, together with the GluN2A and GluN2B subunits of the NMDAR and the GluR1 and GluR2 subunits of the AMPA receptors in the hippocampus and pre-frontal cortex of male and female rats. A MD lasting 24h at PND9 significantly increases the levels of IL-1RI, as well as IL-1RI interaction with GluN2B, at the synapsis of hippocampal neurons at PND 45. The effect is sex-dependent, occurring only in male rats. No such alterations were observed in the prefrontal cortex as well as no enrichment of GluN2B and GluN2A at the synapse is evident in PND 45 MD rats. On the contrary, both GluR1 and GluR2 subunits of the AMPAR at the hippocampal synapse were reduced in 45 PND MD rats. These data reveal a profound modification in the receptors organization at the post-synapses induced by MD in male rats hippocampus, suggesting the setting for an immature synapse which possibly affects neuronal sensitivity to both IL-1_ and the glutamatergic neurotransmission.

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D10-107

SPATIAL LEARNING AND MEMORY DEFICITS IN PLB1$_{TRIPLE}$ MICE

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PLB1$_{triple}$ mouse represents a 3rd generation mouse model of Alzheimer's disease produced by targeted knock-in of single-copy mutated human APP and tau genes. This approach may help circumvent inconsistencies in gene copy number and phenotypes seen in models generated by multiple pro-nuclear injections. Here, spatial learning and memory of PLB1$_{triple}$ mice was assessed at different ages in both water maze and IntelliCage. Methods: Exp. 1: Naïve PLB1$_{triple}$ mice were tested in the open-field water maze (OFWM) at 4 and 12 months in a reference memory paradigm (4 trials/day for five days; ITI 30 min; WT n=16 (4m), n=15 (12m); PLB1$_{triple}$: n=16 each at 4 & 12m). Exp. 2: Longitudinal testing (WT n=14; PLB1$_{triple}$ n=25) at 4, 8 and 12 months took place in a second cohort using an 8-arm radial water maze with a 'trials-to-criterion' protocol (two consecutive trials with no more than two errors; three platform locations) followed by a probe trial (60s free swim) 1hr later. Reference (first entry into wrong arm) and working (re-entry error) memory were discriminated separately. Exp. 3: Spontaneous exploration and spatial learning were determined in the IntelliCage at 4 and 12 months (WT n=11 (4m), n=15 (12m); PLB1$_{triple}$ n=11 (4m), n=13 (12m). After two days of habituation – free access to water in all corners – a 1-day spatial training to the least preferred corner was conducted (trained corner). Results: In the OFWM, PLB1$_{triple}$ mice showed an age-dependent deficit in spatial acquisition training which was significant at 12 months ($P<0.05$). However, they attained asymptotic performance at the end of training. Conversely, in the RAWM, at all ages tested, no deficit was observed in acquisition learning; however, 12m old PLB1$_{triple}$ mice were impaired in short-term memory performance ($P<0.05$). In the IntelliCage, in both age groups tested, PLB1$_{triple}$ mice did not acquire a preference for the trained corner ($P<0.05$ cf. WT).
Conclusions:
PLB1$_{triple}$ mice present with progressive loss of spatial memory in-keeping with that observed in AD. Though this was a more subtle deficit than observed in some established transgenic models, single-copy PLB1$_{triple}$ mice represent a more physiologically relevant experimental model of AD.

D10-108

PREFRONTAL SYNAPTIC ABNORMALITIES IN A MOUSE MODEL OF HYPERPHENYLALANINEMIA

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Dendritic and spine alterations have been found in most genetic syndromes characterized by mental retardation, including phenylketonuria (PKU). Although PKU is the most common genetic cause of mental retardation, the cellular mechanisms underlying impaired brain function are still unclear. Using PAHenu2 mice (ENU2), the genetic mouse model of PKU, we previously demonstrated that high phenylalanine levels interfere during critical postnatal period with brain tryptophan hydroxylase activity by reducing the availability of serotonin (5-hydroxytryptamine, 5-HT), crucial for maturation of neuronal connectivity in the prefrontal cortex (PFC). Moreover, our previous studies showed neuromorphological alterations in medial PFC of adult ENU2 mice. Serotoninergic treatment during critical period of neurodevelopment (P14-21) improves deficient performances in spatial and object recognition and promotes spine maturation of pyramidal neurons in layer V of the prelimbic/infralimbic area of the PFC.

The role of 5-HT on synaptic plasticity processes in prefrontal cortical area is mediated in part by the activity of 5-HT2a receptors. We hypothesized that the dendritic spine alterations in ENU2 mice correlate with deficits of 5-HT2a receptors and of proteins involved in spine matuarationas well as PSD-95, a scaffolding protein, and neuroligins, cell-adhesion molecules.We reported reduction of 5HT2a and alterations of PSD-95 and neuroligins levels in the PFC of ENU2 mice. Altogether, our data suggest that morphologic alterations of dendritic spines in PFC of ENU2 mice depend on 5-HT brain deficits. In particular, 5-HT deficits reduced 5HT2a receptor levels and impair 5-HT2a interaction with important synapse-associated proteins, as well as PSD-95 and neuroligings. In conclusion, these results suggest new molecular targets for mental retardation therapy in PKU.

D10-109

BRAIN PATHOLOGY IN A MOUSE MODEL OF TYPE 2 DIABETES MELLITUS

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Diabetes is a well known risk factor for dementia and Alzheimer's disease. At present many clinical studies have shown a relationship between both illnesses, however it remains unclear whether there is a cause-effect association between both of them and how diabetes might be implicated in the onset and development of Alzheimer's disease. This study seeks to clarify these issues by characterizing central nervous system abnormalities in the leptin receptor null mice, a genetic model of type 2 diabetes mellitus also known as db/db mouse. Two key issues are studied in this model at 2.5 and 6 and months of age: 1- cognitive impairment in these mice, using the new object discrimination task and the Morris water maze test. Both approaches provide information regarding learning abilities as well as working, spatial and episodic memory, that are early affected in dementia, and 2- brain damage, including brain atrophy, and specific morphological alterations of selected relevant areas in learning and memory processes, such as cortex and hippocampus. We also assessed the number and extension of brain haemorrhages in both areas. We have observed that KO db/db mice present significant brain atrophy, when compared with wildtype littermates, that worsens with age, and that brain shrinkage seems to affect cortex and hippocampus sequentially. We also observe severe brain vascular pathology in KO db/db mice with a significant increase in haemorrhagic burden. Altogether our data may set the basis to discern whether specific central nervous system alterations in a type 2 diabetes mellitus animal model can predict the appearance of cognitive alterations underlying the cognitive decline observed in dementia and Alzheimer's disease.

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D10-110

CHOLINERGIC DENERVATION WORSENS BEHAVIOURAL IMPAIRMENT IN APPSWE/PS1DE9 MICE

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Alzheimer's Disease (AD) is a neurodegenerative disease characterized by progressive cognitive and memory impairment. Amyloid-beta (Aß) deposition, as senile plaques (SP), seems to play a key role in the development and progression of the illness. Moreover SP tend to accumulate in cortex and hippocampus, relevant areas in learning and memory. On the other hand neuronal loss, especially relevant in the cholinergic system, is the pathological feature that best correlates with duration and severity of the illness. In the present work we used APPswe/PS1dE9 mice and we assessed the effect of a selective cholinergic lesion of the basal forebrain on learning and memory abilities. We lesioned APPswe/PS1dE9 mice, which profusely deposit Aß as SP by 6 months of age, with murine p-75 saporin, an inmunotoxin that selectively removes cholinergic innervation. We performed intracerebroventricular murine p-75 lesions in animals with an incipient (~3 months) and robust (~7 months of age) Aß deposit and removed ~50% basal forebrain cholinergic innervation to cortex and hippocampus, structures significantly affected in AD and implicated in learning and memory. We observed an increased SP deposition, in vivo and in real time, using multiphoton microscopy as soon as 1 week after the lesion. We corroborated these data with post-mortem inmunohistochemistry for Aß and Aß fibrils. 7 days after the surgery, when the lesion is established, animals were tested in the new object discrimination test and the Morris water maze test. As expected we observed an early memory impairment in young mice (~3 months) and an age dependent evolution that worsened with age, when Aß is more robust (~7 months of age). We further observed significantly worse learning abilities in transgenic lesioned mice when compared with the rest of the groups, suggesting a synergic effect between cholinergic denervation and Aß deposition. Altogether our data suggest that cholinergic denervation may synergically contribute to cognitive impairment observed in AD.

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D10-111

ASSOCIATIVE LEARNING CAPABILITIES OF THE *TAMBALEANTE* MOUSE

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Tambaleante (tbl) recessive mutation affects cerebellar Purkinje cells, leading to its disappearance (Wassef y cols., 1987). The degeneration of Purkinje cells begins from the second month of life, date from which Purkinje cells number decreases dramatically. The mutation causes a severe ataxic syndrome (Wassef y cols., 1987, Rossi y cols., 1995), so that homozygous mutant mice (tbl/tbl) show evidence of tremor, unstable gait and abnormal hindlimb posture. However, the motor phenotype of this mutant mouse is not completely understood. The fact that tbl mutation could only affect to cerebellar Purkinje cells makes it a perfect model for studying the cerebellar involvement in several motor learning tasks. The behaviour and motor learning abilities of three-month old wild-type and tbl/tbl mice were studied by using different motor and associative tasks (fall, horizontal bar, ladder, rotarod, etc.). Wild-type and tbl/tbl mice were also studied in order to determine whether the mutation is associated with other behavioral problems, such as analgesia, deafness, impaired spatial learning, etc. Our preliminary data show that motor coordination problems caused by Purkinje cell loss of the tambaleante mouse did not affect its learning capabilities. Presents results are quite similar to those obtained in Lurcher mutation (Porras-García et al, 2005; 2010), and reinforce our hypothesis that cerebellum interferes on learning processes by its motor deficiencies rather than by acting on the learning capabilities itself.

D10-112

CEREBELLAR TRANSPLANTATION AND MOTOR SKILLS IN LURCHER MICE

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Lurcher mutant mice represent a natural model of olivocerebellar degeneration. They can be used to investigate effects of experimental therapy of the degeneration. Lurchers suffer from cerebellar ataxia deteriorating their motor functions. The aim of the work was to assess the effect of the transplantation of embryonic cerebellar tissue into the cerebellum of Lurcher mice. Adult Lurcher mice of the B6CBA strain were used. The cerebellar tissue was obtained from mouse embryos (E12) without the Lurcher mutation and administered into the cerebellum of host mice as solid pieces or as a cell suspension. 2 months after the surgery motor skills were examined with the suspension wire, rotarod and wooden beam test repeated for 3 days and compared with those in untreated Lurcher mice. In the suspension wire and rotarod test no significant differences between treated and control mice were observed. In the wooden beam test only mice treated with the solid graft reached longer fall latencies on the second day compared with control mice. Mice treated with cell suspension showed significant increase of their fall latencies between the first and the third day of the test on the rotarod and wooden beam while animals that received solid graft and control mice did not change their performance significantly in the course of the experiment. There were only weak effects of the embryonic cerebellar grafts in Lurcher mice. The only marked positive effect was enhancement of motor learning in animals treated with the embryonic cerebellar cell suspension.

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D10-113

THE BEHAVIOURAL IMPAIRMENT IN OLD MICE DECREASES WITH HORMESIS AND HYDROTHERAPY INTERVENTIONS

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The physiological impairment in the aging process affects especially to the homeostatic systems such as the nervous system and the age-related changes of the nervous system functions are reflected in behavioural alterations. Previous studies have shown that several lifestyle strategies, such environmental enrichment (EE), improve nervous system functions and behavioural parameters. The aim of the present work was to study the effects in old mice of two lifestyle strategies: a hormetic intervention with slight infections and a new type of EE, hydrotherapy, on several behaviour parameters. Two groups of old female ICR-CD1 mice as well as an adult group (55_1 weeks of age; age control group: ACG) were used. Several behavioural tests were performed in these animals to determine their motor coordination, muscular vigour, traction capacity and exploratory behaviours, both horizontal activity (total and internal deambulation) and vertical activity (percentage of mice performing rearing and total number of rearings). The wood-rod, tightrope, corner, open-field, hole-board and T-maze tests were used. In a group of old mice a hormesis intervention was carried out. Animals at 55_1 weeks of age received an i.p. injection of 0.1 mg/Kg of Lyppopolisaccharide from Escherichia coli (old hormetic group: OHG) or PBS (old control hormetic group: OCHG) during 2 months with an interval of 15 days. When the animals were old (84_1 weeks) all the behavioural tests mentioned above were performed. In other group of old mice, animals at the age of 76_2 weeks received a hydrotherapy treatment. They were bathing in warm water (37ºC) 15 minutes, five sessions per week during 2 weeks (old bathing group: OBG) or were not submitted to a bath (old control bathing group: OCBG). After these two weeks, all animals performed the behavioural tests mentioned above. The results show an improvement in OHG and OBG mice of motor coordination, muscular vigour, traction capacity and exploratory parameters compared with their corresponding control groups (OCHG and OCBH), and in some cases, reaching similar values to those obtained in ACG mice. In conclusion, both hormesis and hydrotherapy interventions could be two possible strategies to “rejuvenate” the behavioural response in old mice, decreasing age-related impairment of the nervous system. Support: MCINN (BFU2008-04336), UCM (910379ENEROINN), Fundación Mutua Madrileña and RETICEF (RD06/0013/0003).

D10-114

MELATONIN AND PHYSICAL EXERCISE INDUCE SYNERGISTIC NEUROPROTECTION IN THE 3XTG-AD MOUSE

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Alzheimer’s disease (AD) is a devastating age-related neurodegenerative disease with no specific treatment at present. Several healthy lifestyle options and over-the-counter drugs that it has been suggested delay the onset of the disease are in an experimental phase, but it is unclear whether they will have any therapeutic value against AD. We assayed physical exercise and melatonin in 3xTg-AD male mice aged from 6 to 12 months, therefore from moderate to advanced phases of AD pathology. Analysis of behavior and brain tissue at termination showed differential patterns of neuroprotection for the two treatments. Melatonin was effective against the immunosenescence that 3xTg-AD mice present. Voluntary physical exercise protected against behavioral and psychiatric symptoms of dementia such as anxiety, a lack of exploration and emotionality. Both treatments protected against cognitive impairment, brain oxidative stress and a decrease in mtDNA. Interestingly, only the combined treatment of physical exercise plus melatonin was effective against the decrease of mitochondrial complexes and synaptic status markers. Therefore, melatonin plus physical exercise exerted complementary and synergistic effects against disturbances present in AD.

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D10-115

ZINC DIETARY SUPPLEMENTATION ALTERS BEHAVIORAL AND BIOCHEMICAL PROFILES IN HIGH FAT DIET EXPOSED ADULT MICE

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High fat diets (HFD) induce metabolic dysfunction leading to atherosclerosis , fatty liver disease hormonal impairment and mood disorders. Zinc , the essential trace element and participant in many CNS and PNS functions, has proved to protect tissues from metabolic distress, mainly, via antioxidative procedures. The present study aims first to evaluate the role of HFD on specific behavioral and biochemical aspects and second to investigate the impact of dietary supplementation of Zinc on high-fat diet-induced distress. Male C57B6/J mice, age matched, were divided in the following groups: control group-CD (AIN-93G, 30 mg Zn/kg), HFD30 (ZC-HF Zn supplemented diet 30 mgZn/kg, 55% calories from fat, Mucedola Co.), HFD300 (ZS-HF, Zn supplemented diet 300 mgZn/kg, 55% calories from fat, Mucedola Co,). All groups started their diets from 4 weeks of age. Body weight was registered once per week. During adulthood, behavioral responses such as novelty reaction, habituated open field activity, center/periphery preference, object recognition and “depressive-like behavior” were assessed in all mouse groups. ^{1}H NMR-basal lipidemic analysis were also performed in plasma samples of the animals engaged in the experiment. HF diet induced an increase in BW as compared with control diet in mice. HFD mice did not display any statistically significant difference in the habituated open field activity as compared to controls. Interestingly, HFD mice displayed an increased tendency of higher reaction to novelty and a higher preference to periphery as compared to CD mice. Additionally, HFD induced an impaired ability to recognize a novel object as compared with CD. Interestingly, supplementation of zinc reversed the aforementioned behavioral alterations. Findings from the ^{1}H NMR-basal lipidemic analysis of plasma samples support the protective role of Zn in mice exposed to oxidative procedures due to HFD. Our results show that HF diet induced behavioral alterations that are linked to response to stress, stress coping strategies and non- spatial memory performance along with respective metabolic alterations in adulthood. Supplementation of Zn reversed most of the observed alterations, indicating a role of Zinc in emotional/anxiety state and in memory/learning procedures as well.

PHARMACOLOGY AND BEHAVIOUR: D10-116

D10-116

INCREASES OF GLUTAMATE AND GABA LEVELS IN MEDIAL PREFRONTAL CORTEX AFTER ELECTRICAL STIMULATION OF THE PARAFASCICULAR THALAMIC NUCLEUS: AN IN VIVO MICRODIALYSIS STUDY

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The centromedian-parafascicular complex (CM/Pf) in primates or parafascicular nucleus (Pf) in rodents is a posterior intralaminar nucleus (pIL) of the thalamus related to the generation of cortical activation and maintenance of states of consciousness underlying attention, learning and memory. Previous research in humans has suggested that electrical stimulation of CM/Pf may be a useful approach to assisting recovery from severe brain injury. In rats, post-training Pf stimulation has been shown to enhance performance in learning and memory tasks. Therefore, CM/Pf stimulation has been proposed as a method of potentiating cognitive functions, based on its influence on distributed neural networks involving frontal cortex and basal ganglia. The primary expected effect of electrical stimulation of Pf nucleus is depolarization of target cortical neurons, particularly in prefrontal regions, such as the medial prefrontal cortex (mPFC). We used in vivo microdialysis in freely moving Wistar rats to investigate whether electrical stimulation of the Pf affects glutamate release in the mPFC. In addition, the levels of the gamma-aminobutyric acid (GABA) have also been analyzed to elucidate the specificity of electrical stimulation treatment. The stimulation parameters used were similar to those that in previous reports facilitated retention of an avoidance learning task, and neurotransmitters release was determined as a function of stimulation frequency and intensity. During the microdialysis session, and after a 4-h equilibration period, 4 consecutive microdialysates in 10-min intervals were collected for baseline sampling. The concentration of glutamate and GABA was determined using capillary zone electrophoresis with laser-induced fluorescence detection. The results demonstrated that different pulse frequencies of Pf electrical stimulation (50, 100 and 200Hz) had different effects on glutamate and GABA release. Stimulation-induced release was higher at low frequencies (50Hz). Such findings indicate that the Pf modulates glutamate and GABA systems in the mPFC. Therefore, the contribution of the Pf in learning and memory may be linked to its role in the modulation of cortical activity, which in turn may enhance arousal and thereby improve stimuli encoding and sensory-associational information processing.

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Abstracts Posters

SUNDAY September 11th, 2011

D11-1

NEUROANATOMICAL SUBSTRATE TO ASOCIATE ODORANTS AND PHEROMONES IN MICE

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Non-volatile stimuli, like some pheromones, are essential to properly perform social and reproductive behaviors. Pheromones are mainly detected by the vomeronasal organ, while volatiles activate the olfactory epithelium. Each one projects to the accesory olfactory bulb (AOB) and main olfactory bulb (MOB) respectively. AOB and MOB efferents have been traditionaly believed to innervate non-overlaping regions of the amygdala and olfactory cortex. Recent studies carried out in rats and scattered data available in mouse indicate convergence of vomeronasal and olfactory projections in the amygdala. This structure has been proposed as the area where emotional learning take place, and in particular to mediate the asociation of volatile odorants and non-volatile pheromones. The aim of this work is to re-investigate the projections of the olfactory bulbs in mice and its putative convergent pathways to the amygdala, to identify possible chemosensory asociative areas. To this aim, we performed iontophoretic injections of dextranamines in the AOB and MOB, and studied the resulting anterograde transport. In one restricted injection in the AOB, we observed labeling in zones previously described as vomeronasal recipients: anterior amygdala (ventral, AAV, and dorsal, AAD), medial amygdala (anterior, MeA, and posterior MeP), posterior medial nucleus of stria terminalis and posteromedial cortical amygdala. In another injection, not absolutely restricted we distinguished labeling in the bed nucleus of the accesory olfactory tract. Moreover we observed fibers and varicosities in the ventral aspect of the piriform cortex (Pir), cortex-amygdala transition zone (CxA) and anterior cortical amygdala (Aco). The injection obtained in the MOB corroborated the previously observed labeling in areas described as olfactory recipients: Pir, olfactory tubercle, CxA, ACo and posterolateral cortical amygdala. In addition, we observed fibers and varicosities in the AAV and MeA. These results confirmed some convergent areas described in rats and mice by other groups. The labeling found in the amygdala originated by the projections from AOB and MOB, points to possible secondary asociation areas (AAV, CxA, ACo and MeA) directly receiving olfactory and vomeronasal information. To understand the functional role of these amygdaloid structures in olfactory-vomeronasal associative learning, we plan to lesion these convergent areas and study the behavioral consequences in chemosensory learning.

D11-2

A TANDEM AFFINITY TAG APPROACH TO UNCOVER NOVEL INTERACTIONS WITH THE SYNAPTIC PROTEIN, Arc/Arg3.1

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Arc/Arg3.1 is an immediate-early gene whose mRNA is rapidly transcribed, transported to dendritic processes, and locally translated in response to synaptic activity. Arc/Arg3.1 has been mostly implicated in its critical role in hippocampus-dependent long-term memory formation and in the ability of synapses to undergo long-term changes in efficacy, a process known as synaptic plasticity. More specifically, sustained Arc/Arg3.1 synthesis is required for the consolidation of long-term potentiation (LTP) by remodeling of the actin cytoskeleton at the synapse. It is also involved in long-term depression (LTD) by interacting with components of the endocytic machinery (dynamin-2 and endophilin 2/3), which leads to the internalization of surface AMPAR-type glutamate receptors. Despite this knowledge, the precise molecular function of Arc/Arg3.1 protein remains unclear. Identification of novel protein-protein interactions with Arc/Arg3.1 could reveal significant information concerning its cellular pathway, and thus about memory and even associated diseases. To identify Arc/Arg3.1's binding partners, we used Arc/Arg3.1 doubly-tagged with the His tag and glutathione s-transferase (GST) tag. The His tag was exploited in the purification of the bait protein and GST was put to use in GST pull-down experiments. Here we designed a customized protocol for efficient production of the GST-Arc-His bait employed in pull-down assays. Using this enhanced protocol, we are currently performing pull-downs using lysates from various preparations and identifying the proteins via mass spectrometry. These findings are of great interest, as even a single interaction discovery could provide significant insight into how Arc brings about responses which lead to LTP and/or LTD.

D11-3

DRG NEURONS AND PAIN SENSATION IN RELATION TO STRESS PROTEINS

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Dorsal root ganglia (DRG) neurons transmit, from body periphery, sensory information including pain stimuli to the sensory cortex. Stress proteins like heat shock proteins 70 (Hsp70) and metallothioneins 3 (MT3) are considered to initiate protective cell procedures against thermal and other noxious stimuli. The present study aims to investigate whether certain DRG neuronal characteristics and pain sensation are modified in mice overexpressing human Hsp70. Male C57B6/J mice, age matched and divided in 2 groups:1. control wild type group-Wt and 2. transgenic overexpressing hHsp70 group –Tg , were employed in order to study the nociception profile. Open field activity was evaluated in both mouse groups in order to exclude any interference of motor activity in the nociceptive thresholds of Wt and Tg respectively. Hot plate and tail flick test procedures were conducted in both mice groups. Each analgesia-related test was registered once per week, for a period of 2 weeks. Subsequently the animals were killed according to the care guidelines of EC for animal euthanasia (2007/526/EC) and the DRGs were carefully removed and sectioned in a Leica CM1850 cryostat. Immunohistochemically treated slices for Hsp70 and MT3 localisation were observed under a Nikon Eclipse luminescence microscope. Our results have shown that withdrawal latency in both hot plate and tail flick tests was higher in Tg as compared to Wt mice.($p<0.01$; $p<0.01$ respectively). Interestingly, open field experiments have shown that Tg mice were not less active than Wt controls. The immunohistochemical observations showed altered MT3 cell staining in DRGs of Hsp70-overexpressing mice compared to Wt mice. Our results have shown that Tg displayed enhanced nociceptive thresholds, an effect that underlines the protective role of hHsp70 in pain sensitivity. Additionally, the role of the altered MT3 staining on the pain sensitivity of Tg mice cannot be excluded since MT3s are anti-stress proteins and their induction could be modified by the expression of hsp70. Finally our findings further contribute to the concept related to the protective role of Hsp70 against noxious stimulus.

D11-4

EFFECT OF LOCUS COERULEUS ACTIVATION ON STATE-DEPENDENT WHISKER-EVOKED RESPONSES IN BARREL FIELD: INSIGHTS FROM CURRENT SOURCE DENSITY ANALYSIS

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Cortical evoked response can markedly vary across presentation of identical sensory stimuli. Spontaneous subthreshold fluctuations of the membrane potential of cortical neurons are thought to underline this variability. During sleep or under anesthesia the activity of cortical neurons is highly synchronized. Their membrane potential fluctuates between de- and hyperpolarized levels, also known as UP/DOWN states. Previous studies have shown that such intracellular states can be predicted by the local field potential (LFP) and multi unity activity (MUA). This study examined the effect of LC electrical microstimulation on whisker-evoked responses in barrel cortex of urethane anesthetized rats by analyzing sensory response during predicted UP or DOWN states. LFP signal was recorded from 32-channel microelectrode array with 50 microns interchannel distance and Current Source-Density (CSD) profiles were derived. After deflection on and offset of principle whisker (2 mm, 200 ms) current sinks we generated in layer IV of the corresponding barrel field, reflecting thalamic input. The dynamic of current flow markedly differed between UP and DOWN states. Deflection onset produced high amplitude (0.19 ± 0.1 mV/mm^2) and long lasting current sink during DOWN state, while during UP state current sink was significant smaller (0.07 ± 0.2 mV/mm^2) and followed by a long lasting reversion of polarity (100-120 ms). LC stimulation resulted in a systematic shift of cortical LFPs from a synchronized to a desynchronized state. We used trains of biphasic square pulses 0.5 ms, 100 mA, 5 pulses at 100 Hz. The desynchronization was transient and relatively short-lasting. 3 trains (250 ms inter-train interval) produced ~1 sec desynchronization. CSD analysis showed that the cortical response profile followed by a priming LC stimulation was similar to such during UP state. Our results demonstrate that LC electrical stimulation alters the dynamics of cortical network as reflected in LFP signal. Moreover, LC discharge and accompanying noradrenaline (NE) release from the terminal fields of LC-NE neurons may shift the membrane potential of somatosensory neurons toward threshold level. This is consistent with previous observations that LC activation facilitates phasic response of sensory neurons in primary somatosensory cortex. We conclude that the smaller amplitude of current sink during UP state and after LC activation is result of a smaller driving force of the network at the moment of sensory input, and it is not due reduction of synaptic input to the somatosensory network.

D11-5

ROLE OF WHISKERS IN COMPENSATION OF VISUAL DEFICIT IN A MOUSE MODEL OF RETINAL DEGENERATION

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Lurcher mutant mice of the strain C3H suffer from the olivocerebellar degeneration that is manifested by cerebellar ataxia and impairment of cognitive functions. Wild type littermates of these mice serve as healthy controls. Moreover, some of the C3H strain mice are afflicted with retinal degeneration which leads to a massive extinction of retinal photoreceptors. Our previous experiments revealed that the retinal degeneration does not influence motor skills, gait control and spontaneous behavior regardless of the presence of the cerebellar degeneration. From these findings, a question about the role of whiskers in compensation of the visual deficit arose. Our aim is to investigate the effect of the absence of tactile stimuli mediated by whiskers in both seeing and blind animals on motor skills, spontaneous motor activity, gait control and CNS excitability. Here we present our experiments with the wild type mice with the intact cerebellum. Three months old mice were used. Whiskers had been cut regularly from the 2nd postnatal week. The mice were subjected to a standard battery of motor tests: rotarod, beam-walking test and coat hanger test. For gait analysis the CatWalk system was used. Spontaneous motor activity was tested in the open field using the EthoVision system. The method of audiogenic epilepsy was applied to test CNS excitability. The reduction of tactile information due to the absence of whiskers from the early postnatal life lead in the blind mice to the following significant effects: worsening of performance in rotarod test and beam-walking test, increase in the time spent in the central zone of the open field, changes in some gait parameters and increased CNS excitability. In the seeing mice, only insignificant changes in the rotarod test and in CNS excitability were observed. We conclude that the visual deficit due to the retinal degeneration is markedly compensated by tactile inputs from the whiskers. In spite of the fact that vision in not the primary sense in mice, vision itself is efficient for execution of motor tasks. The interesting question of whether this compensatory effect of the whiskers can be influenced by the neurodegenerative disorder in the Lurcher mutant mice is already being addressed in our laboratory.

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D11-6

THE EXTERNAL LATERAL PARABRACHIAL SUBNUCLEUS IN RELATION TO FEEDING INDUCED BY PARTIAL WITHDRAWAL OF GASTRIC FOOD CONTENTS

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Sensory information from the gastrointestinal tract appears to be an essential neurobiological mechanism involved in satiation and meal size control. These afferent signals seem mainly to be processed via the vagus nerve, which projects to the intermediate-caudal part of the nucleus of the solitary tract and later to the parabrachial complex, including the external lateral subnucleus (PBLe). With this background, the goal of our study was to examine the relevance of this subnucleus in food satiation. For this purpose, we analyzed the intake of PBLe-lesioned and control animals following the partial withdrawal of gastric food contents, done shortly after completion of an initial meal (satiation). Unlike the non-lesioned animals, which consumed around the same amount of food as had been removed and maintained a similar meal size, PBLe-lesioned rats were unable to regulate or compensate for the food pumped out and consumed a lower amount of food than had been withdrawn post-satiation. These data suggest that the external lateral parabrachial subnucleus may critically participate in and form part of the neurobiological system involved in satiation control.

D11-7

THE COCHLEAR ROOT NEURONS AND THE CAUDAL PONTINE RETICULAR NUCLEUS PARTAKE IN THE AURICULAR REFLEX OF THE ACOUSTIC STARTLE REFLEX

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The auricular reflex, as a part of the acoustic startle reflex (ASR), is a compensatory ear movement which occurs by fast contraction of the ear muscles when an intense and unexpected stimulus is presented. Movement of the pinna profoundly changes sound location performance orienting ears towards the acoustic startle stimulus, and hence, plays a role as survival mechanism. This reflex is triggered by the medial part of the facial motor nucleus (Mot7), which receives inputs from two essential nuclei of the primary ASR circuit: the caudal pontine reticular nucleus (PnC) and the cochlear root nucleus (CRN). Both nuclei send short latency hearing information, which is consistent with the extraordinary short latency observed in the auricular reflex. To determine the role of PnC and CRN inputs in the auricular reflex, we recorded electromyographic activity in the ear muscles during the ASR tests and after selective-chemical lesions in the auditory area of the PnC. As control of the lesion in the PnC, we performed double tract-tracing experiments, placing an anterograde neurotracer in the PnC and a retrograde neurotracer in the ear muscles. Our results showed that the auditory area of the PnC, which innervate auricular motoneurons, is fundamental for triggering the auricular reflex in the ASR. In the injured animals, the ASR was dramatically decreased. Nevertheless, even large lesions of the PnC still evoked a slight electromyographic activity in auricular muscles. Such a slight activity might be attributed to the direct neuronal connection between the CRN and auricular motoneurons.

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D11-8

THE ATTENTIONAL COMPONENT IN PREPULSE INHIBITION

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The startle reflex (SR) consists of a set of reflexive, involuntary responses to a sudden, intense stimulus. One of the modifications of the startle reaction is the Prepulse inhibition (PPI) that occurs when the startling stimulus is preceded by a prepulse, and is considered to provide an operational index of sensorimotor gating. A variant of the PPI is modification of the SR is the prepulse facilitation (PPF) that occurs when the startling stimulus is preceded by a prepulse by 4500 ms PPF has been suggested to reflect sustained attention or sensory enhancement linked with modality-specific selective attention. A commercial human startle response monitoring system (EMG Human Startle-SR Lab, San Diego, CA) was used for the acoustic startle stimuli and for the recording of the electromyography (EMG) activity from the onset of the stimulus. Stimuli were presented to participants binaurally through headphones (SONY) while they were sitting in a moderately lit soundproof room. The eye blink component of the startle response was indexed by recording EMG activity of the orbicularis oculi muscle by positioning two miniature silver/silver chloride electrodes filled with electrolyte paste directly beneath the right eye. Participants received 118 startle stimuli in all. One hundred and eight trials, in three blocks of 36 trials each, followed the initial pulse-alone trial. There was a range of prepulse to- pulse intervals (prepulse onset to pulse onset) to elicit PPI (from 30 to 480 ms) and PPF (from 1000 to 6000 ms). The present study examined the roles of sex found in sensorimotor gating by examining PPI and PPF in young women with age-matched men. Our results show that prepulse inhibition (PPI) of the startle response is sensitive to sex, with healthy young women showing less PPI compared with age-matched men in all the interstimulus intervals studied. An opposite pattern of effects was found for PPF men showing less PPF. Sex differences in human sensorimotor gating might represent a general downshift in the inhibition curve and upward shift in the facilitation curve in women compared with men.

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D11-9

CHANGES IN THE REPRESENTATION OF INDIVIDUALLY DISTINCTIVE COMMUNICATION SOUNDS IN THE SONGBIRD AUDITORY FOREBRAIN

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Songbirds provide a useful model for studying the neural code underlying the perception of acoustic communication signals. They rely on auditory processing of vocalizations for a number of social behaviors, such as pair-bonding. Vocalizations, songs as well as calls, are multiple cue signals that may convey information about the identity of the bird. An avian brain nucleus that is analogous to the mammalian secondary auditory cortex (the caudo-medial nidopallium or NCM) has recently emerged as part of the neural substrate for sensory representation of conspecific vocalizations. This led us to investigate whether, in the zebra finch, NCM neurons could contribute to the discrimination among vocalizations that convey information about the individual identity of the bird. We focussed on the long distance call. Females can indeed identify their mates on the basis of this call alone. We examined whether NCM neurons in paired females showed a preference for the mate's call over familiar or unfamiliar calls. To this end, adult female zebra finches (n=12) were paired for two months in the aviary while other females (n=5) remained unpaired. Three days prior the electrophysiological investigation, each pair was placed in another cage that allowed visual and acoustic contact with another pair. As a first step, single-unit recordings were performed in both paired and naive anesthetized females. Then, by using a telemetric device, we collected multi-unit responses in freely behaving paired females (n=8). Results indicated that, in both anesthetized and awake paired females, neurons exhibited auditory responses of greater magnitude to either the mate's call or the call of the familiar male than to the unfamiliar call, with no difference between the mate's call and the familiar one. In contrast, no such differential responsiveness was observed in naive females. Also, more cells showed highly selective responses in mated than in naive females suggesting that experience-dependent plasticity in call-evoked responses resulted in enhancing auditory stimuli discrimination. Therefore, the whole set of results provides evidence for major changes in representation of natural vocalizations in NCM within the context of individual recognition.

D11-10

COUPLING BETWEEN EYE AND HAND MOTOR SYSTEMS: A TRANSCRANIAL MAGNETIC STIMULATION (TMS) STUDY

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A tight motor coordination of eyes and hand is mandatory for accurate interactions with objects. Our previous TMS studies showed excitability changes in the corticospinal system (CSS) of the relaxed upper-limb when visual stimuli are targeted by eyes alone. This demonstrates that both systems are activated even when the motor response involves only one effector. We investigated the nature of this coupling by conducting two experiments to assess whether CSS changes are induced whenever a shift of spatial attention is occurring, or are tied to the actual execution of an eye movement. In Experiment 1 (27 participants), the colour of a peripheral stimulus randomly commanded either the execution of a prosaccade, or the maintenance of central fixation. In Experiment 2 (29 participants), stimulus colour determined whether to perform a prosaccade or an antisaccade. A single-pulse TMS was applied on the left motor cortex and motor evoked potentials (MEP) were recorded in three muscles of the contralateral relaxed upper-limb: first dorsal interosseous (FDI), abductor digiti minimi (ADM), extensor carpi radialis (ECR). TMS was randomly delivered before (baseline) or at a variable delay (within 1 s) after the onset of the peripheral stimulus. Experiment 1 showed that CSS excitability did not change in the absence of eye movements. Conversely, direction-dependent modulations of MEP amplitude were found in FDI 120 ms after saccade onset. In Experiment 2, no changes in CSS excitability were observed in antisaccade trials. Instead, a generalized facilitation turned to a long-lasting inhibition in all muscles, in correspondence of prosaccade occurrence. Furthermore, direction-specific changes were observed in FDI and ECR 480 ms after saccade onset. Results reveal that covert shifts of attention are not sufficient to trigger a sub-threshold motor plan in the relaxed upper-limb. CSS excitability changes require that a saccade is actually performed towards a peripheral stimulus and are not elicited when eye movements are driven by cognitive factors, in the absence of a visual target (antisaccade). We can surmise that task familiarity and stimulus-response compatibility determine whether a motor coupling of the two effectors has to be switched on. Moreover, even in prosaccade trials the coupling between eye and hand motor systems in not fixed, but depends on the motor set determined by the task.

D11-11

EFFECTS OF ANODAL AND CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCs) ON SENSORY EVOKED POTENTIAL OF ALERT RABBITS

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Although the effects of transcranial direct current stimulation (tDCs) on the excitability of central nervous system were discovered long time ago, it is only in recent years that the clinical use of this non-invasive technique has increased exponentially. However, little is still known about the mechanisms underlying the neuromodulatory effects observed after tDCs application. The aim of this work was to test the effect of tDCs on somatosensory (SS) local field potentials (LFP) evoked by contralateral whisker stimulation in behaving rabbits. Three male rabbits were prepared for chronic tDCs stimulation and recording of LFPs in the SS cortex. Once LFPs were established for a particular whisker pad region, air pulses were delivered every 10 ± 3 s before, during, and after tDCs application. tDCs stimuli were applied through four silver ball electrodes placed above the skull (targeted active electrode) and a saline-soaked sponge attached to the contralateral ear (targeted counter electrode). Anodal and cathodal stimulation were performed at different current intensities for 100 s to test the direct effects, and at 1 mA during 20 min to see after-effects on SS LFPs. Paired pulse stimulus applied to the ipsilateral ventroposterior medial (VPM) nucleus of the thalamus were used to determine whether presynaptic processes could be affected by anodal or cathodal tDCs. During anodal and cathodal tDCs application, significant differences were observed in evoked LFP amplitude (at 0.5, 1, 1.5 and 2 mA), integrated area (at 1, 1.5 and 2 mA) and duration (at 1.5 and 2 mA) between these two conditions. Anodal current induced an increase in amplitude, whilst cathodal current induced a decrease. Regarding after-effects, only cathodal current effects persisted for more than 30 min after application, whereas no persistent changes were observed after anodal stimulation. Paired pulse test indicated that anodal or cathodal tDCs modulated and even reversed the paired-pulse relation suggesting that tDCs modify thalamo-cortical synapses at presynaptic sites. These results demonstrate for the first time tDCs effects on intracortical LFPs in behaving animals and suggest that presynaptic mechanism seems to be involved. This new model brings the possibility to go forward on the study of neuronal mechanisms involved in tDCs neuromodulatory effects, and represents a valuable tool for the study of tDCs effects on behavioral tasks.

D11-12

STRATEGIC FILTERING: BEHAVIORAL EVIDENCE FOR A SUPRAMODAL MECHANISM

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Spatial attention, a key mechanism mediating interactions between humans and the environment, relies on both stimulus-driven and top-down mechanisms. A wide literature investigates attentional processes by means of target-distracter discrimination tasks, primarily in the visual and, recently, in the tactile modality. Nevertheless, the effect exerted by a potential, yet absent, distracter has rarely been assessed. The aim of our study is to focus on this aspect of strategic top-down attentional control processes in the tactile modality. We suggest that, when an endogenous filtering mechanism is engaged to cope with potential distraction, this might result in a cost regardless of the actual presence of distracters. In our experiments, we introduce a novel approach, whereby we focus our analysis on distracter-free trials in a speeded tactile discrimination task. We present a series of four experiments in which different manipulations of the context, such as distracters' probability, task relevance, and sensory modality, were adopted. Results clearly highlight a cost of a potentially distracting-context, in terms of higher reaction times, in no-distracter trials. The robustness of this effect is proven by its persistence across different manipulations of the context. Moreover, the cost of potentially distracting contexts in no-distracter trials is independent of the presence/absence of a distracter in the previous trial, suggesting a general, rather than contingent, underlying mechanism for the strategic filtering of potential distraction in the human brain. These results are consistent with the hypothesis that a supramodal monitoring and filtering system is engaged whenever potential distraction is foreseen. Although its activation is indisputably beneficial when distraction occurs, it leads to robust costs when distraction is actually expected but currently absent.

D11-13

PERCEPTION CODING OF THE PINEAPPLE "ACCORD" AND ITS COMPONENTS: FROM PERIPHERY TO BEHAVIOR

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A fascinating property of the sense of smell is that odor mixtures often have distinctive emergent qualities, and their individual components are consequently difficult to identify. Here, we make the hypothesis that the emergence of a new quality of an odor mixture is initiated from the peripheral olfactory mucosa. In order to test our hypothesis, "the blending mixture perception" was studied in the Rat at the peripheral and behavioral level. To this aim, single olfactory receptor neurons (ORN) responses were electrophsiologically recorded in response to (1) the binary ethyl maltol (Emalt) + ethyl isobutyrate (Eiso) mixture from which emerge the pineapple fragrance and (2) each of the molecules. Amplitude of the ORNs responses was plotted as a function of concentrations and the curve obtained for the mixture showed a clear dominance of Eiso or a suppressive or an amplifying effect of Emalt regarding the response to Eiso when used alone; these 3 effects being equally observed. For the behavioral study, animals were submitted to a conditioned odor aversion (COA) paradigm consisting of the association between Emalt or Eiso (conditioned stimuli) and the administration of a gastric malaise (0.15 M Lithium chloride i.p. injection). The conditioned aversion to Emalt or Eiso was assessed by presenting successive discriminative two-bottle tests during which the animals had to choose between the conditioned odor versus the mixture Emalt+Eiso. The results showed that animals conditioned to Eiso showed a clear aversion to the mixture suggesting an elemental strategy that corresponds to the detection of one component of a mixture in order to avoid it. By contrast the animals conditioned to Emalt failed to develop a clear aversion to Emalt thus rendering the absence of conditioned Emalt+Eiso aversion difficult to interpret. Our results obtained at the cellular level showed that the pineapple "accord" induced a remarkable ratio of synergy which may sign an "accord" specificity. At the behavioral level, our data suggest that animals developed an elemental strategy coding thus rendering possible the detection of the Eiso in the pineapple "accord". The status of Emalt needs to be precised using other types of conditioning which will use rather reinforcement. As a conclusion even in "accord" the different components can present different status regarding discriminative processes.

D11-14

ON THE QUANTIFICATION OF SSVEP RESPONSE

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The electroencephalography (EEG) becomes increasingly popular in psychological studies. One of the features being investigated are Steady State Visual Evoked Potentials (SSVEP). Visual stimuli that oscillate 5 – 50 Hz may induce corresponding (stimulation and higher harmonics) frequencies in the EEG over visual areas of the scalp. In psychology there are several studies that show relations between magnitude and latency of SSVEP and IQ, working memory tasks and face processing. This phenomenon is also commonly used in Brain – Computer Interface (BCI) systems. In order for SSVEP to be effective physiological indicator, the accurate estimation of the response magnitude is critical. The simplest estimator of SSVEP strength is the Spectral Power. It is often used in neuropsychological experiments, although it has some significant disadvantages. One of the characteristic of EEG spectrum is that the spectral power of EEG decreases with frequency increase. This property means that response to high-frequency SSVEP has less power than response to low-frequency stimulation. Therefore SSVEP strength can be better estimated as a percentage increase in power in the stimulation frequency. The relative power change is computed using reference EEG period with spontaneous activity. This allows an objective assessment of SSVEP strength regardless of the frequency. Presented method was applied to evaluate strength of SSVEP response for a range of frequencies. Presented method allowed obtaining significantly improved results.

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D11-15

TRIAL-BY-TRIAL CHANGES IN A PRIORI INFORMATIONAL VALUE OF SUBJECTIVE BELIEFS AND EXTERNAL CUES IN HUMANS

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Preparatory activity based on a priori probabilities generated in previous trials and subjective beliefs would produce an attentional bias. However, preparation can be correct (valid) or incorrect (invalid) depending on the actual target stimulus. Alternation effect refers to the subjective belief that a target will not be repeated in the same position, causing RTs to increase if the target location is repeated. Our experiment, using the Posner's central cue paradigm, tries to demonstrate that not only the credibility of the cue, but also the subjective beliefs about the next position of the target are changed in a trial by trial basis. Results indicated an increase in RT benefits when sequences of two and three valid trials occurred. Analysis of errors indicated an increase in anticipatory behavior which grows as the number of valid trials is increased. On the other hand, there was also an RT benefit when a trial was preceded by trials in which the position of the target changed with respect to the current trial. A sequence of two changes was still faster than a change preceded by a trial with no change in the target position. Taken together, these results suggest that in Posner's central cue paradigm, and with regard to the anticipatory activity, three independent preparatory processes appeared: 1) attentional preparation to the location indicated by the explicit directional cue, 2) anticipatory activity depending on the validity/invalidity of previous trials and 3) a tendency to prepare for a trial with an opposite location and response to that of the previous trial. Results suggest that Bayesian rules are operating in the generation of anticipatory activity as a function of the previous trial's outcome, but also on subjective biases like the "gambler´s fallacy".

D11-16

DOUBLE BISECTION OF AUDITORY TEMPORAL INTERVALS BY RATS

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Scalar Expectancy Theory (SET) has been the leading theory in timing research, and has also influenced research into human timing. However other timing theories exist, such as Learning to Time (LeT). The double bisection task was designed to test the SET and LeT theories in pigeons, but as the other species timing resembles animal timing; it may be that double bisection also applies to rats. The usual results of the double temporal bisection procedure show that the proportion of responses to the long option increases monotonically as a ogive with increasing stimulus duration, even though both response options are associated with the same absolute duration. The purpose of this experiment was to verify whether similar results emerge from a rat's analogue of the double bisection task. For that, 6 rats were trained on a modified double bisection procedure in which 2 bisections were trained with the same operands but different temporal markers. Both bisections were subsequently presented in one session, and then present all durations of generalization of both bisections with a new temporary marker in a final test phase. The results show that in this final time estimation was more variable: the proportion of "long" responses monotonically increased for some subjects but not for others.

D11-17

SPATIAL VISUAL CUE PROXIMITY AND PERFORMANCE IN RATS WITH THALAMIC LESIONS ON A CHEESEBOARD NAVIGATION TASK

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The literature clearly supports the involvement of the anterior thalamic nuclei (AT) in the processing of spatial memory as part of an extended hippocampal system (Aggleton, 2008). However, few studies have examined the contribution to spatial memory of the laterodorsal thalamic nuclei (LD), an adjacent structure with similar neural connections. Studies have shown that spatial memory performance can be influenced by the proximity of visual cues, but comparisons are often drawn using different task conditions (Brett, 2008; Cánovas et al., 2011; Livingstone and Skelton, 2007; Save and Poucet, 2000). In this study we directly compared the effect of proximal or distal visual cue proximity on spatial memory performance using identical methods on a cheeseboard maze. Rats with AT, LD or sham lesions (N = 54) were trained using a fixed spatial configuration which comprised either proximal or distal visual cues, a beacon on the maze indicating the location of the food reward and a fixed start point relative to the visual cues and beacon. A set of three probes were interspersed between training trials and repeated weekly for four weeks. Performance in each probe emphasised the ability to use particular strategies, i.e. allocentric or egocentric navigation, and were measured using deviation scores and latency to locate the food reward. Learning effects were observed across training with a decrease in both measures. Performance was initially poorer in the proximal cue condition, but stabilised at asymptote, resulting in similar performance across the two task conditions. The AT group (n = 18) had higher deviation scores overall compared to the LD (n = 11) and sham groups (n = 18). Though not statistically significant, the LD group exhibited longer latency when proximal cues guided navigation compared to the AT and sham groups. No lesion effects were observed across the three probes, but there were clear differences between the proximal and distal cue conditions, with poorer performance across both measures in the proximal cue condition. The effect of cue proximity may be due to motion parallax, the perceived displacement rate of cues, while the absence of lesion effects may be due to preferential use of the beacon rather than the spatial configuration present during training trials.

D11-18

THE EFFECT OF PRE AND POSTNATAL ELECTRIC FIELD EXPOSURE ON VISUAL EVOKED POTENTIALS AND COGNITIVE FUNCTIONS

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The purpose of the study was to investigate the effect of pre and postnatal electric field exposure on memory acquisition-retrieval and visual evoked potentials (VEPs). In the present study, 24 female wistar rats, aged 5 months, were divided into 2 equal groups (n = 12 rats/group) as follows; control (C), the group exposed to electric field (50 Hz AC; 12 kV/m) in prenatal and 3 months postnatal period for one hour per day (PRE+PO). In this study, we used paralel plate system to create 50 Hz electric field. In the Y-maze paradigm, rats had to learn which of the two arms forming the Y was baited with food. Rats were trained in the Y maze for 3 days, with two sessions per day, each session containing five trials. After 4 days, memory retention was tested in rats. Rats were exposed to the retention paradigm for two sessions per day for 2 days. Percentage of correct arm choices per session was measured. Visual evoked potentials were recorded with stainless steel subdermal electrodes under ether anesthesia. Peak latencies of the components and amplitudes of successive peaks were measured and statistical analysis were performed. For the first day of the Y-maze test, no significant difference was observed in the correct arm entries among the two groups. Memory acquisition was significantly decreased in the PRE+PO group versus the control group in the following days of the experiment. In the retention test, PRE+PO group showed a reduced performance compared with the control group. Also, latencies of all VEP components were significantly prolonged in the PRE+PO group versus the control group. But, no significant difference was observed in the recorded amplitudes among the two groups. In conclusion, these results show that electric field exposure in the pre and postnatal periods reduced cognitive functions. In addition, the prolongation of VEP latencies clearly indicated that electric field exposure could affect visual system.

D11-19

EFFECTS OF POSTTRAINING EPINEPHRINE AND VOLUNTARY PHYSICAL EXERCISE ON LEARNING AND MEMORY IN A SPATIAL BARNES MAZE TASK

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There are many evidences that posttraining epinephrine can modulate memory for both aversive and appetitive tasks. In turn, many works have shown that physical exercise is capable of improving several learning and memory tasks, including spatial ones. The present work was aimed at examining the effects of voluntary physical exercise (running wheel) and posttraining epinephrine, alone or in combination, on 1) learning and memory, 2) cognitive flexibility, and 3) learning strategy (spatial vs serial vs mixed), in a Barnes maze task, in rats. The Barnes maze consists of a circular platform containing 20 holes around its perimeter, one of them connected to an escape tunnel. Bright lighting and a white noise are used as aversive stimulation. Each animal was subjected to four training sessions (two trials each). Fifteen days later, a memory test (with no escape tunnel) was performed. Finally, in order to test for cognitive flexibility, an additional four-trial training session, with a different position of the escape tunnel, was administered. Physical exercise consisted in free access to a running wheel starting 15 days prior to training and ending on the last training session. Epinephrine or vehicle were administered immediately after the second trial in each training session. Two epinephrine doses were tested: 0.05 and 0.01 mg/kg. The animals were randomly distributed into the following six experimental groups: 1) Exercise-vehicle; 2) Exercise-Epinephrine 0.05; 3) Exercise-Epinephrine 0.01; 4) Sedentary-vehicle; 5) Sedentary-Epinephrine 0.05; 6) Sedentary-Epinephrine 0.01. The main results showed that voluntary physical exercise was capable of improving the acquisition of spatial Barnes maze task, by reducing the time and distance to find the hole connected to the escape tunnel. However, in the memory test performed fifteen days after the end of physical exercise, all the groups showed a similar level of retention, as well as a similar speed in learning the new location of the escape tunnel. In turn, while posttraining epinephrine neither improved learning and memory or cognitive flexibility, there was a higher proportion of rats that used a spatial strategy to solve the task in the epinephrine groups, regardless of the dose and of whether they had physical exercise or were sedentary.

D11-20

EFFECTS OF ELECTRICAL STIMULATION OF THE NORADRENERGIC NUCLEUS LOCUS COERULEUS ON NEURAL ACTIVITY OF THE NORADRENERGIC AND PREFRONTAL NEURONS

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The Locus Coeruleus (LC) is a major source of noradrenaline (NE) for the cerebral cortex. Tonic stimulation of LC typically results in desynchronization of the forebrain EEG and priming phasic activation of LC increases signal-to-noise ratio of sensory cortical and thalamic neurons. Although electrical microstimulation is commonly used, its effects on LC neuronal discharge have not been studied systematically. We sought to compare the local effects of LC microstimulation and its effects on neural activity of its distal cortical targets. We performed a combined recording/stimulation study in urethane-anesthetized rats. We applied monopolar stimulation of LC, delivering biphasic single-pulses (SP, duration range: 0.1-0.5ms; amplitude range: 0.01-0.2mA) and 50-200ms trains of pulses (TR) at 20-50Hz every 4s. Neural activity in the stimulated LC, the contralateral LC and ipsilateral mPFC was recorded simultaneously. LC neurons in close proximity to the stimulation site showed a long-lasting inhibition after SP with no spikes for 40-120ms depending on the stimulation current. Duration of inhibition well exceeded a ~20ms artifact period and decreased at higher currents (196±10ms at 0.01-0.05mA; 131±12ms at 0.07-0.2mA, n=7, $p<0.001$). There was no effect of pulse duration. Neural responses in the contralateral LC showed overall a shorter inhibition (65±6ms). None of the SP affected the firing rate of the ispilateral prefrontal (mPFC) neurons. TR elicited a sustained inhibition in the stimulated LC (488±63ms at 20Hz and 869±69ms at 50Hz, n=4, $p<0.001$). Preliminary analysis revealed no effect in the contralateral LC and mPFC except for occasional brief excitation. In agreement with earlier observations, only relatively long (~500ms) TR affected cortical activity as detected by a transient desynchronization in mPFC. Our results show that a wide range of stimulation parameters may mimic characteristic response of the noradrenergic LC neurons to salient stimuli (a brief excitation followed by a prolonged inhibition), while only relatively strong LC stimulation may affect neural activity in distal cortical targets of LC. Thus, LC microstimulation can be effectively used for phasic activation of LC-NE system in a well-controlled mode in behavioral studies, but careful examination of effects of LC stimulation in the region of interest is essential for the interpretation of results.

D11-21

HIPPOCAMPAL MECHANISMS OF SELF-STIMULATION BEHAVIOR

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In a seminal study carried out in the 50s of the past century, James Olds and Peter Milner reported that rats will respond with a high level performance as a result of the direct electrical stimulation of selected brain sites. The medial septum is one of those sites. Subsequent studies have revealed that many vertebrate species will learn to work for what has come to be called brain stimulation reward (BSR). In the other hand, the hippocampus is a structure classically related with mechanisms underlying learning and memory. In a specific way, it has been described that field excitatory post synaptic potentials (fEPSPs) recorded in the hippocampal CA3-CA1 synapse shows changes in strength (in terms of amplitude or slope) in direct relation with the learning and/or extinction processes. The aim of this work was to describe the functional relationships in an operational task using BSR and the associated changes in hippocampal activity. Mice C57/BL6 with chronically implanted electrodes for recording in CA1 and for stimulation in CA3 and medial septum areas were trained to execute an operant task. Electrical stimulation of the medial septum (train of square pulses, 100 Hz, 200 ms) were used to obtain BSR. Forty ms after the end of each train delivered to the medial septum, a simple square pulse (100_s) was presented to the hippocampal CA3 area (i.e., to the Schaffer's collaterals) to evoke a fEPSP in the CA1 area. With this protocol, we obtained as a main result the diminution of fEPSP amplitude related with the learning process across the training and performance days of BSR. This result represents by first time a report of synaptic activity changes in the hippocampus evoked by the BSR. Results also suggest that the hippocampus presents different levels of inhibition depending on the experimental situation -namely, if it is a learning process or just the execution of an already learned task. It is important to note that these results were collected from a totally free moving animal with synaptic recording in a kind of task not directly related to food or water intake.

D11-22

REINFORCEMENT LEARNING AND DAT1 POLYMORPHISMS: AN ASSOCIATION STUDY OF THE MODERATING EFFECT OF ORIENTING BIAS

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Motivational bias is a fundamental temperamental trait, defined as a predominant tendency towards approach or avoidance behaviors, and reflecting greater sensitivity to positive vs. negative reinforcement, respectively. Although frontostriatal dopamine signaling is known to play an important role in reinforcement learning, it is not clear to what extent it is involved in mediating individual differences in relative sensitivity to positive vs. negative reinforcements. Individual differences in motivational bias were shown to be reliably associated with asymmetric cortical activation patterns. Such asymmetric activation is also reflected by orienting bias, and individual differences in orienting bias are known to reflect individual differences in dopaminergic asymmetry in animals, and possibly in humans too. However, although it appears that dopamine signaling is important for both motivational bias and orienting bias, the underlying factors that contribute to individual differences in these traits are not known. The present study tested the hypothesis that polymorphisms of dopamine-related genes contribute to such differences. Specifically, we investigated the association of a variable number of tandem repeats polymorphism the 3' untranslated region of the dopamine transporter gene (DAT1) with orienting bias, and with relative sensitivity to positive vs. negative feedback in a reinforcement learning task, in 77 healthy individuals. No differences in motivational bias were found between 9-repeat allele carriers and 10-repeat homozygotes. However, Orienting bias moderated the association between DAT1 variation and reinforcement processing. Among carriers of the 9-repeat allele, the magnitude and direction of orienting bias was significantly correlated with the differential sensitivity to reward vs. punishment, such that participants who showed a stronger leftward bias displayed better learning from negative (relative to positive) reinforcement, and a stronger rightward bias was associated with better positive (relative to negative) reinforcement learning. This association was not present among 10-repeat homozygotes (showing either leftward or rightward orienting bias). These results suggest that asymmetric hemispheric activation and the DAT1 gene polymorphism interact in determining the nature of one's reinforcement sensitivity.

D11-23

BRAIN NETWORKS UNDERLYING THE ACQUISTION OF A SINGLE-DAY SPATIAL LEARNING TASK

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Although the dorsal hippocampus has been particularly involved in the acquisition of spatial learning, there is still a lack of precise knowledge of the brain circuitry that underlies spatial learning. To address this issue, we mapped the changes in brain oxidative metabolism using cytochrome oxidase (C.O.) quantitative histochemistry after training rats in a single-day spatial learning task using a water maze. Animals were trained in a massed reference memory protocol consisting of 4 habituation trials using a visible escape platform followed by 12 additional trials using a hidden platform. Single-day training has the advantage of easily discriminate the acquisition from consolidation phases of memory processes. A group of rats that swam during an equivalent time amount without any escape platform was used as a control group. Rats were decapitated after finishing all behavioral tasks and brain tissue was immediately frozen and processed for C.O. histochemistry. Significant increases in C.O. activity were found in the dorsal CA1 hippocampal area, the granular retrosplenial cortex, the lateral mammillary nucleus and the prelimbic cortex. However, C.O. activity significantly decreased in many brain regions including the lateral septum, the anteroventral thalamic nucleus and midbrain nuclei like the ventral tegmental area. Analysis of functional interactions using correlations of C.O. activity between brain regions showed a brain network comprising dorsal hippocampal areas and the striatum only in rats trained in the spatial learning task. Common brain networks including the ventral hippocampal areas, the perirhinal cortex, the entorhinal cortex, amgydala nuclei or accumbens nuclei were found in both control and trained groups. These results suggest that complex brain networks including brain regions involved in spatial navigation, spatial learning and goal-directed behavior are involved in spatial learning. Additional research is required to evaluate the significance of particular brain networks in different components of spatial learning.

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D11-24

MAKING STATE DEPENDENT MEMORIES BY RECONSOLIDATION UPDATE MECHANISMS

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Introduction: Different studies have demonstrated that after retrieval (reactivation), memories enter into a labile state and require a subsequent process of reconsolidation for maintain memory. Recent studies indicate that reconsolidation can modify memory information by updating through external signal (conditioned stimulus) during retrieval. Moreover, classical studies of state-dependent memory indicate that particular internal states could act as a conditioned stimulus. Here, we examined the effects of an internal state induced by water deprivation during reactivation and it subsequent possible memory update in contextual fear conditioning (CAC) task. Methods and Results: In the first experiment, male Wistar rats were conditioned in CAC. Twenty-four hours later, they were divided in two groups (with or without 24h water deprivation) and reexposed to the same context (reactivation) for 3min. Two test sessions were performed in different conditions: in the test 1, animals were conducted without water deprivation, and in the test 2 under water deprivation. Animals under water deprivation during memory reactivation expressed less freezing responses than animals without water deprivation in test 1. In the second test no difference was verified. In the second experiment, the same protocol was performed. However, 30min before of reactivation session, animals were injected with nimodipine or vehicle. Nimodipne prevented memory reconsolidation process. Conclusions: The water deprivation state during reconsolidation changes pre existing internal information and turns a not-depending state memory on a dependent one. Moreover, solely memory retrieval upon water deprivation, without reconsolidation (what occurs upon nimodipine effect) is not capable for promote these phenomenon. These results are the first evidence that the affective state of a memory can be update by reconsolidation.

D11-25

INFLUENCE OF DIFFERENT RATS' EXPLORATORY ACTIVITY ON THE LEARNING ABILITY

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It is known that animals show a various exploratory activity and display different levels of anxiety and responses to certain pharmacological manipulations (Mallo T., et al., 1998). The present study was devoted to the evaluation of how different exploratory activity of male Wistar rats may influence their learning ability. The exploration box test was used by registration of total path length, path length in each of four separate areas, object inspection in each area during 15 minutes. Afterwards the rats' behaviour was assessed in conditioned avoidance response (CAR) test (number of correct responses and latency of avoiding of aversive stimuli were measured, 7 days training), and in Barnes maze spatial memory test (4 days training, total path length to reach the target-hole). The obtained results revealed 3 groups of rat exploratory activity: high (HE), medium (ME) and low (LE). Activity of rats differed by their locomotor activity: LE rats mainly spent exploratory time in the cage and the average path length (distance) was 372 cm; ME rats showed a slight interest to objects placed on 4 arenas and the distance was 1354 cm, whereas HE rats covered average distance was 4024 cm. Considerable differences between activity groups were observed in rats' ability to find the target-hole in Barnes maze during the first 2 testing days (LE needed longer time in comparison to that of HE rats), however on the 4 training day, all groups spent almost equal time to reach the target hole. In 7-days CAR experiment rats' exploratory activity also was comparable. In conclusion, determination of rats' different exploratory activity is very important in acute memory tests when animals demonstrate distinct learning ability, however chronic or subchronic experiments resulted in similar responses.

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D11-26

DIFFERENCES IN INHIBITORY AVOIDANCE LEARNING AMONG CD1 MICE FROM THREE DIFFERENT SUPPLIERS

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The purpose of the present work was to study the possible differences in inhibitory avoidance (also called passive avoidance) learning in male and female CD1 mice acquired from three different suppliers, for which a one-trial step-through version of the paradigm was employed. Mice from Charles River (France), Harlan (The Netherlands) and Janvier (France) laboratories were divided by sex and assigned to group C, H or J, respectively (n = 11-12). The animals were randomly tested in the training phase (foot-shock: 0.3 mA, 5 sec) and again for avoidance (no foot-shock delivered) one week later. Inhibitory avoidance learning (test latencies significantly higher than training latencies) was observed in both C groups (male and female), as well as in the male H and female J groups. On the other hand, a lack of learning was observed in the female H and male J groups. In conclusion, there are differences in inhibitory avoidance learning among CD1 mice from different breeding facilities.

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D11-27

EXPOSURE TO ENVIRONMENTAL ENRICHMENT DURING ADOLESCENCE HAS A GREATER IMPACT ON EXPLORATORY BEHAVIOR THAN WHEN INITIATED AT A LATER AGE

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Behavioral and physiological effects of rearing mice in enriched environments seem to depend on both the total period of rearing and the age at which it is initiated. The period needed to induce behavioral changes varies according to the experimental paradigm used, although few studies have evaluated this question using the hole-board test. Our aim was to assess the impact of exposure to environmental enrichment (EE) on the exploratory behavior displayed by mice exposed to this type of rearing at different ages. NMRI male mice (n=64) arrived at our laboratory on post-natal day (PND) 21 and, after different periods, were exposed to an enriched (EE) or standard environment (SE). Four experimental groups were compared in the current study: 1) Group EE-6: exposure to EE beginning on PND 28 and lasting a total period of 6 months, 2) Group EE-4: exposure to EE beginning on PND 90 and lasting a total period of 4 months, 3) Group EE-2: exposure to EE beginning on PND 155 and lasting a total period of 2 months, 4) Group SE-6: exposure to SE beginning on PND 28 and lasting a total period of 6 months. At 7 months of age, animals were tested in the hole-board apparatus. The parameters recorded were latency to the first head-dip and total number of head-dips at 1, 5 and 10 min. Results indicated that mice in which exposure to EE began on PND 28 displayed a lower number of head-dips during the 5-min test than those which began EE at later ages (EE-4 and EE-2) and those maintained in SE ($p<0.05$). No significant differences were observed in the latency to first head-dip or number of head-dips during the first minute of the test. These results suggest that behavioral changes in exploratory activity are more pronounced when exposure to enriched environments takes place during early adolescence. Future studies should vary the age of exposure to EE and the total time of exposure in order to analyze in more depth the impact of this type of rearing on different behaviors and emotional responses.

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D11-28

ANTERIOR THALAMIC LESIONS AND RECOVERY: ENRICHED ENVIRONMENTS RESTORE SPATIAL MEMORY IN THE RADIAL ARM MAZE

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Postoperative enrichment in rats with anterior thalamic nuclei (ATN) lesions has been shown to ameliorate deficits in forced choice spatial working memory in a cross maze and reference memory in the water maze, but failed to promote recovery of spatial memory in the radial arm maze (Loukavenko et al., EJN, 2007; Wolff et al., Hippocampus, 2008). The current study re-examined the influence of enrichment (Enr) in ATN rats in the radial arm maze. Here, ATN lesions produced severe impairment in spatial working memory in the cross maze immediately after surgery ($F=31.4$; $df=1,36$; $p<0.0001$), which was substantially reduced by 40 days of subsequent enrichment (Enr vs Standard housing [Std]; ATN-Std < ATN-Enr [$p<0.03$, post-hoc Newman-Keuls]; ATN-Enr was not different to Sham-Std and Sham-Enr [$p>0.15$]). As in previous work, we also replicated the improvement in the ATN-Enr rats when tested on "alternate-arm" trials in the cross maze (free choice test run began from the opposite start box to that used for the forced-choice sample run, a test of allocentric memory). The four groups were subsequently trained in a standard 8-arm radial maze, but with one arm never baited (pseudo-randomly varied across rats). In the radial arm maze, the ATN-Std group made more errors than each of the other groups ($p<0.001$; Sham-Std worse than Sham-Enr, $p<0.05$, no other significant pair-wise differences). Also, all ATN-Std rats failed to reach criterion within 35 days of radial arm maze testing; one rat in each of the other three groups failed to reach criterion. The previous negative finding in the radial arm maze may have been due to the addition of vestibular stimulation when the rats remained in the maze during rotation between successive arm visits. The current study confirms that enrichment promotes recovery from severely impaired spatial memory after ATN lesions in rats and extends this influence to spatial memory in the radial arm maze. Histological analysis of CA1 morphology is being examined to determine whether changes in these neurons are associated with impairment and recovery after ATN lesions.

D11-29

LANDMARKS FACILITATE LEARNING ABOUT ENVIRONMENTAL GEOMETRY IN BOTH MALE AND FEMALE RATS

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In navigation tasks females tend to prefer landmark over geometry cues to locate a hidden goal, while this preference is reversed in males. We tested whether landmarks would restrict learning about geometry when both signalled the same reward, and whether sexes would differ in the extent of this cue-competition effect. Rats were trained to locate a submerged platform in one corner of a triangular-shaped watermaze, with landmarks suspended over this corner and another. For half of the animals the landmarks were visually distinct, while for the remainder they were identical. There were equal numbers of each sex in each condition. Contrary to predictions, both males and females learned equally well about geometry, and unexpectedly, those with distinct landmarks learned more about geometry than those in with identical landmarks. The results are discussed with reference to between-cue associations that may influence the extent to which we observe cue-competition in spatial learning.

D11-30

DELIBERATIVE DECISION MAKING IN THE RAT: HIPPOCAMPAL LESIONS REDUCE VICARIOUS TRIAL-AND-ERROR BEHAVIOUR IN A SPATIAL REVERSAL TASK

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When a rat encounters a choice point in a maze, or is faced with two alternatives in a visual discrimination task, it will often move its head back-and-forth between the alternatives before making a response. This behaviour is termed vicarious trial-and-error (VTE), and was described in early studies by Yerkes (1907), Meunzinger (1938), and Tolman (1938). Recent work has suggested that VTEs at a maze choice-point are associated with anticipatory firing of hippocampal place cells (Johnson & Redish, 2007). The goal of the current experiment was to assess whether VTE, a potential marker for decision making in the rodent, requires the hippocampus.11 Lister Hooded rats were pretrained on a spatial serial reversal task on a double Y-maze. Rats were trained to choose a left or right alley at 2 Y-junctions en route to one of 4 possible goal boxes. On each trial, food rewards were available in only one of these goal boxes. The reward remained in the same location across trial until the rat found it. Once it did so, the rat received 9 additional trials with the same reward location. Following this, the reward was moved to a different goal box, and the same process was repeated. Each rat was given 3 different reward locations during each daily training session. When rats reached a performance of 80% returns to the correct location on 2 consecutive days, they received either a control surgery (n=5), or ibotenic acid infusions into the hippocampus (n=6). Following a recovery period, rats were tested for 16 days on the serial reversal task described above on a modified version of the maze in which the alleys between the second Y-junctions and the goal boxes were removed, creating a 14 cm gap that the rats had to cross in order to enter the goal box. Each session consisted of 4 blocks of trials, each with a different goal box rewarded. Rats with hippocampus lesions were consistently impaired in their choice of the correct goal box, and required significantly more trials to find the food reward on each block of trials than the controls. They also exhibited significantly fewer VTEs before finding the correct goal box than controls. Together, these results may indicate that VTEs prior to locating a reward site reflect a consideration of alternatives, and yield more accurate performance. The results also suggest that the hippocampus contributes to this decision-making process.

D11-31

SEX DIFFERENCES IN SPATIAL NAVIGATION: CONTRASTING SEX-SPECIFIC SPATIAL STRATEGIES

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In the present study we analyse spatial navigation abilities in adult male and female Wistar rats in the Morris Water maze to better qualify and contrast possible strategies used by both sexes. The reference condition was place acquisition, retention and match to sample design (daily new position) in a “normal” laboratory environment. For special conditions, we used a controlled environment with a limited number of cues or a partially masked environment. No clear cut sex differences were observed in the reference condition. Nevertheless, in the completely curtained environment with two salient controlled cues (one above the escape platform and another directional shape placed at a fixed position on the pool wall), the females showed slower escape latencies and no evidence of a bias toward the escape position, in contrary to males. Thus, access to the diversity of visual landmarks seems necessary for females to accurately navigate, a peculiarity also observed in BSO treated rats (Bertholet & al, 2011). Several observations showed that males and females rely on different cues to solve spatial problems. One commonly accepted generalization is that females depend more closely on configurations of proximal cues (i.e., directly explored objects) than on distant relational cues. According to the parallel map theory (Jacobs & Schenk, 2003), we hypothesise that males rely more heavily on directional bearing maps and females on sketch maps. It is likely that the available cues in the completely curtained condition offered mainly directional information, thus being favourable to male like strategies. To further qualify this hypothesis, the two following experiments are currently conducted. The first experiment, in the water maze, will show whether, like male rats, females would show accurate escape when the familiar surrounding environment is partially masked by a circular curtain occluding 270-degrees of the pool periphery, with a new opening position for each daily session. If navigating with changing view of the environment requires reference to bearing maps, allowing more abstract navigation, then the females should be impaired in this condition. Finally, the second series of experiment analyses whether male and female navigate differently in a compartmentalized arena containing several removable doors connecting the different arena’s parts.

D11-32

DOES EXPLORATORY PATTERN INFLUENCE GRID CELL ACTIVITY?

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Entorhinal grid cells are spatially selective neurons whose firing fields form a regular triangular pattern across the environment. This activity has been suggested to form a euclidian map-like representation of the rat's location and orientation based on movement-related information. To understand whether and how restrictions on the use of movement-related information and external sensory input affect grid cell firing, we recorded cell activity while the rats explore bidimensional and unidimensional environments in both light and dark conditions. Rats were implanted with a bundle of 4 tetrodes in the dorsolateral part of the medial entorhinal cortex and were trained to freely explore a circular arena (150 cm in diameter). They were then confined to a peripheral rim of the arena and trained to run unidirectional laps, both in light and darkness. The results showed that the grid cells firing pattern changes from bidimensional to unidimensional environment. Moreover the new-established map in the circular track is stable in both light and dark conditions, and the distance between firing fields increases compared to the circular arena. These data indicate that grid cell activity is influenced by the animal's exploratory patterns. The increased distance between the fields observed in the circular track suggests a potential role of grid cells in estimating the effective distance between places (i.e. the distance travelled by the animal) rather than the absolute distance. Moreover, our data indicate that movement related information is sufficient to stabilize the grid map.

D11-33

MAPPING NETWORKS IN THE RAT FOR OBJECT RECOGNITION MEMORY IN THE DARK

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Understanding the neural basis of recognition memory, the ability to discriminate whether a stimulus is novel or familiar, is heavily reliant on animal research. The large majority of such studies have examined object recognition in the light, assuming a reliance on visual recognition. Recent studies have shown that normal rats are very effective at recognising objects in the dark that were previous sampled in the dark, i.e. using nonvisual information (tactile and olfactory). Little is currently known about the neural basis of nonvisual recognition and, in particular, the degree to which it matches systems for visual-based recognition. The present study used the expression of the immediate-early gene c-fos to compare different patterns of brain activity when rats explore either novel (Group Novel) or familiar (Group Familiar) objects in the dark. The bow-tie maze was used to generate robust levels of novelty discrimination in the dark and to provide a matched control condition using familiar objects. C-fos was examined as it shows differential activation for novel visual stimuli over familiar visual stimuli. Group Novel showed a greater preference for novel objects compared to Group Familiar. Increased c-fos activity was found in Group Novel in the CA fields of the hippocampus, the lateral entorhinal cortex, and the rostral perirhinal cortex. The latter finding contrasts with visual recognition where it is the caudal perirhinal cortex that shows c-fos increases. Group Novel also showed c-fos activity increases in the anterior thalamic nuclei, the anterior cingulate cortex, and the granular retrosplenial cortex. These findings (in the dark) reveal a network of activations when rats explore novel objects in the dark that has a common core to that seen for visual recognition, but also differs in a number of key respects e.g. the perirhinal locus, the precise pattern of hippocampal changes, and the greater involvement of the extended hippocampal system.

D11-34

DORSOLATERAL PALLIUM LESIONS IMPAIR EYEBLINK CONDITIONAL DISCRIMINATION LEARNING IN GOLDFISH

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A considerable amount of studies have shown that the hippocampus of mammals plays an important role in complex learning paradigms such as trace conditioning or conditional discrimination but is not required for delay conditioning. In teleost fishes, the dorsolateral pallium has been proposed as the homologue of the medial cortex or hippocampus of land vertebrates on basis of developmental, neuroanatomical and functional data. The present study was aimed to assess the role of teleost hipocampal pallium on trace conditional discrimination learning within an eyeblink-like conditioning procedure. With this purpose, goldfish with lesion of the dorsolateral pallium, the dorsomedial pallium, with telencephalic lobes ablation and sham operated were trained in a trace conditional discrimination paradigm using a light conditional stimulus (S+/S-) and tone conditioned stimulus (CS) separated by a 1-s trace. The results show that whereas sham animals were able to learn the trace conditional discrimination, goldfish with dorsolateral pallium lesion, such as the animals with complete telencephalon ablation, were significantly impaired in the learning of this conditional discrimination. No deficit was observed in dorsomedial pallium (amygdala homologue) ablated animals. The results of the present work reveal that the dorsolateral pallium of teleosts, like the hippocampus of mammals, plays an essential role in complex forms of conditioning. Moreover, these and previous data, showing notable memory-related similarities among the dorsolateral pallium of teleosts and thehippocampus of mammals, suggest a conserved function of this structure in vertebrates.

D11-35

CHANGES IN SYNAPTIC STRENGHT IN THE HIPPOCAMPAL FORMATION DURING THE ACQUISITION OF ASSOCIATIVE LEARNING IN BEHAVING RABBITS

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The role of hippocampus in learning and memory processes has been a matter of discussion for a long time, and there are many works which focus in its importance for the acquisition and storage of new motor and cognitive abilities. We have recorded here the activity-dependent changes taking place at different hippocampal synapses in conscious rabbits during the acquisition and extinction of an associative task. Two groups of rabbits were classically conditioned to evoke eyelid responses using delay and trace paradigms. The conditioned stimuli (CS) consisted of a tone, whilst the unconditioned stimuli (US) consisted of an air puff. In addition, two more groups of rabbits were prepared. In one of them, electrophysiological recordings of hippocampal field EPSPs (fEPSPs) were carried out without applying any conditioning stimulus, to see the putative effects of environmental influences at the different hippocampal synapses (Baseline); and, in the other, a pseudoconditioning paradigm was used (CS and US stimuli presented at random) to check if uncoupled stimuli evoked the same synaptic changes than in their coupled presentation. A pair of electrical pulses were applied to the perforant path (pp), during the CS and before the US in the case of delay paradigm, or during the CS-US interval for trace paradigm, in the CS for pseudoconditioning, and in a fixed interval of time for baseline. The slope of evoked fEPSPs did not change across baseline sessions. In contrast, an increase, or a decrease, tendency was observed in conditioning sessions depending on the synapse and on the paradigm used. Surprisingly, the pseudoconditioning protocol provoked changes in the pp to DG, CA3 and CA1 synapses, similar in magnitude to those obtained with the trace paradigm, but with relevant differences in some nodal points across the acquisition curve. These results show that a constant context does not evoke significant changes in strength at the hippocampal synapses, in contrast with changes evoked by relevant, but uncoupled stimuli, and those evoked because of the associative learning process.

D11-35

CA1 CONTRIBUTION TO MAPPING SPACE IN THE HIPPOCAMPUS

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It is known that the hippocampus plays a central role in the storage and in the retrieval of episodic memories. In particular the study of population dynamics in hippocampal place cells has emerged as one of the most powerful tools for understanding the encoding, storage and retrieval of episodic memories. Place cells are hippocampal neurons whose discharge is strongly related to a rat location in its environment. The existence of place cells has led to the proposal that they are part of an integrated neural system, which involves also parahippocampal regions, dedicated to spatial navigation and memory. Accumulating evidence suggests that environments are generally represented in hippocampal cells as a collection of manifolds associated to real space. Observed phenomena like global remapping and rate remapping can give us insights on the nature of these maps and on the attractor dynamics that governs their storage and retrieval. As the representation of the same environment is differently expressed in hippocampal subregions it becomes important to understand the function of the sequential transmission through the DG, CA3 and CA1. Indeed, while the particular autoassociative operations are ascribed mainly to the recurrent CA3 network, the role of CA1 and of the CA3-to-CA1 connections is not clear. We address these questions, restricted to Schaffer Collaterals connections for clarity, within a simplified mathematical network model. The model network simulates the storage on CA3 of one or more spatial representations, and their transfer to CA1. We quantify through information measures the ability of Schaffer Collaterals connections to reproduce the retrieved representation in CA1 and with which modifications, after a training phase in which they are modified through model Hebbian plasticity, or else after having been structured top-down. In particular we analyzed the way in which correlated or uncorrelated CA3 maps are actually represented in CA1. We find that in the CA1 maps there is a “smoother” representation of space, and that there is substantial difference in the way information is expressed. Finally, we find that even networks of considerable size can only approximate the idealized notion of a 2D quasi-continuous dynamical attractor.

D11-38

ROLE OF THE CORTICO-RUBRAL PATHWAY IN MOTOR LEARNING: A NEURAL AND BEHAVIORAL APPROACH

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There is little information regarding the involvement of motor cortex (MC) and red nucleus (RN) neurons in the acquisition of new motor abilities. To study these relationships, we used the classical eyeblink conditioning of behaving rabbits, a well-known model of associative learning. New Zealand male rabbits, weighing 2.5-3.0 kg were used. Animals were prepared for the chronic recording of identified RN neurons, and drugs infusion through implanted steel cannulae in MC and RN. Recorded neurons were antidromically activated from stimulating electrodes implanted in facial (FN) or accessory abducens (Acc ABD) nuclei. For analysis of motor activity animals were implanted with recording bipolar hook electrodes in the orbicularis oculi (O.O) muscle. A 5 x 5 mm window was drilled on the bone overlying the RN to allow neuronal recordings. As conditioned stimulus (CS) we used a tone (600 Hertz, 80 dB, 350 ms) and as unconditioned stimulus (US) an air puff aimed to the contralateral cornea (3 Kg/cm^2, 100 ms). Both CS and US finished at the same time. Conditioned responses (CRs) were determined from orbicularis oculi (O.O) EMG. Rubral and perirubral neurons were recorded during habituation and conditioning sessions. In two groups, the MC or the RN were infused with 5 µL 4% lidocaine in saline the 4th and 5th conditioning days to block the related neural activity. Conditioned animals were able to produce up to 80% of CRs/session. Identified neurons projecting to the FN or Acc ABD nuclei and related to CRs were located in the dorsal-rostral-lateral portion of the RN and presented short antidromic activation latencies (0.7-1.3 ms) and a tonic basal activity related to O.O EMG. During MC lidocaine infusion some of these neurons presented an increase of EMG related activity, while the CRs acquisition was prevented. CRs were also canceled during RN lidocaine infusion, without any modification in unconditioned responses. Interestingly, after both MC and FN drug treatment, the animals were able to acquire CRs starting from the pre-injection level. These results indicate that blockade of these brain structures prevent the learning process more than its expression. Moreover, the related rubral neurons are tightly controlled by MC activity, without which a stronger role of NR in this motor learning can be enabled.

D11-38

GLUTAMATERGIC DISCONNECTION BETWEEN VENTRAL SUBICULUM AND VENTRAL STRIATUM IMPAIRS LONG-TERM SPATIAL MEMORY IN MICE

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Well known is the role of the hippocampus in spatial learning and memory. The ventral striatum (VS) receives dense glutamatergic projections from the ventral subiculum of the hippocampus (vSub), and we have recently demonstrated that AMPA receptors activation and phosphorylation in this structure is necessary for the long-term stabilization of spatial information. A suggestion of a possible interplay between the hippocampus and the VS in the memorization process comes also from electrophysiological studies demonstrating hippocampal-striatal ensembles reactivation during sleep after learning. However, to our knowledge a functional interplay between the two structures in the long term stabilization of spatial information has never been thoroughly investigated. In a first series of experiments the inactivation of the VS or the vSub of the hippocampus, by bilateral injections of the AMPA receptor antagonist NBQX (0.00095 µg/side), before a massed training in the water maze task, impaired performance during the probe test 24 hours later. Then, in order to functionally disconnect the two brain regions, we performed focal administrations of the AMPA antagonist into the vSub on one side of the brain and into the VS on the other side, before training in the same task. The functional disconnection significantly impaired the ability to locate the correct quadrant on probe test 24 hour later. As control experiment were performed unilateral administrations of the AMPA antagonists in one or the other of the two structures. In both case mice did not performed differently from saline controls. These data confirm the role of VS and vSub in the processing of spatial information. Further they suggest that a serial transmission of information between the two brain regions is necessary in order to acquire and/or consolidate the information necessary to locate the platform 24 hours later.

D11-39

CONTEXT, LOCATION AND THE ANTERIOR THALAMIC NUCLEI

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The spatial functions of the rodent anterior thalamic nuclei appear to be very closely linked to its role in navigation. This association is underlined by the presence of head-direction cells in the anterior dorsal nucleus, and raises the question of whether these thalamic nuclei are required for spatial tasks that do not tax navigation and, if so, what is the nature of that involvement. Rats with anterior thalamic nuclei lesions (ATNx) were trained on two classes of spatial tasks; i) biconditional discriminations using different types of contextual and location cues (Experiments 1 and 2), and ii) a passively learnt spatial escape task (Experiment 3). Neither class of task taxed navigation. In Experiment 1, rats were trained in operant chambers to learn a biconditional association between an auditory stimulus (tone or click) and either a visual (spot or checked wall-paper) or a thermal (cool or warm) context. In Experiment 2, rats dug in one of two cups containing either beads or shredded paper; the correct cup was determined by its location within the room (i.e. choose cup A in location X, but cup B in location Y; a location-item association). Next, the rats learnt to dig inside a particular cup placed in one of two boxes with distinctive local cues that were in the same location (i.e. choose cup A in box X, but cup B in box Y; a context-item association). The ATNx rats were unimpaired on the biconditional tasks whenever local cues solved the context-item associations (Experiments 1 and 2). In contrast, the ATNx rats were severely impaired when the biconditional task required the formation of location-item associations. The ATNx rats also failed to use the geometrical properties of an environment to learn a specific location when passively placed on a platform in one of two corners of a rectangular shaped pool during the learning phase of Experiment 3. These findings show that while the anterior thalamic nuclei are critical for spatial learning, navigation is not a pre-requisite for such deficits to emerge. The experiments also show how the anterior thalamic nuclei are not needed for learning about discrete, local cues that define contexts but appear necessary when learning about more distal cues that define different locations.

D11-40

CORRELATIONS IN ACTIVATION OF STRUCTURES OF THE THALAMOCORTICAL NETWORK IN A SIMPLE LEARNING PARADIGM

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Learning and learning-dependent changes in behaviour are the result of interactions between different brain regions rather than isolated processes at local neuronal populations (McIntosh, 2000). These interactions and the issue of how these interactions depend upon the sensorimotor or cognitive context are described in terms of functional integration. Functional integration is usually assessed by examining the correlations among activity in different brain areas or by explaining the activity in one area in relation to others. In the thalamo-cortcial network arousal-related attenuation of the correlation strength (coupling strength) of thalamo-cortical input was recently observed with electrophysiological recordings. Here we examined the correlations between metabolic activation of the barrel cortex, posterior parietal cortex (PPC) and thalamic nuclei: ventral postero-medial (VPM), posterior (PO) and reticular (Rt) in a delay conditioning paradigm, where stimulation of the facial vibrissae in mice was paired with a tail shock. During the conditioning session the [^{14}C]-2-deoxyglucose (2DG) brain mapping was performed. 2DG uptake was examined in the first and the third (final) session of conditioning, in the group that received only the stimulation of vibrissae (CS only) and in unstimulated control group. We found that stimulation of whiskers (CS only) evokes correlated activity of the studied structures. As a consequence of repetitive delivery of stimuli in the consecutive stimulation sessions brain structures discontinue to act in the correlated mode. On the contrary, learning process produce high activity of all structures studied and correlations among activities in these brain areas get stronger progressively in the course of the training. In the final phase of the training the correlation between activity of the barrel cortex and PO becomes significant. Activation of PPC and barrel cortex was significantly correlated during learning, both during the initial and final phase of the training. Our results seem to be consistent with the idea that the cortico-thalamic network, including (primary somatosensory cortex and PPC plays a crucial role in the complex neuronal network related to the attentional processes. It might be also possible that coordinated interactions between the structures studied, expressed as correlations among their activity, underlie the active maintenance of a memory trace and its operation during the training.

D11-41

UPDATING THE VALENCE OF A SPATIAL GOAL: ARE THE MEDIAL PREFRONTAL CORTEX AND THE DORSAL HIPPOCAMPUS INVOLVED?

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Recent electrophysiological unit-recording data suggest joined coding of goal location by the dorsal Hippocampus (dHpc) and medial Prefrontal Cortex (mPFC) (Hok et al. 2005) The present work ask how these two anatomically connected structures, are involved in updating the valence of a goal zone during spatial navigation. In the continuous spatial navigation task, Long Evans rats had to cross a non-cued area, the goal zone (GZ), to release one pellet in the openfield (appetitive condition). Once the learning was completed, the valence of GZ was reversed as crossing the GZ triggered an aversive stroboscopic light (aversive condition) instead of pellet release. During this session, mPFC or dHpc were temporary inactivated by bilateral injections of muscimol. Sham animals were injected with vehicle. During the aversive session, the decrease of GZ crossings observed for all groups (mPFC, dHpc, Sham) revealed that the valence of GZ was correctly updated. On the next day, updating retention was tested in the appetitive version, by measuring the latency of the first GZ cross. On this retention test, mPFC animals quickly crossed the GZ, whereas the Sham and dHpc animals delayed their first GZ crossing. These results suggest that the mPFC and the dorsal dHpc are not required to update the valence of a goal zone, but that the mPFC is necessary for the long-term retention of this updating.

D11-42

ABSOLUTE RISK PREDICTION ERROR CODING IN THE ORBITOFRONTAL CORTEX

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An important aspect of reinforcement learning is the reward value prediction error, which indicates the difference between the experienced reward and the predicted reward. An additional aspect of reinforcement learning emerging in the literature is the risk prediction error, which indicates the difference between the experienced risk and the predicted risk. We show that neurons in the orbitofrontal cortex code deviations of the experienced risk from the predicted risk.

D11-43

ROLE OF THE ROSTRAL MEDIAL PREFRONTAL CORTEX IN THE CLASSICAL CONDITIONING OF EYELID RESPONSES IN BEHAVING RABBITS

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We have studied the role of the rostral medial prefrontal cortex (mPFC) in the classical conditioning of eyelid responses in alert behaving rabbits. The rostral mPFC was identified by its afferent projections from the medial half of the thalamic medio-dorsal nuclear complex, and by the firing rate synchronization of mPFC neurons evoked by the stimulation of this thalamic nucleus. Classical conditioning consisted of a delay paradigm using a 370-ms tone as the conditioned stimulus (CS) and a 100-ms air puff directed to the left cornea as the unconditioned stimulus (US). The CS co-terminated with the US. Electrical train stimulation of the contralateral rostral mPFC produced a significant inhibition of air puff-evoked blinks. The same train stimulation of the rostral mPFC presented at the CS-US interval for 10 successive conditioning sessions significantly reduced the generation of conditioned responses (CRs) as compared with values reached by control animals. Interestingly, the percentage of CRs reached almost control values when train stimulation of the rostral mPFC was removed from the 5th conditioning session on. The electrical stimulation of the rostral mPFC in well-conditioned animals produced a significant decrease in the percentage of CRs. Moreover, the stimulation of the rostral mPFC also was able to modify the kinematics (latency, amplitude, and velocity) of evoked CRs. These results suggest that the rostral mPFC is a potent inhibitor of reflexively evoked and classically conditioned eyeblinks _ namely; its activation only prevents the expression of CRs, but not its latent acquisition. We also recorded single unit activity of mPFC neurons during classical eyeblink conditioning sessions. The firing rate of recorded mPFC neurons increases during the CS-US intervals in simultaneity with the presence of CRs. These results seem to point out the need of the activation of the mPFC to execute the acquired motor response (i.e., the conditioned eyeblink) in an appropriate and timed way. But when mPFC activation is too high, then it exerts an inhibitory effect on all (possible) motor responses including reflexively evoked ones.

D11-44

TOWARDS AN INFINITE CHAIN OF ASSOCIATIONS: A NEURAL MODEL FOR THE CORTEX

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The investigation of complex cognitive functions can not leave aside the study of general collective behaviours generated by the presence of interacting units. In this study we focus on the dynamics underlying a free association between two memories. At the computational level this process can be viewed as a spontaneous jump between attractive configurations of a Potts network, an autoassociative network sketching out the salient features of interacting patches of cortex. In the net each constitutive unit stands for a local patch of cortex. Thus, the connection of these units can be regarded as a global network of local subnetworks. In the system the jump between two memories is elicited by an adaptive process, which weakens the stability of memories representation. The “latching process” so generated results a spontaneous consecutive retrieval of stored memories. Acting on the parameters of the model (such the units connectivity, the number of stored memories, the noise) it is possible to explore a variety of behaviours that goes from a “finite latching” region, in which the system, governed by its relaxation time and the global memories structure, allows only finite sequences of memories retrievals, to an “infinite latching” region, in which this jumping dynamics go on indefinitely.

D11-45

DRIVING OF COGNITIVE PROCESSES BY BRAIN STIMULATION IN MICE

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In a continuously changing world, it is essential to learn the relationships between an action and its consequence, in order to produce the precise behavior to obtain the best benefits or to avoid undesirable results. This can be learnt through own experiences or from experiences of a co-specific individual. The neural structures involved in appetitive observational learning remains largely unknown. For observational learning, the observer was located in a Skinner box in the presence of a well-trained demonstrator for 4 successive 20-minute sessions. The observer was separated from the demonstrator by a grid similar to the one covering the floor of the box. After this pre-training, observers were trained with the above-mentioned operant conditioning task until the expected criterion (FR 1:1) was reached. During the demonstration sessions, the observer received a train of stimulus in the medial prefrontal cortex (mPFC), the nucleus accumbens septi (NAc), and in the CA1 area of hippocampus, just in a key moment of the demonstration (i.e., when the demonstrator press the lever). Results show that the electrical stimulation of observer´s NAc during the demonstration produced perceptual enhancement effects. Mice stimulated in NAc draw more attention to the lever and feeder area. In contrast, the stimulation of observer´s mPFC, at the same moment of the demonstration session, prevented observational learning. The stimulation was not blocking learning over the long term because observers stimulated in infralimbic prefrontal cortex acquired the task at the same time than control mice which observer naive mice as demonstrator. However, the stimulation of observer´s CA1 area of hippocampus neither enhanced learning nor blocked it. In additional experiments, demonstrators were stimulated at the same moment of the task (i.e., when they pressed the lever) at the same areas of the brain. The stimulation of demonstrators´ mPFC prevented mice of visiting the feeder to eat the pellet as soon as they press the lever. Apparently, those mice lost the temporal sequence of their ongoing behaviors. Whereas the stimulation of demonstrators´ NAc generated a compulsive lever press behavior and repeated visit the feeder, without eaten the delivered pellets. The stimulation of the hippocampal CA1 area does not disturb the execution of this instrumental learning task. These results provide direct evidences that NAc and mPFC are brain regions involved in observational learning and that these region are necessary for the correct performance of this instrumental learning task.

D11-46

A TEST FOR JUDGMENT BIAS - POSSIBLY INDICATING (TRAIT) ANXIETY IN MICE

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Judgement bias is one of the cognitive effects known to occur in individuals that are highly anxious or in a negative emotional state; i.e. high trait anxious and pathologically anxious people have a more negative interpretation of ambiguous stimuli than low trait anxious people. Trait anxiety can be defined as the basal emotional trait, while state anxiety is the anxiety level expressed at a particular moment in time. In animals state anxiety is relatively easy to asses, however the behaviour that is generally studied remains species specific. Further, in animals it is more difficult to assess how they generally feel (trait anxiety). Judgement bias might be a phenomenon that could be used to identify trait anxiety. Indications of judgement bias have already been found in several animal species. In the present experiments a potential test for judgement bias in mice was investigated. In this test mice were trained with one odour as a conditioned stimulus (CS+) predicting a palatable almond piece and another odour predicting an unpalatable bitter almond piece (CS-). During testing the reaction time to a mixture of these odours was investigated (ambiguous cue). Mice of the BALB/cJ and 129P3/J inbred mouse strains (previously indicated to be high trait or pathologically anxious respectively) were investigated on the ability to discriminate between the odours. While BALB/cJ mice learned the odour associations and showed indications of bias to the ambiguous cues, 129P3/J mice did not discriminate between the cues. On the central nervous level by means of c-Fos immunohistochemistry, indications of differences in information processing between the strains were found in response to the ambiguous cues in brain area's that are known to be involved in emotions such as the lateral amygdala and the prelimbic cortex. These experiments indicate that this test for judgement bias might be useful to indicate basal emotional trait in at least BALB/cJ mice. Further research is necessary to increase the reliability of the test for this specific strain and in order to adapt it for the testing of other mouse strains as well.

D11-47

A MOUSE MODEL FOR "HELPLESSNESS", A MAJOR CONCEPT IN DEPRESSION

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Emotional-cognitive control over aversive events underlies mental health, and loss of such control and generalized helplessness are of major importance in theories and treatment of depression. Establishing an animal model of generalized loss of aversive control requires two basic components: (1) A behavioural assay for impaired control over aversive stimuli. (2) An environmental manipulation that induces a robust deficit in this assay, and where the manipulation takes a different form of aversive stimulation from that used in the assay. Here we present our development to-date of such a two-stage model in C57BL/6 mice. For 15 days, chronic social defeat (CSD) mice were in visual and olfactory contact with an aggressive CD1 mouse and for 10 min/day they were in physical contact and attacked. Relative to controls, CSD mice exhibited: decreased 2-way operant control of e-shock stimuli and freezing to context; increased day-to-day body-weight changes; increased relative adrenal gland weight; increased serum titres of the pro-inflammatory cytokines IL-6 and IFN-□. This mouse model of generalized loss of aversive control is being studied to elucidate underlying circuitry and etio-pathophysiology and to identify novel targets for its neuropharmacological reversal.

D11-48

INCREASED HIPPOCAMPAL OXIDATIVE STRESS, IMPAIRED CELL PROLIFERATION AND SPATIAL MEMORY IN LPA_1-NULL MICE IN RESPONSE TO CHRONIC IMMOBILIZATION

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Lysophosphatidic acid (LPA) is a simple, bioactive phospholipid involved in several biological activities that can act as an extracellular signal through 6 G-protein coupled receptors (LPA_{1-6}). LPA_1 receptor is expressed in hippocampal progenitors involved in their differentiation, but it is also expressed by other neural cells such as neurones and glial cells in the adulthood. Functionally, LPA_1 receptor has been demonstrated to be an important modulator for the normal hippocampal plasticity and neurogenesis. On the other hand, the hippocampus is particularly susceptible to oxidative stress. In this way, some works demonstrated that oxidative stress induced by chronic stress in this brain region may have some detrimental consequences in the hippocampal neurogenesis and dependent-behaviour. The present work was conducted to study the LPA_1 receptor signalling pathway as a modulator of the hippocampal redox in chronic stress situations. To address this issue, we used LPA_1 null mice and their wild-type (WT) littermates submitted to either chronic restraint (3h of daily restraint for 21 days) or control conditions (undisturbed in their homecages). The total antioxidant capacity of tissue (ETAX), lipid hydroperoxides (LOOH) and catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPX) and cytochrome c oxidase activity were assessed in these groups. In addition, hippocampal cell proliferation (BrdU immunoreactive cells), apoptosis and spatial memory using the hole-board test were assessed in the same experimental conditions and groups. Results showed that chronic stress induced lipid peroxidation, increased GPX and SOD activity and reduced cytochrome c oxidase activity in the hippocampus in absence of LPA_1 receptor. In addition, chronic stress only in absence of LPA_1 receptor, reduced cell proliferation and increased apoptosis in the dentate gyrus of the hippocampus. Those hippocampal alterations may be, in part, responsible for the severe impairment in the spatial long-term memory observed in mice lacking LPA_1 receptor after chronic stress.
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D11-49

THE ABSENCE OF LPA_1 RECEPTOR IMPAIRS EXTINCTION OF CONDITIONED FEAR AND COMPROMISES THE INTEGRITY OF CORTICOLIMBIC CIRCUIT

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LPA_1 receptor is one of the 6 characterized G-protein coupled receptors (LPA_{1-6}) trough which acts lysophosphatidic acid (LPA, 1-acyl-2-*sn*-glycerol-3-phosphate) as an intercellular signalling molecule. It has been proposed that the LPA_1 receptor has a role in generating or controlling anxiety-like behavior and it has been implicated in the detrimental consequences of stress. In fact, the lack of LPA_1-receptors reduces ability to filter out irrelevant auditory stimulation, compromises the capacity to adaptively cope with stress and impairs exploration and increase anxiety-like responses in behavioral test. Extinction deficit is a core feature of anxiety disorders. From a neurobiological point of view, extinction process depends on integrity of corticolimbic circuit, focussing on the amygdala, prefrontal cortex, and hippocampus. Although the absence of LPA_1 receptor induces anxiety-like behavior and impairs hippocampal integrity, at the present, the involvement of LPA_1 receptor in extinction process has not been examined. Therefore, in this study, we conducted a survey of fear extinction across LPA_1-null mice and their wild-type littermates. Two different experimental procedures were carried out (cued fear extinction and contextual fear extinction). The mice were submitted to three phases of training: Fear conditioning, extinction, and retrieval testing (Days 3 and 5). The training used was the same for all animals, except for phase 2 (extinction), which differed according to the experimental group: cued extinction group, contextual extinction group and control group (these mice remained in the homecage on day 2). Freezing (as an index of conditioned fear) was measured. Additionally, morphologic examination of amygdala and prefrontal cortex was carried out. Our behavioral data clearly indicate the involvement of the LPA_1 receptor on extinction of aversive memories. The absence of LPA_1 receptor induces significant deficits on acquisition and consolidation of extinction that could be associated, at least in part, with morphological abnormalities observed in amygdala, a key loci of corticolimbic circuit mediating the fear extinction.

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D11-50

NEONATALLY STRESSED MICE INJECTED WITH DEXAMETHASONE DISPLAY LESS ANXIETY IN THE ADULT LIFE

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Stress suffered during development of the nervous system may influence emotionality and behavior of adult animals. We examined permanent effects of maternal separation and administration of dexamethasone on the rate of development of pups and emotionality of adult male mice. Male pups were separated from their mothers and littermates for 2 hours daily from P1 till P7. Some of stressed pups were injected with various doses of dexamethasone prior to separation. When mice were 3-4 months old they were subjected to behavioral tests that assessed their anxiety and fear. We found that the highest dose of dexamethasone that we used (2 mg/kg) was lethal. The rate of development and final body weight did not differ among four other investigated groups (stressed-only, stressed and 0.1 mg/kg dexamethasone-treated, stressed and saline-injected and not stressed). In the open field test stressed mice displayed hyperactivity and spent more time in the central area of the open field than not stressed animals. The highest locomotor activity was observed in mice treated with dexamethasone before separation. In the elevated plus maze all stressed mice spent more time in open arms than unstressed controls. Western blot analysis showed that the level of expression of the glucocorticoid and mineralocorticoid receptors in the hippocampus and hypothalamus of adult mice stressed and unstressed in early life did not differ. In conclusion, maternal separation introduced the permanent trait of hyperactivity and risky behavior into males that grew out of stressed pups. This disturbance is similar to attention deficit hyperactivity disorder (ADHD) and therefore maternal separation may be a model for investigation of this condition.

D11-51

DISCRIMINATIVE ABILITY: A ROLE FOR THE MINERALOCORTICOID RECEPTOR

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The glucocorticoids cortisol and corticosterone enhance memory consolidation for emotional experiences, but also impair retrieval and working memory during emotionally arousing situations. Both steroids bind to two distinct steroid receptor types in the brain, the mineralocorticoid receptor (MR) and the glucocorticoid receptor (GR), which operate as transcription factors. As the affinity of the nuclear MR to corticosterone is higher than that of GR, MRs are always occupied whereas GRs become activated during stress. This property of the receptors and distinct distribution in the brain underlines their function in emotion and cognition: while GR is responsible for consolidation of newly learned information, MR is involved in the appraisal and risk assessment in novel situations, behavioral flexibility and memory retrieval. Here, we raised the question whether MR affects the ability to discriminate between stimuli during the initial processing of environmental cues. Here, mice deficient in limbic MR ($MR^{CaMKCre}$) were tested in two tasks: social approach and fear conditioning. First, social interest was measured by time spent in close proximity to an unfamiliar mouse1; after 10 minutes another unfamiliar mouse2 was introduced to examine discriminative ability between the two mice. $MR^{CaMKCre}$ mice were hyper-responsive in their encounter with the unfamiliar mouse1. However, they did not discriminate between mouse1 and mouse2. Second, in the fear conditioning paradigm, we measured the initial emotional fear (freezing) response during acquisition, and the ability of the mice to discriminate between context and cue during memory tests on the following days. Both $MR^{CaMKCre}$ and control littermates showed high freezing at the end of training; during memory testing both genotypes discriminated between context and cue. However, $MR^{CaMKCre}$ mice showed stronger freezing to context and enhanced and persistent freezing instead of extinction towards the cue. The deficit of limbic MR (1) alters emotional responses in both tasks, (2) interferes with the ability to discriminate between stimuli that are processed within the same brain area, the hippocampus - as revealed by the social approach task, however (3) allows discrimination of emotional fear responses that rely on the hippocampus (context) and amygdala (cue). We conclude that appropriate social interactions as well as fear memory rely on functional brain mineralocorticoid receptor signaling.

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D11-52

DELETION OF THE P66^{Shc} GENE PROMOTES LONGEVITY IN LABORATORY MICE BUT DECREASES SURVIVAL IN MICE EXPOSED TO FOOD COMPETITION AND WINTER TEMPERATURES IN THE WILD

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P66$^{Shc-/-}$ mice are characterised by increased longevity and reduced oxidative stress. P66^{Shc} plays also a role in energetic metabolism promoting fat accumulation, p66$^{Shc-/-}$ mice resulting lean and healthy. The lack of this gene is indeed favourable without any “side effect” raising the question of why p66^{Shc} might have been selected, and what is its physiological role. Caloric restriction and cold affect early survival of the species and fecundity while reproduction is a high energy-cost process that relies on energetic and endocrine fat functions. We hypothesize that p66^{Shc} might play a role in these process. To address these issues we studied survival, reproduction and fecundity of p66$^{Shc-/-}$ mice both in a population living in an outdoor enclosure - exposed to food competition and winter temperatures - and under controlled laboratory conditions - with specific regard to maternal behaviour -. Results show that under natural conditions the deletion of p66^{Shc} is strongly counter-selected while in the laboratory p66$^{Shc-/-}$ mice have deficits in fat and reproductive behaviour. These findings indicate that p66^{Shc} has been conserved through evolution because of its role in energy metabolism, and caution should be exercised against premature conclusions regarding gene functions which have only been observed in controlled laboratory conditions.

D11-53

EFFECTS OF BRIEF *VS* PROLONGED CHRONIC STRESS ON NEUROENDOCRINE-IMMUNE RESPONSES AND DEPRESSION-LIKE BEHAVIOURS IN A MOUSE MODEL OF CANCER

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Psychological stress can unleash a cascade of events with multiple effects on central and peripheral targets leading to different pathologies including depression and cancer. Abundant evidence suggests that the sustained activation of the hypothalamic-pituitary-adrenal (HPA) axis following stress, and the consequent suppression of the immune function mediated by glucocorticoid (GCs) hormones, can render vulnerable individuals more susceptible to neoplastic processes. In this regard the neurotrophin Brain-Derived Neurotrophic Factor (BDNF) has been identified as a neuroendocrine effector involved in the response to stress and the associated neurobiological and behavioural changes. We investigated the effect of brief -7 - vs. prolonged -21 days - stress as a risk factor for tumor progression. In particular 4-month-old C57 male mice underwent either restraint stress (RS) or chronic disruption of social hierarchy (SS) and neuroendocrine (corticosterone), neurobiological (BDNF) and immune (cytokines levels and splenocyte apoptosis) function were assessed. In addition mice undergoing social stress were tested for behavioural despair in a forced swim procedure and for emotional reactivity in a social interaction test. Results show that SS subjects do not differ from group-housed controls either for depression-like behaviour or neuroendocrine activation. By contrast, the RS group, when compared to SS, shows more efficient neuroendocrine and immune responses. In particular, we observed reduced corticosterone levels on day 7 (short-term stress), followed by an increase on day 21 (long-term procedure); this response is associated to an inverted “U” shape activation of the immune function and of hippocampal BDNF levels. When the RS paradigm was applied to a transgenic model of tumor (p53-/- mice) we found reduced splenocyte apoptosis, in addition to a stronger neuroendocrine activation. These data point to a different role played by brief vs. prolonged stress in modulating the crosstalk between the neuroendocrine and immune system and suggest that the extent of the stress period might affect tumor progression and the severity of the disease in different directions.

D11-54

EFFECTS OF EARLY-LIFE STRESS ON SOCIAL BEHAVIOR AND nCAM EXPRESSION IN THE HIPPOCAMPUS

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Aversive events, especially when experienced early in life, lead to predispositions to develop affective and personality disorders. Mental disorders are often accompanied by intense and rapidly changing mood states as well as impulsivity and aggression. The trans-synaptic cell adhesion molecules Neuroligin 1-3 (Nlgn 1-3) and Neuroplastin (Nptn) play a pivotal role in synaptic plasticity and may modulate the effects of early-life stress on social behavior and aggression. The aim of the current study was to assess the involvement of neuronal cell adhesion molecules in mediating the effects of early-life stress on social behaviors, including social motivation, social memory and aggression. Therefore, we subjected male C57/Bl6 mice to early-life stress (ELS) from postnatal day 2 to 9. During ELS, nesting and bedding material is remarkably reduced, which results in an impoverished nursing of pups by the mothers. Animals were then tested regarding social behavior in adulthood. Brains were removed under basal conditions for the analysis of hippocampal nCAM expression levels. We showed that ELS specifically increased aggression-related behavior in adulthood, whereas sociability and social memory were not affected. Regarding nCAM expression levels, we observed a specific upregulation of Nlgn2 in the ventral hippocampus induced by ELS, whereas Nlgn1 and Nlgn3 remained unaffected. In addition, Nptn expression levels were found to be upregulated both in the dorsal and the ventral hippocampus. These findings led us to hypothesize a crucial role for Nlgn2 and Nptn dynamics in modulating aggressive behavior following ELS. Ongoing studies are addressed to test the potential of Nlgn2-overexpression and –knockdown to modulate or prevent stress-induced alterations in aggression-related behavior. Our future aim is to elucidate the role of specific nCAMs as mediators of stress on social behavior in rodents. This might elicit further important insights into mechanisms underlying affective and personality disorders and give rise to new targets for therapeutic treatment.

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D11-55

INDIVIDUAL DIFFERENCES IN THE EFFECTS OF SOCIAL STRESS INDUCED BY CHRONIC DEFEAT ON THE HYPOTHALAMIC-PITUITARY-ADRENOCORTICAL AXIS IN MICE. EFFECTS OF TREATMENT WITH A CRHR1 ANTAGONIST

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The aim of this study was to analyze the effects of chronic social defeat at different levels of the hypothalamic-pituitary-adrenocortical (HPA) axis in accordance with the behavioral strategy adopted by subjects. The study also analyzed the effects of a short treatment of antalarmin, a CRH1R antagonist. Male adult mice were exposed to repeated defeat experiences for 21 days, using a sensorial contact model. After 18 days of defeat, 2 groups of subjects were established, active and passive, in accordance with the behavior manifested during social confrontation, and treatment was initiated with antalarmin for 4 and 6 days. On the 22nd day, the animals were subjected to an anhedonic test (the novel palatable test). Two days later the subjects were exposed to another social defeat. The results showed that exposure to chronic defeat increased mRNA CRH levels in the hypothalamus and amygdale, along with plasma levels of corticosterone and spleen weight following the last defeat. Moreover, subjects adopting a passive strategy were found to have a greater spleen weight than active subjects and controls. CRH hypothalamic rest levels in passive subjects were higher than in active ones, while plasma corticosterone levels were lower than in controls. The results also revealed reduced ingestion of a palatable food in all stressed subjects. The drug did not affect the behavioral and physiological variables measured.

D11-56

EFFECTS OF GALANIN AND ITS PEPTIDE ANTAGONIST ON THE BEHAVIOR OF RATS IN THE OPEN FIELD: EFFECT OF RESTRAINT STRESS

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The galanin peptide system is widely distributed throughout the brain and periphery. Galanin is considered to be one of the neuropeptides potentially involved in neuroendocrine and behavior functions. Galanin, a 29 or 30 amino acid neuropeptide, and its three receptor subtypes have been implicated in numerous central and peripheral physiologic functions, including behavioral, cognitive and affective processes. It is expressed in brain structures known to regulate the emotionality and has been suggested to modulate anxiety-like behavioral responses to stress. Evidence from pharmacological and genetic studies obtained in various paradigms for assessment of anxiety-related behaviors has shown that the involvement of the galaninergic system in the stress-induced behavioral responses largely depends on the dose, site and route of drug administration. The present study examined the efficacy of systemic intraperitoneal galanin administration on behavior of male Wistar rats in the open field test. When compared with controls, galanin (0.3 mg/kg) increased locomotor activity recorded 1 hr after the injection. Galanin peptide antagonist M40 blocked the effect of galanin. The locomotion increase caused by galanin persisted 48 hr later without any treatment. Rats exposed to restraint stress for three consecutive days were tested 1 hr after stress termination. Galanin (0.3 or 1.0 mg/kg) administration immediately after stress prevented the decrease of locomotion induced by stress in each trial. In the test repeated 6 days later without stress and galanin treatment the reduction of locomotion level produced by stress still persisted; the anti-stress behavioral effect of both galanin doses persisted. These results suggest that galanin elicited behavioral responses in the open field paradigm indicate stress attenuating action of galanin after intraperitoneal administration. The available data from our behavioral studies suggest that targeting the galanin system might be of therapeutic benefit in anxiety disorders and for stress-related disorders.

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D11-57

OPPOSITE EFFECTS OF CORTICOSTERONE ON FEAR MEMORIES IN DORSAL VS. VENTRAL HIPPOCAMPUS

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Numerous studies indicate that high release of corticosterone (CORT) can alter memory consolidation for emotional events. The hippocampus, both required in memory consolidation and key targeted brain structure for CORT, may mediate this deleterious effect of CORT. However, recent data have shown that stress, as well as CORT, promotes and inhibits synaptic plasticity in the ventral and dorsal hippocampus (vHPC vs. dHPC), respectively. Consequently, we hypothesized that the effects of intra-hippocampal CORT on memory consolidation may be dependent on the hippocampal sector targeted. We have thus compared the effects of CORT injections into the dHPC and vHPC on the consolidation of an aversive conditioning either to a simple tone (tone as predictor of a footshock) or to the context (context as predictor of the footshock). Intra-hippocampal injections of CORT abolished the selection of the right predictor of the aversive stimulus. Specifically, injections of CORT into the dHPC produced a deficit in contextual conditioning and induced a conditioning to the tone in mice yet objectively submitted to the predicting context situation. Reciprocally, injections of CORT into the vHPC produced the exact opposite pattern of responses: a deficit of tone conditioning associated with an increased conditioning to the context was observed in mice yet submitted to the predicting tone situation. In addition, injections of the glucocorticoid receptors (GR) agonist dexamethasone into the dHPC and vHPC mimic the opposite effects of CORT on the conditioned fear responses. In conclusion, supporting a functional dissociation between the dHPC and vHPC our study unveils deleterious and opposite GR-dependent effects of CORT on fear memory as a function of the hippocampal sector targeted.

D11-58

ANXIETY AND COGNITIVE PERFORMANCE: A POPULATION STUDY IN WISTAR RATS

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Human subjects display a great variability in the predisposition to respond anxiogenically to different stimuli, i.e. trait anxiety. This susceptibility has been studied in rodents through the creation of selected strains for anxiety-like behaviour, to obtain extremes anxiety traits. Moreover, anxiety has been shown to variously affect cognitive performance both in humans and selected rodents strain. However, interindividual differences in basal anxiety level in naïve rats and how they may affect cognitive functioning have been poorly investigated. Therefore, the aim of this study is to provide an evidence of the huge interindividual differences in anxiety levels in naïve Wistar rats and demonstrate how they can affect a widely used cognitive test. Primarily, we run a population study, testing 182 Wistar rats for their anxiety-like behaviour in Elevated Plus Maze (EPM), which can provide a measure for animals "basal" anxiety level. Anxiety level was inferred by the amount of time spent by each rat in the open arms and in the centre of the EPM apparatus. Secondly, 60 rats, among those previously exposed to EPM, performed a Novel Object Recognition test (NOR), used to assess cognitive abilities in general, particularly recognition memory. NOR test provided an evaluation of recognition memory through measure of the discrimination between a familiar and a novel object. Basing on EPM data, we obtained a population, which matched a Gaussian distribution and we identified three main groups: a high anxiety group (HA), a medium anxiety group (MA) and a low anxiety group (LA). The performance of the three groups in the NOR test was compared and the results showed a significant difference between the HA group and the MA and LA group in the discrimination of novelty. First and foremost, these data show that a large interindividual variability in basal anxiety level in naïve animals. Moreover, we found that anxiety level significantly affect animals' performance on cognitive tasks, possibly leading to misinterpretation of the results obtained in that task. Therefore we claim the need to consider interindividual differences in emotionality (e.g. anxiety) in general, and the need to assess anxiety level while studying rats' cognitive abilities.

D11-59

MARKED GENDER DIFFERENCES IN THE BEHAVIOURAL AND HYPOTHALAMIC-PITUITARY-ADRENAL RESPONSE TO SHOCK-INDUCED CONTEXTUAL FEAR CONDITIONING AND THE DEGREE OF GENERALIZATION

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There is evidence that male rats are more sensitive than females to both tone and context fear conditioning, but nothing is known about gender differences in generalization of fear to other novel environments or the concomitant hypothalamic-pituitary-adrenal axis (HPA) response to those situations. In the present experiment male and female Wistar rats were exposed to 3 shocks of 1.5 mA over a 15 min period and then behavioural and HPA responses to a novel environment or to repeated exposure to the shock context (without shock) were studied some days after training. Rats receiving shocks showed a much greater ACTH and corticosterone responses than those merely exposed to the shock chamber without shocks and the response to both situations was greater in female than male rats. When tested for shock-induced context fear conditioning (CFC), time spent freezing was greater in male than females. Females also showed higher extinction rate of freezing than males, but, on the contrary, HPA activation more rapidly declined over extinction sessions in male than females. During exposure to the novel environment, that markedly differs from the shock chamber, previously shocked males showed hypoactivity whereas females not, suggesting that behavioural sensitization aftershock or fear generalization is greater in males than females. However, shocked male and female rats showed a similar level of HPA sensitization in response to the novel environment. It can be concluded that gender differences after fear conditioning included not only freezing but also HPA activation, but the two sets of variables are not influenced in parallel.

D11-60

REACTIVATING FEAR MEMORY UNDER PROPRANOLOL REDUCES THE AVERSIVE CONTENT OF LONG TERM MEMORY AND DECREASES NEURONAL CONNECTIVITY IN THE AMYGDALA

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Re-exposure to traumatic situations under drugs which decrease anxiety and/or block reconsolidation of fear experience has been shown to attenuate the aversive content of long term memory traces, especially in situations of post traumatic stress disorder (PTSD). However, whether these treatments also modify the neural support of fear memory is still unclear. In this study, we examine the possibility that reactivating fear memory under propranolol reduces long term fear memory and modifies neuronal connectivity in brain regions governing the formation and the storage of fear representations. Mice were trained for tone fear conditioning and then subjected 24 h later to a reactivation trial with saline or propranolol (10 mg/kg) injected either pre- or post- trial. Their memory was then assessed 48 h later (retention trial) by measuring their freezing response to the tone delivered in another context. Afterwards, their brains were processed for Golgi-Cox staining to visualize spine density in the amygdala. Results show that pre-reactivation injections of propranolol reduced freezing to the tone on the retention trial and decreased spine density in the amygdala. Conversely, propranolol administered post-trial was ineffective. These data suggest that focusing on structural changes occurring in neuronal circuits mediating fear memory should help in (i) describing the wiring properties of those circuits in situations of abnormally long-lasting fear like those generating PTSD and (ii) monitor the efficacy of PTSD treatments through the re-instatement of pre-trauma neuronal connectivity in key brain regions for aversive memory.

D11-61

MODULATION OF SPATIAL ATTENTION BY MEANS OF EMOTIONAL FACIAL AND BODILY EXPRESSIONS IN HEMISPATIAL NEGLECT PATIENTS AND HEALTHY SUBJECTS

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Previous studies showed that fearful and happy facial and bodily expressions may summon attention and overcome leftward bias in patients with hemispatial neglect (Tamietto et al., 2005, 2007; Vuilleumier et al., 2001, 2002). Here we tested the biologically-inspired hypothesis that faces are more effective than bodies in reducing neglect when presented in the near space, whereas bodily expressions are more effective when displayed in the far space. We studied 24 patients with hemispatial neglect consequent to right cerebral lesions (mean age: 67.5 ± 9.48 years; mean level of education: 7.62 ± 4.53 years), 19 with a prevailing deficit in the near space (NS) and 5 with deficit in the far space (FS). Besides, 20 healthy participants were enrolled (mean age: 63 ± 8.84; mean level of education: 9.5 ± 2.4 years). Fearful, happy and neutral facial or bodily expressions were used as lateral cues during a line bisection task. Lines could be placed either at a near (60 cm) or far (150 cm) distance from participants, who were asked to mark the line midpoint regardless of the presence or nature of the lateral cues. Moreover, global cognitive level, hemispatial neglect and overt recognition of emotional facial expressions were evaluated. A paired t-test showed, in the patients with NS neglect, a significant effect in reducing rightward bisection errors with both fearful and happy facial expressions in the near space, and with fearful and happy bodies in the far space. Conversely, in the patients showing FS neglect, the only significant reduction was observed for left-side fearful bodies shown in the far space. No significant effects of emotional cueing were found with regard to healthy participants. Emotional faces and bodies are both efficient in pre-attentively summon spatial attention. Our preliminary results suggest that faces seem especially informative when seen in the near space, whereas bodies are particularly effective in the far space.

D11-62

PROSPECTIVE DURATION JUDGEMENTS: THE ROLE OF THE ATTENTION AND SECONDARY TASKS

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It is known that concurrent secondary (non-temporal) executive tasks or attentionally salient stimuli shorten the reproduced durations. Attentional Gate Model (Block & Zakay, 2006) was theoretical background to interpret the results of our experiments. In four experiments, three duration lengths were used in multi-seconds scale which are 15-30 and 45 sec. Exp-1 was the control experiment and subjects were asked to reproduce an almost empty interval. Exp-2 was conducted to observe the role of the secondary temporal task and revealed decreased reproduced durations. Moreover, we intended to replicate the already known effect of executive tasks on time perception in remaining experiments with probably new duration lengths and with a new executive task that is Simon task. We found very clear shortened reproductions due to the Simon task. We can conclude that secondary temporal tasks as well can lead to decreased duration judgements, but executive tasks have a greater impact on time perception.

D11-63

DOPAMINERGIC INFLUENCE ON NOVELTY PROCESSING

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Evidence has suggested that mesocortical dopamine (DA) plays a role in the processing of novel stimuli (Duzel, Bunzeck, Guitart-Masip, & Duzel, 2010). However, this evidence is mainly correlational, and no study has systematically manipulated dopamine levels in order to assess its effect on novelty processing. In the current psychopharmacological study involving healthy volunteers dopamine level were manipulated by administering D1 and D2 receptor agonist Apomorphine. Twenty-six healthy participants with no history of psychopathology participated in the study. A counterbalanced within-subject (placebo controlled) design was used, in which participants performed a verbal learning task, once after administration of Apomorphine, and once after administration of a placebo. Apomorphine was subcutaneously administered using a dose of 0.005 mg/kg, immediately before testing. A pretreatment of domperidone (40 mg, at 0,5 hrs before Apomorphine), a D2 receptor antagonist, was given in order to reduce side effects of Apomorphine. In the verbal learning task, to-be-studied words were presented visually, either in a frequent black font (standard) or in an infrequent larger and coloured font (novel). Simultaneously, standard and novel sounds were presented in the background. Processing of novelty has been found to be reflected in enhanced N2 and P3 ERP components. We therefore assessed novelty-related activity by analysing the amplitude of the N2-P3 complex elicited by novel and familiar stimuli (presented in the visual and auditory modalities). We hypothesized that the increased levels of dopamine would affect the electrophysiological correlates of novelty processing. The data confirmed our predictions; the administration of Apomorphine changed the amplitude of the N2, P3a and P3b components, both for novel and standard stimuli, in the visual and auditory modality. These results provide further evidence for the involvement of dopamine in novelty processing.

-Duzel, E., Bunzeck, N., Guitart-Masip, M. and Duzel, S. (2010). Novelty-related motivation of anticipation and exploration by dopamine (NOMAD): implications for healthy aging. *Neurosci Biobehav Rev*, *34*(5), 660-669.

D11-64

BRAIN ACTIVITY IN PHONOLOGICAL AWARENESS TASKS - AN fMRI STUDY

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Phonological awareness refers to an individual's awareness of the phonological structure of spoken words and involves the detection of sounds at different levels of word structure, like syllables, phonemes and rimes. The neuroanatomy of phonological awareness is still not clearly established in existing literature studies. The aim of our study was to identify brain regions involved in phonological processing in healthy volunteers, using fMRI method. Five subjects (4 female, 1 male, aged from 50 to 65 years) participated in our block design study. Participants performed *two visual* and *two auditory* tasks. For each modality both experimental and control tasks were applied. The *visual task* required rime detection (experimental task) or stimulus detection (control task). The *auditory task* required identification of words that started with a given letter (experimental task) or detection of a rising/ falling tone (control task). Subjects' answers were given by pressing one of two buttons after each stimulus presentation (responses: YES or NO). The fMRI procedure (BOLD fMRI:10 min) was proceeded by imaging of brain structures (structural MRI: 16 min). Two contrasts were considered: visual experimental *vs.* visual control task or auditory experimental *vs.* auditory control task. Next, the conjunction analysis was used to map the common region activated in both *visual* and *auditory* experimental tasks, thus, to find the region involved in phonological processing, independently of the sensory modality. The preliminary results revealed the common region activated in both *visual* and *auditory* tasks. This region comprised BA 21 and BA 22 of the left hemisphere. These results indicate that phonological awareness is represented in the classical Wernicke's area involved in broad aspects of auditory comprehension.

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D11-65

SEX HORMONES MODULATE INTER- AND INTRA-HEMISPHERIC FUNCTIONAL CONNECTIVITY DURING COGNITIVE PROCESSING

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Functional cerebral asymmetries (FCAs) in women have been shown to vary with changing levels of sex hormones during the menstrual cycle. Previous studies have suggested that inter-hemispheric interaction forms a key component in generating FCAs and it has been shown behaviorally and by functional imaging that inter-hemispheric interaction changes during the menstrual cycle. We used functional MRI and an analysis of functional connectivity to examine the neural correlates of cyclic changes of interhemispheric inhibition, both for a left hemisphere dominant verbal and a right hemisphere dominant visuo-spatial task. Women were examined three times during the menstrual cycle, during the menstrual, follicular and luteal phases and behavioral data confirmed changes of hemispheric advantage during the menstrual cycle. For the verbal task, the connectivity analysis revealed a change of the inhibitory influence of left-hemispheric language areas on homotopic areas of the right hemisphere with a pronounced lateralization during the menstrual phase and a reduction of inhibition and FCAs during the luteal phase. For the visuo-spatial task, imaging data showed cycle phase-related changes in lateralized brain activation within the task-dominant hemisphere and changes in connectivity between nonhomotopic areas of both hemispheres, suggesting that changes in functional brain organization in women during the menstrual cycle are not only restricted to hormone-related changes of interhemispheric inhibition between homotopic areas, as has been proposed earlier, but might additionally apply to changes of neuronal processes within the hemispheres which seem to be modulated by heterotopic functional connectivity between hemispheres. These results reveal a powerful neuromodulatory action of sex hormones on the dynamics of functional brain organization in the female brain.

D11-66

NEURAL CORRELATES OF STIMULUS-SPECIFIC PREPARATORY PROCESSING

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Visual attention is controlled by top-down factors such as expectation, and bottom-up factors such as stimulus salience. We examined whether the response to an endogenous cue would recruit stimulus-specific areas needed to process the expected task. We used EEG and fMRI to identify neural correlates of perception of visual and spatial aspects of the same object, and of preparation to process specific features. Two coloured shapes were presented on the left and right with an instruction letter in the centre. Participants had to indicate whether the two stimuli were the same or different in terms of their angle of orientation (indicated by instruction letter A) or their colour (instruction letter C). Prior to the appearance of the stimuli, a cue appeared which either indicated which task was coming (valid condition) or was uninformative about the task (neutral condition). Precuneus, middle frontal gyrus, and posterior cingulate showed decreases in BOLD signal in the valid compared to the neutral condition during the colour task, but not the orientation task. Insula, lingual gyrus, and medial frontal gyrus showed decreases in BOLD signal in the valid compared to the neutral condition during the orientation task, but not the colour task. ERP analysis showed a contingent negative variation (CNV) over the vertex, which was larger in the valid compared to the neutral condition, and larger in the colour compared to the orientation condition. These results show that different brain regions are involved in preparing to process different features of the same stimulus. This preparatory processing seems to involve suppression of regions which are specialized for processing the task-irrelevant feature.

D11-67

PROGESTERONE-RELATED CHANGES IN LACTATE USING 3T MRS

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Background: The menstrual cycle has been implicated in the modulation of both neural structure (Hagerman et al, 2011; Peper et al, in press) and function (Halpern, 2000). Research demonstrates that the gonadal-hormone progesterone can effect essential neurotransmitters such as glutamate and GABA (Hausmann & Güntürkün, 2000), and is involved in various affective disorders (e.g. Andréen et al, 2009; Keisner, 2010). However, the underlying effect of progesterone on brain chemistry remains largely unknown. Magnetic resonance spectroscopy (MRS) has been useful in assessing the role of cerebral metabolites (e.g. glutamine, glutamate and lactate) in affective disorders such as bipolar disorder (Strakowski, DelBello & Adler, 2005; Yüksel & Öngür, 2010), and depression (Hasler et al, 2005). It is assumed that monitoring MRS signal may help elucidate underlying metabolic changes by which the gonadal-hormones affect neural structure and function. This will have significant implications on clinical research, particularly those that manifest themselves in a sex-specific manner. We hypothesise that progesterone is linked to cerebral metabolite concentrations in the menstrual cycle. We show here a link between progesterone and lactate (a metabolite linked to bipolar disorder (Dager et al, 2004)) but not between progesterone and glutamate and glutamine; metabolites highly implicated in affective disorders (e.g. Hasler et al, 2005) as well as having established links to progesterone (Andréen et al, 2009). Methods: 9 naturally menstruating women (18-30years) were tested twice; once during their mid-follicular phase (≈day 7) and once during their mid-luteal phase (≈day 21). Days associated with very low and high progesterone levels respectively. Saliva samples were taken on the day of testing and were assessed by radio-immuno-assay for progesterone levels. Short echo-time single-voxel MRS data (ROI: anterior intraparietal sulcus) was collected using a 3T Siemens scanner (PRESS; TE=30ms; TR=1500ms). Results: Paired t-tests revealed a significant difference in lactate (t(8),2.71,p=.03) which increased from low progesterone (0.55±0.19) to high progesterone (0.91±0.26). There was no significant difference in glutamine (p=.82) or glutamate levels (p=.25). Conclusion: Recently it has been shown the patients with bipolar disorder have elevated levels of lactate (Dager et al, 2004; Regenold et al, 2009), a similar increase in lactate over the female menstrual cycle warrants further investigation in combination with mood questionnaires. Understanding the effect of gonadal hormones is imperative if we are to fully understand the extent of sex-related differences in cognitive and clinical disorders. The present research suggests future MRS studies should control and account for the impact of gonadal-hormones.

D11-68

EFFECTS OF TASK COMPLEXITY ON HIGH-FREQUENCY AND LOW-FREQUENCY HEART RATE VARIABILITY AS INDICATORS OF MENTAL LOAD

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Heart rate variability (HRV), particularly the high-frequency-band (HF), has been found to be a stable indicator for mental load. In contrary, literature analysis reveals mixed results for the low-frequency-band (LF) of HRV. In this study we aimed to 1) replicate findings for HF-HRV in a complex control task with multiple attention foci and 2) further clarify the role of LF-HRV in mental load. Forty young, healthy, male participants (age between 20 and 34 years) participated in the experiment. Participants performed 60 minutes of a complex task using the software CAMS (Cabin Air Management System), a computer simulation of a spacecrafts supply system. After a baseline measure, we varied three levels of complexity by programming different system-faults, which were either practiced in a training session before (level 1), or just named but not practiced (level 2), or a complex combination of multiple faults (level 3). ECG was continuously measured during the experiment. As expected we found a main effect of task complexity on HF-HRV ($p<.01$). Post-hoc analyses showed a significant decrease of HF-HRV for level 3 and on trend level for levels 1 and 2 compared to the baseline. No effect was found for LF-HRV. Results confirm the applicability of HF-HRV as an indicator for mental load also for complex control tasks. No clear conclusion can be drawn for LF-HRV due to lacking test-power. More participants will be needed in future studies to clarify the role of LF-HRV in mental load situations.

D11-69

DIFFERENT STRATEGIES OF CHOICES IN THE RAT GAMBLING TASK REVEAL INDIVIDUAL PROFILES RELATED TO HUMAN PSYCHIATRIC DISORDERS

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Make advantageous decisions in complex, uncertain and conflicting situation of choice can be highly problematic in patients with psychiatric disorders such as attention deficit and hyperactivity disorder, substance abuse or obsessive-compulsive disorder. In the laboratory, such decision making impairments are detected in patients but also in a minority of healthy individuals using the Iowa Gambling Task (IGT). Based on the principle of this test, we have developed a decision-making task in rats (Rat Gambling Task, RGT) that assesses in one session their ability to choose under conditions of uncertainty and between several conflicting options that differ with respect to long term gain. Like in humans, some healthy rats are spontaneously making poor decisions in this task as they choose immediate gratification over long-term gain. Considering the existence of a continuum between normality and pathology, excessive or inadequate behaviors observed within a healthy population possibly model some of the key aspects of psychiatric conditions. Based on this concept we compared several behavioral functions related to psychiatric conditions, between good and poor decision-makers such as risk-taking (Dark light emergence test), reward hypersensitivity (Progressive Ratio schedule), cognitive inflexibility (RGT-reversal procedure) and different aspects of impulsivity (Delay discounting task, Fixed Consecutive Number of lever presses, Fixed interval-extinction schedule task). We found that all of these behaviors except some aspects of impulsivity were associated with poor decision making while good performers never expressed more than two of such characteristics. Poor decision making rats present a combination of behavioural traits similar to those observed in decision making related psychiatric disorders in clinic. Complementary studies are currently conducted for understanding the neuronal and emotional mechanisms underlying this specific behavioral profile as it could represent an intermediate phenotype of mental disorder.

D11-70

IMPAIRED DECISION-MAKING PROCESS IN PATIENTS WITH CUSHING'S SYNDROME AS ASSESSED BY THE IOWA GAMBLING TASK

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Context and Objective: Cushing's syndrome (CS) is a rare disease due to endogenous glucocorticoid (GC) excess. This hypercortisolism has been associated with deficits in cognitive function, especially memory and attention impairments. It has been recently shown that CS patients display different and less effective coping strategies compared with healthy controls. It is known that prefrontal cortex has glucocorticoid receptors. Since GC excess in CS affects all frontal functions our aim was to evaluate decision-making function in CS, by using Iowa Gambling Task. Subjects and methods: Thirty-three patients with cured CS (6 males), 11 patients with active CS (2 males) and 33 healthy controls (6 males) were evaluated by Iowa Gambling Task. The test challenge consisted of four card groups having different profile of money wins and losses (two safer card deck groups and two riskier card deck groups). Patients were asked to choose the options to win more money. An increase in both the amount of lost money and the number of riskier cards reflect a poorer decision-making function. Results: Active CS were slower than controls to complete the test ($p<0.05$). Cured CS showed more difficulties than controls to learn the correct profile of wins and losses for each card deck group ($p<0.01$). No difference between active and cured was observed. In general, both active and cured patients presented an impaired decision-making process compared with controls, as reflected by higher number of riskier cards ($p<0.05$) and smaller amount of gained money ($p<0.02$). In addition, CS patients presented more depressive symptoms ($p<0.001$) and more anxiety symptoms ($p<0.001$) than healthy controls. Conclusions: We have demonstrated, for the first time that endogenous glucocorticiod excess is associated with altered risk decision-making. CS patients failed to learn advantageous strategy and their behaviour was only driven by short-term reward, in according with a possible negative impact of GC excess on prefrontal cortex.
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D11-71

CORTICAL DYNAMICS DURING CNV AND GAP. WHAT PREDICTS THE RESPONSE TIMES?

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Response times (RT) in the execution of motor tasks are variable and depend on attention and motor preparation. In two-stimulus paradigms, in which the first stimulus cues a second stimulus which occurs after a predictable time interval, RT have been associated with a fronto-central cortical negativity known as contingent negative variation (CNV). In these tasks the disappearance of the cue before the imperative stimulus (GAP), induces a shortening of RT. Here we studied cortical potentials during this type of paradigm in oculomotor tasks, establishing relationships between cortical dynamics during the CNV and GAP periods and the RT. Eye movements were recorded by video-oculography and cortical activity by 64 EEG electrodes in 21 healthy subjects during a three-block of mixed visuomotor tasks. Subjects seated in front of a display monitor, fixed their gaze on a central color point for a random period from 1900 to 2500 ms. At the end of this period, the color point disappeared for 370 ms and a black peripheral dot appeared 8 degrees left or right at random. The color of the central point (green, red or yellow) indicated the type of task (prosaccadic, antisaccadic and no-go) in each trial. During the cue period, a CNV developed which amplitude was larger during antisaccades, somewhat less during prosaccades and even less during no-go. Trial to trial, both the amplitude and the slope of the CNV correlated linearly with RT during prosaccades and antisaccades, although the latter relationship tended to saturate. The negativity achieved by the CNV increased sharply during the GAP and seemed to follow a relationship similar to the CNV in the three tasks. However, when the negativity of the GAP was corrected by the slope of the CNV in each trial, the GAP amplitude showed an inverse correlation with RT and CNV. These results indicate that the CNV corresponds, in tasks of this length, with a motor preparation whose slope predicts RT. By contrast, the GAP seems to induce a cortical synchronization that shortens RT but its amplitude depends on the previous CNV and is unrelated to RT.

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D11-72

HUMAN NAVIGATION IN DISSOCIATED REFERENCE FRAMES

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When moving in an environment, a remembered spatial representation of this environment enables us to plan how to reach invisible goals. Movement can dissociate two such representations, e.g. rotation in a carousel. This dissociation creates two frames of reference – the stable one and the moving one. People are usually oriented in both frames of reference, but can either be oriented in both of these frames of reference at the same time or we can be continuously switching between them and in one moment in time be oriented only in one of them. To answer this question in human, we developed a new virtual reality test of spatial navigation performed in a square room. The task of the subject is to navigate in a given order to four places (goals) hidden on a slowly rotating circular arena. Two of these places are rotating with the arena, while other two places are stable in the room. The subject navigates alternately to the visible goal in centre of the circular arena and to one of the hidden goals. To which hidden goal the subject should navigate depends on a notice with the name of the goal and shown on the screen each time after reaching the centre of the arena. Before reaching the arena centre, the subject does not know which goal to navigate. Test consists of four phases, during which the subject learns positions of the two places rotating with the arena, two places stable in the room and then navigates alternately to all four places. In the last phase of the test, before navigating from the arena centre to one of the four hidden goal places, the subject should point with a cross in the centre of the screen on the momentary putative goal position. Results show that the time to point to a hidden goal is strongly influenced by the previous hidden goal: if the previous goal was defined in the same reference frame (stable or rotating) as the current one, the time to point is significantly shorter than if the previous goal was defined in the other reference frame. This difference suggests that we are not oriented in both reference frames at the same time, but need some time to switch from one reference frame to another.

D11-73

IMPAIRED REARRANGEMENT OF THE ALLOCENTRIC AND EGOCENTRIC SPATIAL REPRESENTATION IN PATIENT WITH THE PARIETAL, TEMPORAL AND OCCIPITAL BRAIN LESION

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Mental operation, such is a rearrangement of a spatial representation, is a basic precondition for a successful navigation. In real environments, process of rearrangement of the spatial representation includes mental rotation (MR) of a set of a relevant orientation cues in 3D space. MR was extensivelly studied in many neuropsychological paradigms, but only few of them used as a substrate for MR 3D environment. Two types of representation of space have been distinguished: egocentric which is dependent on the subject position and uses representation of the space relative to the subject's body. Allocentric representation is independent of the position of the subject and uses a representation of the space in the form of a map containing important landmarks. Despite of well knowledge of the participating brain structures, which are consistently activated in various mental rotation tasks, comprehension of universal mechanism is still unclear (for review see Zacks, 2008). We describe a case of right-handed patient PB with an acute focal brain lesion due to an ischemia in 1 - left inferior parietal lobule and 2- left posterior temporal and 3- anterior occipital lobe. The patient exhibited executive impairment, dysfasia (and consecutive impairment in verbal memory test) and slight visuo-spatial impairment. Patient was repeatedly tested in a simple and rotate versions of cued navigation test(CNT) –landmark was near a goal position, egocentric navigation test(ENT) – goal position was determined by means of starting position, and allocentric navigation test (ANT) – goal position was distant from the landmark. All tests were designed in spatial experimental room environment and also in 2D image computer environment. P.B. has been showed a severe impairment in both allocentric and egocentric version of the tasks, where the goal and landmark location changed (rotated) after each trial. Inspite of severe impairment of the rearrangement of both the ego- and allocentric representations, the ability of mental rotation test (e.g. when subject solved mental rotation with snapshot from the virtual arena) were unimpaired. Supported by GACR grants 309/05/0693 and 309/06/1231, MSMT CR 1M0517 and research project AV0Z50110509.

-Zacks JM.(2008) Neuroimaging studies of mental rotation: a meta-analysis and review. J Cogn Neurosci.,20(1):1-19. Review.

D11-74

SPECIFIC DEFICIT IN COGNITIVE COORDINATION AFTER SYSTEMIC INJECTION OF DIZOCILPINE (MK-801): SUPPORT FOR PHENOMENOLOGICAL VALIDITY OF A PHARMACOLOGICAL ANIMAL MODEL OF COGNITIVE SYMPTOMS IN SCHIZOPHRENIA

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Animal spatial behavior is used to model human cognitive functions such as learning and memory. Systemic administration of non-competitive NMDA receptor antagonists is used to model symptoms of schizophrenia in animals and humans. One of these antagonists, dizocilpine (MK-801), disrupts place avoidance on a rotating arena (Carousel Maze), where rats foraging on a continuously rotating circular arena avoid an unmarked place defined in stable room coordinates. To avoid successfully, animals have to distinguish room and arena stimuli and selectively use the former. This hippocampus-dependent ability called segregation facilitates behavior by organizing information into coherent subsets. Is MK-801-induced Carousel Maze deficit due to impaired segregation? We manipulated the need for segregation of spatial stimuli. Young (~3months) male Long-Evans rats from the Institute's breeding colony were food-restricted and trained to forage on a smooth metallic arena (82cm). Then they were trained to avoid a room-defined place (3 sessions), punishing each entrance by a mild foot-shock. The arena was stable or rotated 1rpm and a 5cm lip could hold shallow (<1cm) water. Rats received saline or MK-801 (0.15mg/kg i.p.) 30min before the session. The number of entrances and the distance traversed during each 20min session measured avoidance. Contribution of altered locomotion to the avoidance deficit was examined using distance/entrance ratio. MK-801 disrupted segregation of room and arena stimuli. It impaired avoidance on a rotating arena, where the need for segregation was high, but not on a stable arena, where it was low. The deficit was milder when water compromised arena cues and attenuated need for segregation. The Carousel Maze represents an animal model of cognitive abilities possibly impaired in schizophrenia. Supported by GACR grants P303/10/191 and 309/09/0286, and MSMT center 1M0517. All procedures were approved by local animal care committee and conformed to the Czech Animal Protection Code, EU directive 86/609/EEC, and NIH guidelines.

D11-75

EFFECT OF BODY RATIO ON SEXUAL ATTRACTIVENESS IN MALES AND FEMALES

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Investigations on the processing of whole bodies or body parts, (as well as body motions, or body expressions) have shown that human bodies can be processed at a very early visual stage, as reflected by the N190 component in surface EEG recordings and the N260 component in intracranial EEG recordings in the lateral occipital temporal lobe and the posterior fusiform gyrus. By contrast, only few behavioural investigations have studied how the secondary sexual variations in shape (e.g., in terms of waist-to-hip ratios (WHR) and waist-to-shoulder (WSR) ratios) affect processing. One hypothesis is that these factors influence attractiveness, probably because they convey information about reproductive/genetic potential. We performed two distinct behavioral (rating) and ERP studies on a group of right handed heterosexual healthy participants (50% men) while they viewed female models with four different WHRs (0.6, 0.7, 0.8 and 0.9), and male models with four different WSRs (0.5, 0.6, 0.7 and 0.8). In the behavioral experiments participants had to rate the attractiveness of 192 pictures of women and 96 pictures of men. In the EEG experiments (go, no-go task) subjects were presented with stimuli comprising female or male bodies as well as distracter targets (pseudo-animals), to which they were asked to respond manually. Behavioral results showed preferred WHRs of 0.7 and 0.6 for men and women and furthermore naked bodies were judged more sexually attractive than dressed ones. A different trend of WSR preferences was found between male and female views. Taken together our results substantiate the hypothesis that WHR and WSR are measures of physical attractiveness. EEG results showed that naked bodies elicited a greater negativity (N190) than dressed ones over occipital-temporal sites. The occipital P1 (135 ms) was sensitive to different WHRs but not to WSRs, showing a different pattern of activation between male and female groups when they viewed the opposite gender. Our ERP data are in agreement with the view that the N190 is sensitive to whole body shapes while the P1 appears to respond mainly to other, biologically-.relevant features, such as WHRs, also indicating a very rapid processing of these secondary sexual traits in the perception of female and male bodies.

D11-76

CHIMPANZEES AND GORILLAS VARY THEIR PREFERENTIAL USE OF HANDS BASED ON TARGET ANIMACY

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The most prominent manifestation of human cerebral asymmetry is right-handedness, which is widespread in the 90% of the population. The right-handed manual bias appears to be highly correlated (95%) with dominant left hemisphere regions for language function. Recent findings of hand preference in non-human primates are beginning to challenge the view that handedness is a unique hallmark characteristic of humans. Additionally, comparative human and ape studies have demonstrated that we share much of the neural architecture underlying speech perception and some of the mechanisms humans use to learn language. Nevertheless, the causal link between human right-handedness and language skills is still poorly understood. One current theory argues that the brain areas implicated in human language functions may have built upon already existing tool-use and manufacture areas in the left hemisphere of a common human/ape ancestor. The theory refers mainly on the basic common organization underlying both areas, which relay on structured order processing of events that imply a goal (e.g. a simple syntax). Additionally, the right hemisphere has been claimed to be involved during emotional processes which may contribute disproportionately to manual actions that involve emotive stimuli (e.g. social partners) versus those that do not (e.g. inanimate objects). For this study we collected information about lateralized spontaneous manual activities of 9 chimpanzees, hosted at Parco Natura Viva (Bussolengo, Italy), and 12 western lowland gorillas, hosted at Port Lympne Park (Kent, U.K.), using a continuous 10-minute focal animal sampling method. In particular, we distinguished the target of the manual action as inanimate (not living things) and animate (social partners and the self) and unimanual actions as left or right. A 2x2 ANOVA revealed significant differences in hand preference based on target animacy ($p = 0.012$) and a post-hoc t-test demonstrated that right-handed manual actions were only dominant for actions towards inanimate objects ($p = 0.010$). Our findings suggest a hemispheric specialization for categorical meaning in great apes linked to animacy, where the left hemisphere plays a dominant role in processing order-structure actions (e.g. tool-use and food preparation) and the right hemisphere contributes proportionately during emotive actions to animate targets.

D11-77

ANTIDEPRESSANT TREATMENT IMPROVES COGNITIVE FUNCTION IN THE R6/2 MOUSE MODEL OF HUNTINGTON'S DISEASE

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Cognitive dysfunction represents a core deficit in Huntington's disease (HD), and a number of studies illustrate how cognitive deficits may strongly influence the clinical presentation and daily functioning of people with this illness. Despite this, cognitive dysfunction shows only modest improvement with currently available therapies. Furthermore, HD has been shown to have a high comorbidity with depression and relieving its symptoms in someone with HD may be the single most effective intervention available. Here we examined the cognitive enhancing abilities of two available antidepressants; rolipram and agomelatine. A number of studies have shown that chronic treatment with rolipram, a phosphodiesterase type IV inhibitor that increases CREB phosphorylation, has been shown to improve the motor phenotype, inhibit the sequestration of CREB-binding protein into intranuclear inclusions and improve survival in the R6/2 mouse model of HD. However, the effects of rolipram treatment on the cognitive abnormalities expressed by R6/2 mice have not been investigated. Agomelatine is a melatonergic agonist (MT1 and MT2 receptors) and 5-HT2C antagonist which acts as an anitidepressant; one which has not been studied in R6/2 mice. We sought to determine whether or not chronic treatment with either rolipram or agomelatine had beneficial effects on acquisition and reversal learning in a 2-choice swim tank. R6/2 mice were given either 1.5mg/kg rolipram or 50mg/kg agomelatine daily, with treatment starting at 7 weeks of age, 3 weeks before commencement of testing in the 2-choice swim tank. While there were subtle genotype differences during acquisition and retention testing, there was no effect of either drug. However, both rolipram- and agomelatine-treated R6/2 mice performed significantly better than their corresponding vehicle groups during reversal testing, where genotype-dependent deficits were more profound. It is interesting that both drugs resulted in a similar improvement in cognition. This raises the possibility that these agents mediate their beneficial effects on cognition in R6/2 mice via a common mechanism involving noradrenaline. Antagonism of 5-HT_{2C} receptors by agomelatine results in an increase of dopamine and noradrenaline activity in the frontal cortex while rolipram causes an increased release of noradrenaline due to a cAMP-mediated stimulation of tyrosine hydroxylase. Our findings show that the cognitive enhancing properties of antidepressants should be considered as valid therapeutic approaches for treating cognitive abnormalities in addition to depressive symptoms in HD.

D11-78

TOPOLOGICAL ORGANIZATION OF STRUCTURAL AND FUNCTIONAL CORTICAL NETWORKS

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The repertoire of complex behaviors in higher mammals has evolved linearly with the development of highly specialized anatomo-functional cortical networks. Therefore, determining how cortical organization underlies cognition is critical in contemporary neuroscience. Evidence suggests that cortical regions are densely interconnected with nearby areas to facilitate information exchange, whereas a drastically lower density of long-range connections are required to integrate information previously processed in specialized areas. This study represents a preliminary effort to understand how structural and functional cortical networks specifically contribute to this biological organization by studying their efficiency and robustness. To aim this goal, we employed structural MRI and FDG-PET images acquired in 30 cognitively intact elders. By using an optimal parcellation of the cortical mantle, we established connectivity patterns considering significant partial correlations between cortical thickness values (structural connectivity) and glucose consumption (functional connectivity). Criteria for determining local and long-range connectivity maps were purely anatomical: local (U-fibres, shorter than 30 mm) and long-distant connections (fibres larger than 30 mm) were separated to study their effects on network efficiency. Network robustness was determined by removing regions (simulating a cortical lesion) showing a high number of local or global connections (cortical hubs). Our approach revealed that visual areas exhibit dense functional connections with surrounding regions, whereas association areas, as the cingulated cortex, were predominantly connected with distant regions at a functional level. Integration of distant information was similarly performed by functional and structural networks, but the latter was more efficient in transmitting information locally. Structural connectivity patterns appeared to be more robust to local and global attacks when compared to those derived from functional networks. Taking together, our results suggest that the anatomical organization of the cortical mantle provides better topological properties, in terms of efficiency and robustness, than the functional network. Further research is clearly needed to better understand the emergence of anatomo-functional properties by integrating the excellence of both networks.

D11-79

ACTION MONITORING: CORRECT AND ERRONEOUS DECISIONS ARE REFLECTED IN EVENT RELATED POTENTIALS IN HUMANS

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An important function of the human brain is to adapt behavioral actions based on both correct and erroneous decisions. Event related potentials (ERP) have been revealed to be a powerful tool for studying performance monitoring associated with correct and erroneous outcomes. Two ERP components associated with errors have been described, but their functional meaning remains unclear. The first ERP component associated with errors is called error-related negativity (ERN) or error negativity (Ne) and peaks about 80-100 ms after human subjects make errors in a reaction time task. The second component, called error positivity (Pe), is a slow positive wave that peaks about 200-450 ms after an incorrect response, which usually follows the ERN. The ERN/Ne can be elicited following presentation of error feedback and it is called feedback-related negativity (FRN). FRN is a front-central negative deflection that occurs at approximately 250-350 ms after the negative feedback stimuli. The main objective of this study is to understand the functional meaning of error-related ERPs. Electroencephalography (EEG) was recorded from 60 standard channels while participants (N=12, 8 females, 4 males, aged 22.63 years) performed in a visual discrimination reaction-time task. Trial-by-trial analysis confirmed previous findings about significant differences between correct and incorrect trials after receiving feedback reflected on FRN. Moreover, we have found a positive deflection that appears about 450 ms after the feedback onset (feedback related positivity, FRP) whose amplitude is significantly greater after incorrect trials in comparison with correct trials. Furthermore, the difficulty of the discrimination affects the FRN and FRP components in different ways: the latency of FRN is significantly shorter for easy than for difficult discriminations whereas the amplitude of FRP is higher for easier than for difficult discriminations. These results suggest that the FRN and FRP components are related to performance monitoring but reflect different cognitive processes. We propose that the FRN could be related to an automatic error detection system that is faster when the errors are more evident (i.e., in the easy trials). This system would be responsible for fast behavioral corrections. On the other hand, FRP could reflect conscious evaluation of the previous decision process; this evaluation would be related to long-term changes in the decision process and could be useful for improving future decisions.

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D11-80

PERSONALITY AND REWARD BIAS LINKED TO INDIVIDUAL'S CONNECTIVITY PROFILES WITHIN THE MESOLIMBIC REWARD SYSTEM

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Introduction: We noticed marked inter-individual differences in seeking and avoiding reward outcomes in the Frank 'Carrot & Stick' task (Frank et al. 2004). We adapted the Frank probabilistic learning paradigm to acquire a Reward Bias Coefficient (RBc) which measures the strength of bias for seeking positive outcomes or avoiding negative outcomes during the learning process. We hypothesized RBc would predict the levels of functional connectivity between regions mediating normal reward learning. The ventro-medial-pre-frontal-cortex (VMPFC) and the striatum are both regions shown to be implicated in compulsive gambling behaviour, a dysfunction of the reward learning system (Reuter et al. 2005). The striatum is known to encode prediction error (Schultz et al. 1997), as described by the Rescorla-Wagner formal theory of learning (Rescorla & Wagner 1972). Weight and error as predicted by individual response history are therefore incorporated into the experimental design. Method: Behavioural data showed a strong negative correlation between RBc and Neuroticism (Pearson's $R = -0.44$, $P < 0.01$, $n=41$) and strong positive correlation between RBc and Extroversion in males (Pearson's R = 0.45, P < 0.01, n=38). Eighteen participants also undertook the experiment during functional magnetic resonance brain image acquisition. Normal reward related activation networks were identified utilizing a 'win > lose' contrast of the reward feedback component of the task (P < 0.001, uncorrected). Areas of increased BOLD response in VMPFC (*xyz = -4 36 -10*) and the posterior ventral striatum (PVS, *xyz = -10 7 -5*) were used as seed loci for connectivity analysis using a psychophysio-interaction approach. Results: Connectivity between VMPFC and striatum increased with increasing positive RBc and decreased with increasing negative RBc (P < 0.05, FDR & SVC). Therefore, RBc predicts connectivity between dopamine dependent components of the reward system. The analysis suggests that VMPFC-caudate connectivity is linked with the 'strength of association' parameters in Rescorla-Wagners formal theory of learning. Conclusion: RBc appears to be a useful behavioural metric which correlates both with neural connectivity profiles within the dopaminergic mesolimbic system and aspects of personality.

-Frank, M. J. et al. (2004). *Science 306*(5703): 1940-3.
-Rescorla, R. A. and Wagner, A. R. (1972). In: *Classical Conditioning* II.(A. H. Black and W. F. Prokasy). New York.
-Reuter, J. *et al.* (2005). *Nat Neurosci 8*(2): 147-8.

D11-81

REPRESENTATION OF TACTILE BODY SPACE IN SPATIAL NEGLECT: COMPRESSION AND ANISOMETRY

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Background - There is increasing evidence that space perception is distorted in unilateral neglect. The representation of object space was shown to be anisometric, the grain becoming coarser and coarser from right to left. The projection of body space in front space appeared shifted toward the ipsilesional side and possibly reduced in width. Here, the representation of body itself was directly investigated by means of a tactile localization task. The errors were analyzed using the method of independent contrasts in order to test both the compression and the anisometry hypotheses. Method - Thirteen healthy controls and fifteen patients who suffered a right hemisphere lesion were included. Nine patients neglected left space according to classical paper and pencil tests, and six did not. All the participants were right-handed and signed an informed consent. Five points were drawn in each of four areas of the trunk skin: at navel and shoulder heights, on front and back sides. For each area the points were horizontally aligned and placed at -40% and -20% (left), 0% (centre), +20% and +40% (right)of the body width. Each area was tested separately and there were six trials per point (random order). In each trial, the participant had to localize the touched point (verbal response). He/she was helped by a mannequin where eleven points were drawn (-50% to +50%, with 10% intervals) and labelled in order to avoid any mix-up. Results - Constant (CE) and variable errors (VE) were greater in the patients and even greater in the neglect group. In the latter only, the pattern of CEs fitted both the compression (linear contrast, $p < 0.001$) and the anisometry (quadratic contrast, $p < 0.001$) hypotheses. The pattern of VEs also varied according to the group ($p = 0.021$): VE was much lesser for the central point in healthy controls and non-neglect patients, but not in the neglect group. Conclusions - Body representation appeared profoundly affected by unilateral neglect. Beyond the lateral shift previously reported, the data of the present study suggest a reduction of body width and an anisometric impairment of the grain of body space. These changes appear consistent with the deficits that neglect patients show in neuropsychological tests and daily activities.

D11-82

RIGHT CORTEX CEREBELLUM VOLUME LOSS IN CUSHING'S SYNDROME

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Introduction: Cushing's syndrome (CS) is caused by an excess of circulating cortisol. Cognitive decline, mainly related to memory and frontal functions have been described in these patients. Cerebellar atrophy has been suggested, without a correlation with neuropsychological tests. Cerebellum has classically been related to motor control, but more recently it has also been linked to executive functions, visuospacial abilities, fluency and emotional processing.
Aim: Evaluate cerebellar volumes in CS patients, by using 3tesla Magnetic Resonance imaging (3T MRI) and correlate them with neuropsychological tests. Patients and methods: 16 active CS (2males), 26 cured CS after surgery (4 males), 26 healthy controls (6 males) were studied. Frontal functions (WCST, TOL, CPT-II, Digit Span, TMTB, Animals, FAS), visuospatial functions (Block design, Object Assambly), motor function (Grooved Pegboard, TMTA), language (Boston), information processing speed (SDMT), depression (BDI) and anxiety (STAI) have been evaluated. Cerebellar volumes (left cerebellar cortex (LCC), right cerebellar cortex (RCC), left cerebellar white matter (LCWM) and right cerebellar white matter (RCWM)) were calculated using FreeSurfer software.
Results: The RCC was reduced in active hypercortisolism compared to healthy controls ($p=0.019$), while a trend was observed for the LCC ($p=0.051$). RCWM, LCWM and all neuropsychological tests did not differ between groups. BDI in both active and cured CS patients scored higher, indicating more depressive symptoms than in healthy controls ($p\leq0.001$). Both RCC and LCC correlated with frontal functions (WCST, TOL, Digits Forward, TMTB; $p<0.05$), Motor function (Grooved Pegboard, dominant hand; $p<0.05$) and Information processing speed (SDMT; $p<0.05$). RCC also correlated with another frontal test (Animals; $p<0.05$) and BDI ($p<0.05$), while LCC also correlated with Visuospatial functions (Block design; $p<0.05$).
Conclusion: The reduced right cerebellar cortex may be related to the subclinical depression in active CS patients. Moreover, cerebellar cortex is correlated with frontal functions, visomotor speed and depressive symptoms.

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D11-83

LANGUAGE ABILITY IN HEALTHY AND EPILEPSY PARTICIPANTS: AN fMRI INVESTIGATION

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High language ability in healthy participants has been linked in our previous work to increased activation in the right inferior frontal gyrus (IFG), left middle temporal gyrus (MTG) and right posterior temporal lobe. In this study, we investigated whether similar neural distinctions between high and low language ability emerge in 23 epilepsy participants and 23 healthy controls. Individual linguistic performance was measured with the FAS word fluency test and a test battery to measure complex language skills (BeSS). Brain activation was measured with functional magnetic resonance imaging (fMRI) with a word fluency paradigm (WORD) and a sentence reading paradigm (SEN). The fMRI paradigms manipulated effort, through varying the dictionary frequency of the cue letter in WORD (low versus high) and the difficulty of sentences in SEN (correct versus incorrect). This resulted in two between-group conditions (epilepsy/healthy and linguistic ability scores) and one within-group condition (effort level). WORD elicited activation in left IFG, cingulate gyrus and supplementary motor cortex. SEN elicited activation in left IFG, Wernicke's area, BA 46, fusiform and lingual gyrus. Comparing healthy participants to the epilepsy group, a trend was observed of increased activation for epilepsy participants in the left BA 39 (SEN) and left insula and supramarginal gyrus (WORD). Including the FAS performance scores in a multiple regression analysis of the WORD paradigm, a trend towards increased activation in left BA 39 or angular gyrus was seen in high ability healthy participants. Increased activation was observed in Wernicke's area and the left lingual and fusiform gyrus in high ability epilepsy participants. When BeSS was entered as a regressor in the SEN analysis; high ability epilepsy participants showed a trend for increased activation in Wernicke's area (left MTG) and the right IFG. The within-group effort condition (hard > easy sentences) resulted in increased bilateral activation in BA 46 for all participants. Our preliminary results replicate our previous findings of right-hemispheric IFG, Wernicke's area and dorsolateral prefrontal cortex (DLPFC) activity related to increased language ability. Bilateral BA 46 in the DLPFC (an attentional center important for response selections) shows increased activation when participants are confronted with more difficult sentences.

D11-84

EARLY ERP MODULATION PRODUCED BY ATTENTION SHIFTING TOWARDS TASK-IRRELEVANT EMOTIONAL FACES

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ERP studies investigating the Posner paradigm have shown that spatial re-orientation of attention is associated with modulations notably on the P1 and N1 components. In recent years, it has also been suggested that emotional faces are powerful attracters of attention, although this has been disputed. In this ERP study, we used an endogenous cueing paradigm in which subjects were asked to respond to the onset of task-irrelevant emotional faces. We hypothesised that RTs would be faster for emotional faces and that this would be associated with modulations of early ERP components. Leftward or rightward pointing arrows were presented at the centre of a computer screen, followed by a target face (fearful, happy, neutral or scrambled faces from the Ekman series) in a valid (80%) or invalid location (20%). Participants (n=14) were asked to respond with a single button-press, irrespectively of the type of stimulus (total number of trials N=1400). A 64-channel EEG recording was performed and average-referenced ERPs, time-locked to the target, were then computed for each condition. The peak P1 and N1 amplitudes were then computed and compared across conditions using standard ANOVAs for repeated measures. Reaction times (RTs) were significantly faster for validly-cued locations. Importantly, in the invalid trials, RTs were significantly shorter ($p<.01$) for real faces than scrambled ones, and for emotional faces than neutral ones. P1 amplitudes were significantly smaller for invalidly-cued stimuli ($p>.00001$). For valid targets, no differences in P1 appeared across categories, while for invalid targets, P1 differed significantly across categories with largest amplitudes for scrambled faces, followed by happy, then neutral and fearful faces. The N170 was also significantly less negative for invalid than valid faces ($p<.01$), also differing across emotional faces. Finally, scrambled faces produced a smaller N1 response which did not differ between valid and invalid trials. In line with our hypothesis, emotional faces attracted attention more efficiently, producing shorter RTs in the invalid trials, an effect that was mirrored by modulation in P1 amplitudes across stimulus categories for the invalidly-cued locations alone. These findings confirm that emotional faces impinge on spatial attention at an early period in time by modulating extrastriate visual areas. This most likely leads to an improved detectability of behaviourally-relevant stimuli when they appear at unattended locations.

D11-65

OPPOSING EFFECTS OF 5,7-DHT LESIONS TO THE CORE AND SHELL OF THE NUCLEUS ACCUMBENS ON THE PROCESSING OF IRRELEVANT STIMULI

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There is good evidence that forebrain serotonergic systems modulate cognitive flexibility. Latent inhibition (LI) is a cross species phenomenon which manifests as poor conditioning to a stimulus that has previously been experienced without consequence and is widely considered an index of the ability to ignore irrelevant stimuli. While much research has focused on dopaminergic mechanisms underlying LI, there is equally good evidence of serotonergic modulation. However, the anatomical locus of these effects remains poorly understood. Previous work has identified the nucleus accumbens (NAc) as a key component of the neural circuitry underpinning LI and furthermore this work has shown that the core and shell sub-regions of the NAc contribute differentially to the expression of LI. To examine the role of the serotonergic input to NAc in LI, we tested animals with 5,7-dihydroxytryptamine (5,7-DHT) lesions to the core and shell sub-regions NAc on LI in two experiments. In Experiment 1, the effects of these 5,7-DHT lesions were assessed under experimental conditions which produced LI in shams. Then in Experiment 2, lesion effects on LI were further examined using a procedural manipulation - reduced number of stimulus pre-exposures - designed to prevent the emergence of LI in shams. The 5,7-DHT lesions to the medial shell were anatomically highly selective in that they produced significant 5-HT depletions within the shell (-65.5%) but only minimal changes in the adjacent core (+13%). The core lesion depleted core 5-HT (-76.0%) but also resulted in significant 5-HT loss in the shell sample (-33.4%). In Experiment 1, serotonergic deafferentation of the core(+shell) disrupted LI whist the LI effect was clearly demonstrated in the sham and shell-lesioned groups. In Experiment 2, in which (as expected) the reduced number of stimulus pre-exposures successfully precluded LI in the shams, the shell lesion potentiated LI. The dissociation in function between the core and shell (in disrupting and potentiating LI) is diametrically opposed to that which is found with electrolytic and excitotoxic lesions. The overall pattern of findings underscores the importance of neuromodulation within key brain structures. Moreover, the present neuropsychopharmacological data complement emerging evidence for the modulation of cognitive flexibility by forebrain serotonergic systems.

D11-86

DEPRESSIVE-LIKE BEHAVIOUR INDUCED BY CHRONIC STRESS IN CB1 KNOCKOUT MICE: A PET STUDY WITH [11C]-DASB

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Chronic stress represents a risk factor for anxiety and depression and the neurobiological mechanisms underlying these psychiatric disorders may involve gene expression alterations. Serotonergic and endocannabinoid systems are important substrates for the control of emotional behaviour. The serotonin transporter (5-HTT) plays a critical role in the regulation of serotonin neurotransmission and has been implicated in the pathophysiology of major depression. On the other hand, the lack of CB1 receptor produces an anxiety and depressive-like phenotype in mice. In the present study, CB1 knockout (KO) and WT mice were exposed to chronic restraint stress for a long period. Chronic stress produced depressive-like symptoms, such as anhedonia and learned helpless, as well as short-term memory impairment in a novel object recognition task in both genotypes. Under basal conditions, KO mice also presented depressive-like behaviour and a better memory performance than WT non-stressed mice. In addition, brain levels of serotonin transporter (5-HTT) were assessed by using the selective 5-HTT ligand, [11C]-DASB for PET study. A decrease in brain 5-HTT has revealed in KO and WT mice only after chronic stress. No changes between genotypes were revealed in brain 5-HTT levels in basal conditions. In conclusion, our results show that chronic restraint stress induced depressive-like behavioural alterations and brain changes in the levels of 5-HTT. These results underline the relevance of chronic environmental stress on serotonergic transmission in development of major depression.

D11-87

EFFECT OF HIGH DOSES OF METHYLXANTHINES ON MOTOR PARAMETERS AND ANXIETY: IMPLICATIONS FOR THEIR THERAPEUTICAL EFFECT ON BRADYKINESIA INDUCED BY DOPAMINE ANTAGONISTS

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Caffeine and theophylline are methylxanthines that act as nonselective adenosine antagonists. Adenosine receptors in the central nervous system are mainly of the A_1 and A_{2A} subtype, and are colocalized with dopamine (DA) receptors in the caudate/putamen and nucleus accumbens, thus regulating aspects of motivation and motor control. Methylxanthines have been shown to improve psychomotor slowing induced by DA antagonism in animal models. In rats and mice, caffeine and theophylline attenuate the suppression of locomotion induced by D1 and D2 antagonists. However, exposure to high levels of caffeine can produce anxiogenic effects and motor impairments, which could limit the therapeutic utility of adenosine antagonists. In this regard, the effects of theophylline are less well characterized. In the present work we evaluated the impact of high doses of acute (intraperitoneal, IP) and chronic (oral) caffeine and theophylline on measures of locomotion (open field, running wheel (RW), and rotarod) and anxiety and stress parameters (elevated plus maze, dark and light paradigms and blood corticosterone levels) in CD1 mice. Chronic caffeine and theophylline (0.3 g/l) consumption for 60 days did not change motor activity in the RW. Acutely, theophylline increased locomotion at 50 mg/kg, while caffeine at 100 mg/kg reduced locomotion compared to control. The RW generates high levels of spontaneous locomotion, and with this paradigm, caffeine reduced locomotion at all doses tested, while theophylline only was effective in suppressing locomotion at the two highest doses (50 and 100 mg/kg). In the rotarod both drugs impaired performance at the highest doses and caffeine was more effective at this effect. With measures of anxiety, both substances produced a very similar pattern, increasing anxiety in the elevated plus-maze both acutely and chronically. However, caffeine induced corticosterone release at all doses, while theophylline only did so at the highest dose. In summary, theophylline had fewer disruptive effects than caffeine on motor and anxiety parameters, and therefore could be a better adenosine antagonist than caffeine for the treatment of motivational and motor symptoms induced by DA antagonists.

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D11-88

DEPRESSION-LIKE BEHAVIOR IN MICE DURING ABSTINENCE FOLLOWING ALCOHOL DRINKING AND A POTENTIAL ROLE OF SIGMA$_1$ RECEPTORS

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Clinical evidence has indicated high degrees of comorbidity of alcoholism and depression and has shown that emergence of depression during abstinence increases the likelihood of relapse. Some recent data have demonstrated the depression-like behavior in mice during abstinence following voluntary alcohol drinking. The depression-like behavior (i.e., the increased immobility time in the forced swim test /FST/) was observed 14 days after alcohol withdrawal. It has been recognized that σ receptor ligands (especially σ_1 agonists) reveal a potential antidepressant activity in experimental models (FST, tail suspension test) and that targeting σ receptors alone is sufficient (but not requisite) for production of antidepressant-like actions. As recently found, σ_1 receptor knockout mice display a depressive-like phenotype. The aim of this study was to estimate the potential role of σ_1 receptors in the depression-like behavior following voluntary alcohol drinking in male C57BL/6J mice. To this end, mice were allowed to self-administer ethanol (in raising concentrations of 4%, 8% and 10% v/v) in their home cages for 16 days. Then alcohol was withdrawn for 14 days (abstinence period) and desipramine (used as a standard antidepressant drug) or a σ receptor ligand (fluvoxamine and PB190) were given repeatedly (intraperitoneally, once daily) for 14 days. FST was performed on the 1st and 14th day after ethanol withdrawal. The results indicated that abstinence from voluntary alcohol drinking led to prolongation of immobility time (depression-like behavior) in alcohol drinking mice vs. control non-drinking animals. Desipramine, a classical, tricyclic antidepressant, at the dose of 10 mg/kg (but not 20 mg/kg) counteracted that effect. Fluvoxamine, a selective serotonin reuptake inhibitor, with a relatively high affinity for σ_1 receptors, at the dose of 10 mg/kg, induced no modification of depression-like behavior in alcohol-abstinent mice similarly as PB190, used as a selective σ_1 receptor agonist. The obtained preliminary results did not support the importance of σ_1 receptors in depression-like symptoms in mice during abstinence, but further studies are required to exclude such a possibility.

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D11-89

COMPARATIVE PHARMACOLOGICAL ACTIVITY OF OPTICAL ISOMERS OF PHENOTROPIL

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Phenotropil (N-carmamoylmethyl-4-aryl-2-pyrrolidone (2-(2-oxo-4-phenyl-pyrrolidin -1-yl) acetamide; carphedon)) racemate is used clinically as a nootropic drug for improvement of physical condition and cognition. Although the racemic substance can be separated into R- and S-enantiomers, thus far it is clinically used only in the racemic form. Information concerning the comparative pharmacological activity of R- and S-phenotropil is not available. Because phenotropil is structurally related to piracetam, a known drug that increases both physical and cognition-related capacities, we tested the pharmacological activity of racemic phenotropil and its enantiomers in experimental set-ups related to those activities. The compounds were tested in mice for locomotor, antidepressant and memory-improving activity in open-field, forced-swim and passive avoidance response (PAR) tests, respectively. Moreover, the contents of R- and S- phenotropil in brain tissue after single administration where determined by ultra performance liquid chromatography-tandem mass spectrometry (UPLC/MS/MS) in a positive ion electrospray mode. R-phenotropil significantly enhanced memory function in PAR test at dose of 1 mg/kg; the S-enantiomer did not show any activity in this test. Single administration of R-phenotropil increased locomotor activity significantly in open field test at doses of 10 and 50 mg/kg while S- enantiomer exhibited the same effect at a dose of 50 mg/kg. Antidepressant activity of R-phenotropil in forced swim test was observed at doses of 50 and 100 mg/kg; but S-phenotropil exerted similar activity only at a dose of 100 mg/kg. The results of the present study provide evidence that R-phenotropil is the most active enantiomer of phenotropil. Racemic phenotropil and S-phenotropil also stimulate locomotor activity and induce some antidepressant effect after acute administration, but the effects are achieved at 2-5 times higher doses in comparison to effects of R-phenotropil. Interestingly, S-phenotropil did not exert any memory enhancing activity in the PAR test, although the amount of the enantiomers in brain tissue was similar as shown by UPLC/MS/MS. In conclusion, only R-phenotropil exerts memory-improving activity, but both R- and S- isomers of phenotropil possess antidepressant and increased locomotor activity, R-phenotropil being the most active isomer. These results may be important for the clinical use of optically pure isomers of phenotropil.

D11-90

ANTIDEPRESSANT- AND ANXIOLYTIC-LIKE EFFECTS FOLLOWING TREATMENT WITH RISPERIDONE AND FLUOXETINE IN BEHAVIORAL MODELS IN RATS

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Several clinical reports have suggested a beneficial effect of the addition of a low dose of an atypical antipsychotic drug (e.g., risperidone) to the ongoing treatment with antidepressant drugs, particularly of the selective serotonin reuptake inhibitors (e.g., fluoxetine, fluvoxamine and poroxetine) in the treatment of drug-resistant depression. In anxiety disorders, like post-traumatic stress disorder, some studies found that atypical antipsychotics improved certain symptoms, while others failed to reach the same conclusion. Preclinical evidence on the intrinsic anxiolytic-like property of atypical antipsychotics is also inconclusive. To understand the mechanism of clinical efficacy of a combination therapy with an antidepressant drug and an atypical antipsychotic in treatment-resistant depression and anxiety disorders, in the present study we examined the effect of treatment with a low dose of risperidone, given separately or jointly with fluoxetine in the forced swimming test (an animal model of depression) and in the elevated plus-maze test (an animal model of anxiety) in male Wistar rats. The obtained results showed that treatment with risperidone (0.05 and 0.1 mg/kg) and fluoxamine (10 mg/kg) did not induce any antidepressant-like effect in the forced swimming test. Moreover, co-treatment with both drugs induced a more potent inhibition immobility time, and increase swimming behavior than treatment with either drug alone, and that serotonin 5-HT_{1A} receptors might play some role in these effects. Active behavior in that test was not a consequence of an increase in general activity, since the combined treatment with fluoxetine and risperidone failed to enhance the locomotor activity of animals. Risperidone (0.1 and 0.3 mg/kg) and fluoxetine (5 and 10 mg/kg) induced anxiolytic-like effect in the elevated plus-maze test. In contrast, co-administration of risperidone and fluoxetine was unaffected in that test. This finding indicates that a low dose risperidone enhances the action of ADs in an animal model of depression, and that 5-HT_{1A} receptors may play some role in these effects. Furthermore, they may be of particular importance to the pharmacotherapy of drug-resistant depression. In contrast, risperidone and fluoxetine may each be clinically effective in treating anxiety disorders, but their effects may be attenuated in the combination treatment with both medications.

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D11-91

COMPARATIVE STUDY OF ANTIDEPRESSANTS WITH DIFFERENT MECHANISM OF ACTION ON MEMORY MODELS: INFLUENCE OF MOTOR PERFORMANCE

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The purpose of the present study was to investigate the effect of various antidepressants on cognition in relation with their specific mechanism of action. The antidepressants studied were reboxetine (RBX 4-64mg/kg, and i.p.) (selective NA reuptake inhibitor, SNRI), fluoxetine (FLX 4-64mg/kg, i.p.) (selective 5-HT reuptake inhibitor, SSRI) and the dual antidepressants duloxetine (DLX 4-64mg/kg, i.p.), milnacipran (MLN 4-64mg/kg, i.p.) and venlafaxine (VLX 4-64 mg/kg, i.p.) (5-HT/NA reuptake inhibitors, SNSRI, dual action). The antidepressant-like efficacy was measured by means of the forced swimming test (FST) and the tail suspension test (TST), The Morris water maze test was used to test the effect of antidepressants on cognition. Motor activity was monitorized in each case. The results showed: *Motor activity:* RBX 64mg/kg; FLX 32, 64mg/kg; DLX 8-32 mg/kg; MLN 64mg/kg produced a decrease in motor activity. *Depression models:* i) FST: RBX 4-64mg/kg; FLX 32, 64mg/kg; DLX 4-64mg/kg; MLN 32, 64mg/kg and VLX 16-64 mg/kg significantly decreased the immobility time versus saline, as expected. ii) TST: RBX 4-64mg/kg; FLX 32, 64mg/kg; DLX 4-64mg/kg; MLN 16-64mg/kg and VLX 16-64 mg/kg significantly decreased the immobility time respect to saline. *Cognition models:* any antidepressant produced memory deficit in the cognition test, except at high doses in 8-arm radial maze (RBX 64 mg/kg; FLX 64 mg/kg and DLX 64 mg/kg). Therefore, the results showed that the SNRI, reboxetine; the SSRI, fluoxetine; the SNSRI, milnacipran and duloxetine decreased the motor activity. All antidepressant induced antidepressant-like effects in a similar range of doses. In conclusion, RBX, FLX and DLX produced a cognitive impairment but at high doses but this may due to the induction of a sedative effects.

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D11-92

BINGE ETHANOL AND MDMA COMBINATION: BEHAVIORAL AND NEUROINFLAMMATORY AFFECTATIONS

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Binge drinking is a common pattern of alcohol consumption among young people that can induce alcohol dependence. Binge drinkers are especially susceptible to brain damage when other substances are co-administered, in particular MDMA (3, 4-methylendioxymethamphetamine) and it is of special relevance and severity in the case of adolescents and young adults. The aim of the study was to evaluate the behavioral and neuroinflammatory consequences of the voluntary binge ethanol consumption, alone and in combination to MDMA in mice. To study this, the drinking in the dark (DID) procedure has been employed as a model of alcohol binge drinking. Some groups of mice also received a MDMA treatment. The behavioural influence of this treatment was evaluated on body temperature, locomotor activity, motor coordination and anxiety-like and despair behavior in adolescent mice 48, 72 hours and 7 days after the treatment. Astrocytic and microglial response in the striatum was also evaluated in the same groups of animals. The hyperthermia observed in MDMA-treated mice was abolished by pre-exposition to ethanol. MDMA-treated mice showed less locomotor activity 48 hours after treatment but no differences were found after that. Ethanol-treated mice showed motor coordination impairment and increased despair behavior. Anxiety-like behavior was only seen in animals treated with both drugs. All these alterations were seen after 72 hours and after 7 days of the treatment but not after 48 hours. Additionally, MDMA-induced glial reactivity was higher in those mice pre-exposed to ethanol. The combination of both drugs increases the side effects of each one of the drugs evaluated.

D11-93

INVOLVEMENT OF NEUROPEPTIDE FF (NPFF) SYSTEM IN AMPHETAMINE-INDUCED REWARD AND WITHDRAWAL

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Although neuronal mechanism of amphetamine is mainly connected with inhibition of re-uptake of dopamine, noradrenaline and serotonin, many data indicate that endogenous opioid system is involved in amphetamine-induced seeking behavior and amphetamine reward. Published data indicate that neuropeptide FF (NPFF, FLFQPQRF), an endogenous peptide with anti-opioid efficacy inhibited/attenuated effects of several drugs of abuse. The aim of the present study was to investigate whether NPFF system is involved in the expression of the rewarding effect of amphetamine and the amphetamine withdrawal-induced anxiety-like behavior. Rewarding effect of amphetamine was measured in the biased conditioned place preference (CPP) paradigm in male Wistar rats. After establishing an initial preference of animals to one of the two compartments of CPP apparatus, acquisition of amphetamine-induced CPP was initiated. Thus, amphetamine (1 mg/kg, i.p.) was administered for 7 consecutive days to rats before confine them to the drug-paired (non-preferred) compartment (30min). After 4 h interval, rats received saline injection immediately before confinement in the vehicle-paired (preferred) compartment (30 min). One day after conditioning the time spent by rats in each compartment was measured (the expression of CPP)**.** Single intracerebroventricular (i.c.v.) injection of NPFF (5, 10, 20 nmol) inhibited the expression of amphetamine CPP at the doses of 10 and 20 nmol. RF9, the NPFF receptors antagonist, reversed the inhibitory effect of NPFF (20 nmol) at the dose of 10 and 20 nmol, i.c.v. Anxiety-like effect of amphetamine withdrawal was measured for 5 min 24 h after the last (14 days) amphetamine (2.5 mg/kg, i.p.) treatment in the elevated plus-maze test (EPM). In the EPM test, amphetamine withdrawal decreased the percent of time spent by rats in the open arms and decreased the percent of open arms entries. RF9 (5 - 20 nmol, i.c.v.) significantly attenuated the anxiety-like effect of amphetamine withdrawal in all doses used. NPFF (20 nmol) reversed the effect of RF9 (10 nmol). Our results suggest that the NPFF anti-opioid system participates in the amphetamine reward and amphetamine withdrawal-induced anxiety-like behavior.

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D11-94

CHRONIC TREATMENT WITH CAFFEINE BLOCKS NEUROINFLAMMATION INDUCED BY MDMA

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Previous research suggests that under conditions of chronic daily caffeine administration, caffeine protects against brain injury in different animal models of neurodegenerative disorders, such as Parkinson and Alzheimer diseases, ischemic brain injury and allergic encephalitis. However, little is known about the effects of chronic caffeine administration on MDMA-induced neuroinflammation. The present study examined whether a chronic caffeine pretreatment (10 mg/kg, i.p, for 21 consecutive days) protects against MDMA-induced astrocytic and microglial activation, impairing its neuroinflammatory effects. Additionally, in order to assess possible behavioral alterations due to caffeine administration, locomotor activity, sensoriomotor reflexes and anxiety were evaluated after caffeine injection on days 1, 7, 14 and 21 of the chronic treatment. On day 21, mice pretreated with caffeine or saline received a neurotoxic regimen of MDMA (3 x 20mg/kg, i.p., 2 hours interval) or vehicle. 48 hours after last MDMA or vehicle injection, microglia and astroglia activation were evaluated in mice striatum. Caffeine pretreatment blocked MDMA-induced glial activation without having any effect on behavior. Together, these findings suggest that chronic caffeine consumption has anti-inflammatory effects and prevents MDMA-induced neuroinflammation.

D11-95

ACUTE TREATMENT WITH MDMA ENHANCED LATENT INHIBITION PRODUCED WITH FEW PRE-EXPOSURES

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Latent inhibition (LI) refers to the reduction in conditioning to a stimulus that has received non-reinforced pre-exposure, an effect typically abolished by amphetamines and enhanced by antipsychotics. Similarly, LI can be abolished by disruption to the serotonergic (5-HT) system, for example, through lesions to the medial raphe, and by pharmacological treatments which reduce 5-HT release or block its actions postsynaptically. Conversely, LI enhancement - demonstrated when LI in controls has been systematically weakened using a reduced number of stimulus pre-exposures - has been shown using the 5-HT reuptake blocker sertraline. To our knowledge the effects of treatment with pharmacological agents which mimic the actions of 5-HT postsynaptically have not been further tested. The cognitive effects of MDMA ('Ecstasy') are controversial, particularly in the case of acute administration of low doses, known to increase 5-HT release. Therefore MDMA (6 mg/kg, within the range comparable to human doses) was examined using 10 and 40 pre-exposures to produce weak and strong LI in controls, respectively. Seven days post MDMA administration, fresh brain samples were taken by micropunch from the following regions; nucleus accumbens, medial prefrontal cortex (mPFC) and amygdala. Tissue samples were analysed for neurotransmitter and metabolite levels determined by HPLC. MDMA (injected twice, prior to pre-exposure and conditioning) significantly enhanced LI in that the effect was clearly demonstrated after only 10 pre-exposures, when it was absent in the saline controls. There was some evidence of neurotoxicity in that there were small but significant reductions in 5-HT in the mPFC and amygdala assayed 7 days post MDMA administration (2 x 6 mg/kg, 24 hrs apart). With respect to the underlying cognitive mechanisms, we conclude that the enhancement of (weakened) LI after treatment with MDMA reflects an increased tendency to switch from presently dominant to (weakly established) prior contingencies, which could in principle contribute to potential therapeutic efficacy as an adjunct to psychotherapy. However, the significant reduction in 5-HT found 7 days subsequent to a total dose of 12 mg/kg would be a contraindication. Thus the therapeutic implications of the present study require further experimental examination, also in animal models more directly relevant to extinction-based exposure treatments.

D11-96

BLOCKADE OF 2-ARACHIDONOYLGLYCEROL HYDROLYSIS: EFFECTS ON LOCOMOTION AND ANXIETY

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Anandamide (ANA) and 2-arachydonoylglycerol (2-AG) are endogenous ligands of the CB1 cannabinoid receptor (CB1R). Activating this receptor with direct agonists can induce multiple behavioral effects, however ligand-specificity of these effects is yet to be investigated. Selective inhibition of the hydrolysis of CB1R ligands allows studying mechanisms mediated by this receptor in a ligand-specific manner. A number of papers showed that inhibiting the activity of fatty acid amide hydrolase, the ANA degrading enzyme, promotes similar behavioral effects as CB1R agonists. With the recently developed molecule, JZL184, the 2-AG degrading enzyme monoacylglycerol lipase can be blocked, allowing studying 2-AG specific CB1R behavioral effects. In recent studies JZL184 treatment induced behavioral changes which were also induced by the exogenous CB1R agonist Δ9-tetrahydrocannabinol, but could not be induced by blocking ANA hydrolysis, suggesting ligand-specific CB1R effects. In the present study we treated CD1 mice with 4 doses of JZL184 to investigate its effects on locomotion in the open-field paradigm. We also studied the effects of the above treatment on anxiety on the elevated plus-maze, first in the literature, to the best of our knowledge. Selectively manipulating the metabolism of endocannabinoids allows studying interactions of ligand-specific CB1R mechanisms. The better understanding of these mechanisms might open a new perspective in the medication of psychiatrical disorders.

D11-97

EFFECTS OF AN ACUTE HIGH-DOSE OF ALCOHOL ON MANUAL DEXTERITY IN A YOUNG POPULATION

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Alcohol is a social drug widely consumed among young people. Impaired psychomotor performance is a common adverse effect of alcohol consumption and can also interfere with daily activities that require full alertness. The objective of the present research was to use the Purdue Pegboard Test (PPT) to evaluate the effects of alcohol on manual dexterity in a young population. This task requires participants to move pins from a recessed well to a series of holes on a laminated board. Left and right unimanual, bimanual and assembly versions of the test are administered, and the test score is commonly used as an index of manual dexterity. A total of 31 healthy young volunteers (18 women and 13 men; mean age 20±0.97) were submitted to the PPT, before (test) and after (retest) taking a drink (120 ml alcohol, 40%). The control group did not consume alcohol. The results showed sex differences in the task performance, with women obtaining higher scores than men. The non-consumers improved their test-retest performance, but no improvement was observed among the consumers. This lack of improvement in manual dexterity due to alcohol intake could affect activities that require full alertness, such as driving or operating machinery, in a risk population such as young people.

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D11-98

DIFFERENTIAL ROLES FOR SEROTONIN AND DOPAMINE IN SUBCONSCIOUS INSTRUMENTAL LEARNING: EVIDENCE FROM OBSESSIVE-COMPULSIVE DISORDER AND GILLES DE LA TOURETTE SYNDROME

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Whereas a consensus exists about the role of dopamine in reinforcement learning, the role of the other major midbrain neuromodulator serotonin is less understood. Many pharmacological studies using dopaminergic drugs converged to the idea that dopamine is specifically driving reward learning. One of the most influential hypotheses regarding the role of serotonin states that it mirrors that of dopamine but for punishment learning. To test this hypothesis, we examined the effects of serotonergic and dopaminergic medications in a same subliminal conditioning task that enables dissociating reward and punishment learning. The task was administered to patients with obsessive-compulsive disorder (OCD) and to patients with Gilles de la Tourette’s syndrome (GTS). Half of OCD patients were treated with serotonin reuptake inhibitors (SRI), half of GTS patients were treated with dopamine receptor antagonists (neuroleptics). GTS results confirmed the role of dopamine in reward learning, since neuroleptics impaired reward learning and favored punishment learning. In contrast, OCD results showed that SRI restored normal perfomance in both reward and punishment learning. Thus, contrary to dopamine, the role of serotonin in reinforcement learning is independent of outcome valence.

D11-99

REAL-TIME OXYGEN AMPEROMETRY CONFIRMS HUMAN NEUROIMAGING EVIDENCE FOR A ROLE OF THE ANTERIOR CINGULATE CORTEX IN VIGILANT ATTENTION

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Vigilant attention, the most basic aspect of attention, probably is a prerequisite for the more complex domains of cognition. A typical task to assess vigilant attention is a simple reaction time measurement. Interestingly, a slowing in reaction time has been found in many neuropsychiatric diseases such as schizophrenia. Evidence from both animal and human studies suggests that this form of attention relies on fronto-parietal interactions involving the anterior cingulate cortex (ACC), and may therefore represent a useful substrate for translational research. To investigate this, we decided to record both the behavioural performances and the oxygen amperometric responses in naïve and drug-treated rats trained to perform a simple reaction time task. Rats were trained to focus their attention and wait until a visual stimulus appears to nosepoke and receive food reward; the time taken to respond is called the reaction time. Rats were systemically treated with either vehicle or ketamine; a drug known to induce schizophrenia symptomatology in human healthy volunteers. Oxygen responses were simultaneously measured in the ACC using *in-vivo* oxygen amperometry, a technique allowing real time monitoring of tissue oxygen changes in freely-moving animals in a manner homologous to human fMRI. As in human fMRI studies, an increase in the oxygen signal was observed in the ACC during correct responding. Moreover, reaction time and oxygen increase seemed positively correlated, suggesting a direct relationship between the oxygen signal and the behavioural outcome. Compared to vehicle controls, ketamine-treated rats showed a significant increase in reaction time, clearly indicating a slowing of response. This slowing was also reflected in the oxygen signal, as the ACC oxygen increase during correct responding was significantly delayed following ketamine treatment. Overall, oxygen responses observed were similar to those obtained in human fMRI experimentation, corroborating the use of *in-vivo* oxygen amperometry as a viable animal surrogate for human fMRI. Moreover, the acute administration of ketamine considered to induce schizophrenia-like cognitive deficits in human healthy volunteers induced a slowing in reaction time. The ketamine-induced behavioural deficit correlated with a delay in the activation of the ACC as indexed by the oxygen amperometric signal; therefore giving us a useful biomarker against which to assess the effect of potential new cognitive therapies.

D11-100

MAPK PATHWAY INHIBITION TARGETS THE SEROTONINERGIC SYSTEM TO POTENCIATE THE ANTIDEPRESSANT-LIKE EFFECT OF DESIPRAMINE

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A high percentage of depressed patients do not achieve satisfactory alleviation with the current antidepressants available. The efficacy and onset of action of these drugs are mechanistically conditioned by modulation of monoaminergic system and long-term adaptative intracellular signalling changes. Indeed, all effective antidepressants cause a decrease of the activity of locus coeruleus (LC) neurons, the major source of noradrenaline in the brain. Furthermore, long term synaptic plasticity in LC and specifically in response to stress situations has been closely related with mitogen-activated protein kinases (MAPK) pathway modulation. Previous reports have implicated components of this signalling cascade in the antidepressant behavioural effects. Therefore, the aim of this study was evaluate the effect of MAPK pathway inhibition on the effectiveness of antidepressant treatment. To this end, the effect of SL327 (selective MAPK inhibitor) and/or the antidepressant desipramine (noradrenaline reuptake inhibitor) were studied. The modified forced swimming test (mFST) was used as a model predictive of antidepressant-like activity combined with electrophysiological recording of LC neurons. The administration of PCPA (para-chloro-phenylalanine), a serotonin synthesis inhibitor, was used to evaluate the serotoninergic system implication. The results showed that SL327 did not modify neither behavioural nor electrophysiological patterns. However, SL327 in combination with desipramine enhanced the antidepressant-like effect of desipramine in the mFST, decreasing the immobility and increasing the swimming behaviour. These behavioural changes are not due to an increase of locomotor activity and are counteracted by PCPA treatment. Single-unit extracellular recording showed that pre-treatment with SL327 increased desipramine inhibitory effect on LC activity. It caused a shift of the desipramine dose-response to the left, decreasing the ED_{50} by 63 % compared to vehicle group. These findings showed that SL327 potentiates the antidepressant-like behavioural effect of desipramine through an increase of serotoninergic neurotransmission. Futhermore, desipramine inhibitory effect on LC neurons is potentiated by SL327. Overally these data suggest that MAPK pathway inhibition may potentiate antidepressant effect, opening novel therapeutic approaches to depression.

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D11-101

ANXIETY, SOCIAL HIERARCHY, AND MITOCHONDRIAL FUNCTION IN MALE WISTAR RATS

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Social hierarchies are an integral component of societies. Hierarchy formation is linked to the establishment and understanding of behavioral patterns, in addition to being closely associated with health. Prominent social status affords individuals greater access to contested resources, and in humans, can become intimately associated with physiology and health. Despite the far-reaching consequences of social hierarchies, little is known about the underlying mechanisms of hierarchy formations. As anxiety has been implicated as a contributing factor in an individual's social status, we investigated the molecular consequences of inherent trait anxiety differences on the outcome of a social interaction between male Wistar rats. A vast body of literature has found inherent differences in anxiety levels in rats that can be detected in tests such as the Elevated Plus Maze (EPM) and open field. In our study, we characterized trait anxiety in rats with the EPM and classified adult male Wistar rats as either high (HA) or low (LA) anxious. Rats were then matched for weight and paired into dyads such that HA rats were always paired with LA rats. These dyads were allowed to socially interact for a period of twenty minutes in an empty, clean, and previously habituated cage. Following this interaction, we investigated whether such anxiety differences might have influenced social rank by inducing changes in motivational behavior mediated by changes in mitochondrial output in the nucleus accumbens. Our results indicate a role for energy deficiency as a mechanism underlying the propensity of highly anxious rats to develop subordinate behavior.

D11-102

ELECTRIC FOOTSHOCK IN RATS LEADS TO SIMILAR BEHAVIORAL RESPONSES BUT DIFFERENT ACUTE AND LONG-TERM CHANGES IN BRAIN ACTIVATION PATTERNS: IMPLICATIONS FOR PTSD

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Mechanisms underlying shock-induced conditioned fear -a laboratory model of post-traumatic stress disorder (PTSD)- are usually studied shortly after shock exposure. Brain regions relevant to this disorder were activated in each study, but their number was restricted, and showed little overlap across studies. As PTSD develops after a long incubation time, we hypothesized that a more consistent picture would be obtained at later time-points. Therefore, we exposed rats to a single session of footshocks and studied their conditioned fear response 1 and 28 days later. Fear-induced neuronal activation patterns were studied by c-Fos immunocytochemistry in 29 brain regions relevant for the expression of conditioned fear. The duration of contextual freezing was similar at the two time-points, but the associated neuronal changes were qualitatively different. A restricted number of brain areas were affected 1 day after shocks; freezing was associated with, and likely due to an enhanced activation of the anterior hypothalamus (a component of the hypothalamic defense system), and/or to changed periaqueductal gray activation. 28 days after shocks, almost all the systems involved in conditioned fear were activated. Increased activations were seen in the medial prefrontal cortex, hippocampus, medial and basolateral amygdala, ventromedial hypothalamic nucleus (another component of the hypothalamic defense system), hypothalamic paraventricular nucleus, dorsomedial periaqueductal grey, median raphe and locus coeruleus. The sharp contrast between the similarity in behavior and the markedly different neuronal activation patterns might be the result of the temporal evolution of shock-induced changes, suggesting the importance of incubation time for modeling PTSD.

D11-103

WITHDRAWAL FROM THE OPERANT CHAMBER DURING EXTINCTION OF FOOD-REINFORCED LEVER-PRESSING AS A MEASURE OF "DESPAIR": INFLUENCE OF ANTIDEPRESSANT DRUGS

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There are few practicable animal models for studying the efficacy of antidepressant drugs which exhibit face as well as construct validity. Depressive symptoms such as low mood, suicidal intentions, inability to experience pleasure, hopelessness, cognitive impairment and increased avoidance behaviour can be a consequence of the absence of an expected reward (extinction). Our first approach to modelling extinction-induced "despair/depression" employed extinction of a negatively reinforced behaviour, namely the escape from water onto a platform in the Morris water maze. Extinction of water maze escape behaviour led to behavioural changes, such as increased immobility, which were positively influenced by antidepressants (Huston et al., 2009). Here we present the results of an attempt to examine possible extinction-induced "despair/depression" using extinction of a positively reinforced behaviour, namely lever-pressing reinforced by food reward. We employed a conventional Skinner-box attached to a second empty "withdrawal" compartment of the same size. We measured number of entries and duration of time spent in the withdrawal chamber. We found that the tricyclic antidepressant imipramine (20 mg/kg) as well as the selective serotonin reuptake inhibitor citalopram (20 mg/kg) reduced the number of entries and time spent in the withdrawal compartment over repeated extinction trials. Rearing behaviour was also reduced by antidepressant treatment during extinction. We postulate that entries and time spent in the withdrawal compartment can be a measure of avoidance, a main symptom of major depression. Additionally the attenuation in vertical activity (rearing behaviour) may indicate less emotional arousal during extinction in the antidepressant treated rats. These results lend support to the hypothesis that extinction of operantly reinforced responses induces behaviours that may reflect elements of "despair/depression", since these behaviours are modulated by antidepressant treatment. Particularly the avoidance of the operant chamber as a consequence of extinction seems to be a useful paradigm for the testing of antidepressant treatments.

-Huston JP, Schulz D, Topic B. (2009). Toward an animal model of extinction-induced despair: focus on aging and physiological indices. *J Neural Transm*. 116(8):1029-36.

D11-103

BEHAVIOURAL EFFECTS OF ANTIDEPRESSANT TREATMENT DURING EXTINCTION OF A RUNWAY RESPONSE

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Previously, we found that extinction of negative reinforcement in the Morris water maze resulted in behavioural immobility which was attenuated by antidepressant treatment. We suggested that the process of extinction induces a state akin to despair (extinction-induced despair, EID), and, thus, might be a useful model of human depression as a consequence of the loss of reinforcement. Here, we examined whether antidepressant treatment also modifies behaviour during extinction of positively reinforced behaviour, that might potentially also be relevant as a behavioural marker of despair/depression. 20 adult Wistar rats were food deprived (10 g/day lab chow). After habituation to the runway (grey rectangular box; 192 cm x 14 cm x 22.5 cm), rats were trained to run down the alley for 7 days to gain food reward (per trial 10 sucrose pellets, 45mg). They then received daily injections (i.p.) of either vehicle (water; n=6), citalopram or imipramine (10 mg/kg; n=7 per group) 30 min prior to experiment. Acquisition training was continued for 3 more days, followed by 5 days of non-reinforced extinction trials. All rats reached asymptotic level of runway performance by day 7. The groups did not differ in acquisition under antidepressant treatment. Over the extinction trials, the time to reach the food cup steadily increased in all groups, indicating extinction of the runway response. The vehicle treated rats reached the food cup earlier compared to the group treated with imipramine or citalopram. Rearing behaviour was decreased in both antidepressant groups. Animals treated with citalopram exhibited more grooming. The group treated with imipramine moved a shorter overall distance than the controls. Thus, several behaviors during runway extinction were sensitive to antidepressant treatment, in support of the hypothesis that extinction of reinforced behaviour induces a state akin to "depression/despair". These results complement our finding that during extinction of Skinner-box lever-pressing, vehicle-treated rats enter an adjoining "withdrawal" compartment more than antidepressant-treated animals.

D11-105

FUNCTIONAL CONNECTIVITY IN DESCENDING HIPPOCAMPAL PROJECTIONS TO CORTEX AND SEPTUM DURING ANXIETY IN MICE

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The brain structures and neural circuits regulating anxiety behavior are poorly understood. A large body of evidence shows that the hippocampus is involved in the inhibition of motivated behavior in the face of unexpected environmental contingencies and the septo-hippocampal behavioral inhibition theory has been proposed as a unified explanation for these apparent disparate functions (McNaughton and Gray, 2000). The hippocampus has two major outputs: 1) projections to the adjoining entorhinal cortex, and 2) descending efferents, directed mainly from the ventral hippocampus to the lateral septum and frontal cortex. Recent electrophysiological data suggest that modulation of hippocampus-frontal cortex connectivity is critically involved in anxiety (Gordon et al., 2006; Adhikari et al., 2010) and suggests that these descending outputs may be critical for novelty-induced behavioral inhibition. However, it is not clear what the contributions of septal and frontal cortical outputs are to anxiety because, until now, no manipulations were available to selectively inhibit these pathways. In order to characterize the role of these two descending projections in anxiety, recording electrodes were chronically implanted in the ventral hippocampus (vHIP), prelimbic area of the medial prefrontal cortex (mPFC), and rostral lateral septum (rLS). Anxiety behavior and local field potentials (LFP) were assessed in the elevated plus maze and open field and prior to these tests in a familiar open arena. Both vHIP-mPFC and vHIP-rLS synchronization were increased during the anxiety tests when compared to the familiar arena suggesting that both projections are recruited during anxiety. In all environments, vHIP-rLS coherence was higher than vHIP-mPFC coherence pointing to a particular role for vHIP-rLS projections in these behaviors. Future studies are aimed at using the hM4D DREADD receptor pharmacogenetic inhibition tool to selectively manipulate these projections.

D11-106

KAINIC ACID- AND PILOCARPINE-TREATED EPILEPTIC RATS DISPLAY DIFFERENT TYPES OF HIPPOCAMPAL RHYTHM DISRUPTION

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Previous studies have reported disruption of theta activity in the pilocarpine model of temporal lobe epilepsy (TLE) and related this deficit with spatial memory impairment. Here, we compared theta rhythm disruption in epileptic rats using two experimental models of TLE. Chronic epileptic rats were generated using the model of status epilepticus induced by intra-peritoneal injections of either kainic acid (KA) or lithium-pilocarpine (LIP). Control rats received saline injection instead of the convulsivants. All tests started after about 4 weeks post-status, when the animals already exhibited spontaneous seizures. Rats were implanted with either 16-channel silicon probes or wire tetrodes to measure local field potentials and single-cell activity, respectively. The relationship between the theta power and the rat speed was evaluated using a treadmill at increasing speeds from 10 to 25 cm/s. In control rats, the theta power at the strata lacunosum moleculare and radiatum of CA1 was positively correlated with the walking speed. In contrast, the LIP group was either negatively correlated or uncorrelated with the walking speed in the treadmill while the power of theta oscillations was significantly lower compared with control group. Interestingly, the KA group exhibited variability in the degree of modulation between theta and walking speed, not presenting significant differences in the theta power with the control group. Theta modulation of CA1 pyramidal cell firing was lower in both the KA- and the LIP-treated groups compared to control. Histological analysis revealed different alterations in the two experimental model of TLE. Our results indicate that disruption of the hippocampal theta rhythm is model-dependent and reflects the underlying reorganization of the neuronal circuit after the status.

D11-107

THE NEW FAAH INHIBITOR ST4070 (1-biphenyl-4-ylethenyl piperidine-1-carboxilate) REDUCES ACUTE AND NEUROPATHIC PAIN IN ANIMAL MODELS

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Recent research has focused on targeting the endogenous cannabinoid system, elevating anandamide (AEA) levels through pharmacological inhibition of its principal catabolic enzyme: fatty acid amide hydrolase (FAAH). FAAH inhibitors are efficacious in rodent models of inflammatory and neuropathic pain, without any apparent motor deficit or general pharmacological effects associated with direct cannabinoid agonist (Schlosburg et al., 2009). In the present study a new reversible and selective inhibitor of FAAH (Gattinoni et al., 2010) ST4070, (1-biphenyl-4-ylethenyl piperidine-1-carboxilate) was tested on acute pain in rats and chronic neuropathic pain in diabetic mice models. ST4070 at oral doses of 10, 30 and 100 mg/kg in the Randall-Selitto Acute pain test increased dose-dependently the nociceptive threshold after 60 and 120 min in rats. ST4070 also reduced diabetes induced neuropathic pain in mice by increasing, in a dose-dependent manner, the mechanical withdrawal threshold in the Von Frey test, although statistical significance was only reached at the highest dose of 100 mg/kg. This study highlights the potential therapeutic efficacy of ST4070 to treat acute and neuropathic pain.

-Schlosburg et al. AAPS J 2009; 11:39-44.
-Gattinoni et al. Chem Med Chem 2010; 5:357-60.

D11-108

EXOGENOUS ERYTHROPOIETIN EXERTS OPPOSITE EFFECTS ON ANXIETY IN EPILEPTIC RATS DEPENDING ON THE QUALITY OF THE LIVING ENVIRONMENT

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Anxiety can precede onset of epilepsy in children with severe cognitive disorders, motivating the search for therapeutic approaches to reduce the severity of anxiety disorders in these children. We showed in prior preclinical studies that rats subjected to lithium/pilocarpine-induced *status epilepticus* (Li/Pilo-SE) at weaning develop anxiety-like disorders before spontaneous recurrent seizures (SRS) occur, and severe learning and memory impairments as measured in the Morris Water Maze after the first SRS. We also reported that: 1) treatment with recombinant human erythropoietin (rEPO) can exert neuroprotective properties following SE, and 2) housing in enriched Marlau™ cages can decrease the severity of anxiety-like disorders and prevent the development of learning and memory deficits following Li/Pilo-SE at weaning, we tested the hypothesis that rEPO treatment after Li/Pilo-SE can further improve the beneficial effects of enriched housing on anxiety without affecting learning and memory. We show that rEPO treatment in rats reared in conventional housing conditions has slight protective effects on anxiety-like disorders, but prevents the development of learning and memory deficits. In rats reared in enriched Marlau™ cages, rEPO treatment exacerbates anxiety-like disorders, without affecting learning and memory performances. Altogether, these data indicate that rEpo treatment given after SE at immature stages may counteract the development of anxiety and cognitive deficits once SRS occurred and when living in an impoverished (i.e. conventional) environment. Such positive effects may thus be expected in patients with epilepsy, whose majority is reporting poor quality of live, with increased feelings of social isolation. However, our results also reveal that rEpo may be a double-edged sword in the treatment of individuals prone to SRS. Indeed, while producing positive effects in rats reared in impoverished environments, rEpo turned out to exacerbate anxiety-like disorders in rats reared in enriched/complex environments.

D11-109

GABA-A ANTAGONIST INJECTIONS IN THE CEA INCREASE ANXIETY AND IMPAIR AVOIDANCE LEARNING IN THE TRANSGENIC RAT MODEL FOR HUNTINGTON'S DISEASE

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Huntington disease (HD) is caused by an expansion of CAG repeat in the Huntingtin gene and induces a triad of motor, cognitive and psychiatric symptoms. A transgenic rat model (tgHD rats), carrying 51 CAG repeats, demonstrates progressive striatal degeneration and polyglutamine aggregates in limbic structures. In this model, we previously showed emotional blunting and hypersensitivity to negative emotional situations in symptomatic tgHD animals, as well as a selective shrinkage of the central nucleus of the amygdala (CeA; Faure et al, 2011). These results suggest that some of the emotional symptoms in patients may be related to amygdala dysfunction. The aim of the present study was to evaluate the role of CeA on performance in different tasks evaluating both emotional and cognitive alterations in tgHD animals. Wild type (WT), heterozygous (HT) and homozygous (HO) rats were first trained in a social interaction task. HO animals spent more time sniffing the unfamiliar conspecific than WT rats. HO rats injected with picrotoxine significantly reduced exploratory behavior compared to saline injected animals. However, picrotoxine had no effect on social interactions. Animals were then trained in a signaled avoidance task in which a tone (20 sec) preceded a tone+shock period (20 sec). Rats could avoid or escape by pushing a bar which stops both the tone and the shocks. Transgenic rats were injected either with picrotoxin or saline during the first five sessions of learning and were then trained for 8 more sessions without injections. The results show that (1) Homozygous rats performed more inter trial responses, showing hyperactivity compared to WT and HT rats. (2) Homozygous animals learned the avoidance response faster than WT and HT, suggesting a reduced level of anxiety in these animals. (3) Picrotoxin significantly prevents avoidance learning selectively in HO animals. These data suggest that increasing neuronal activity in the CeA by blocking GABAA receptors may have increased emotional responses and thus induced an impairment of rats' ability to learn the behavioral meaning of the avoidance signal.

D11-110

BLOCKADE OF SEIZURE-LIKE EVENTS BY SK-CHANNEL ENHANCER IN RAT HIPPOCAMPAL SLICES

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Small conductance calcium-activated potassium channel (sK-channel) belongs to a family of Ca^{2+}-activated K^+ channel and plays an important role in regulation of neuronal excitability. Activation of sK channel results in the hyperpolarisation of membrane resulting in the reduction of excitability, thus may have an anticonvulsant action. In the present study we have evaluated the anticonvulsant action of sK-channel enhancers by inducing seizure-like events (SLEs) in acute hippocampal slices of rat using 4-aminopyridine and low magnesium. Once the SLEs were stable, CyPPA (50μM and 100μM) and SKa-31 (100μM and 150μM) were tested. Field potential recording from entorhinal cortex was performed in an interface setup. CyPPA at dose of 50μM didn't block SLE, rather delayed the interval between SLEs, whereas at the dose of 100μM SLE were completely blocked. Similarly SKa-31 didn't suppress 4-AP induced SLEs at dose of 100 μM but suppressed at dose of 150 μM. Both drugs failed to block SLEs induced by low Magnesium- Based on these findings we suggest that sK-enhancer plays a role in reducing membrane hyperexcitability and thus may have potential to be an anticonvulsant agent.

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Abstracts Posters

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D12-1

THE IMPORTANCE OF SELF-MOTION CUES ON THE ABILITY OF RATS TO LEARN PLACES WITH RESPECT TO MOVING ORIENTATION CUES

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The active place avoidance task tests the ability of rats to navigate in a moving world. A rat, placed on a rotating circular arena, should avoid an unmarked sector defined with respect to stable extra-arena cues. Recently, we have showed that rats learn the task easily if the arena rotates in a stable world (standard task) while they do not learn if the world rotates around the stable arena (modified task). One possible explanation suggests that rats need to perceive the distal extra-arena cues as stable in order to associate the position of the sector with these cues. Another explanation stresses the importance of inertial stimulation (perception of acceleration and deceleration) on the preparedness of the nervous system to process spatial information and to generate behavioral actions. Rats trained in the active place avoidance task typically alternate short periods of no movement with short periods of running against the arena rotation. The short runs (the avoidance actions) are initiated before the rat is transported into the to-be-avoided sector. Motionless rats perceive inertial stimulation in the standard task but not in the modified task. Forcing the rats to move actively during the whole session would make the inertial stimulation generated by the arena rotation less important because the stimuli generated by self-motion (including inertial stimuli) would also provide constant information to the subject that its position in the environment is changing and therefore new information may be comming and new behavioral responses required. We motivated food-deprived rats to move actively by pellet chasing. One group of rats was trained in the standard task while another group was trained in the modified task. Our preliminary data obtained on four rats in each group showed that both groups learned the active place avoidance task equally well. We conclude that constant information about motion is sufficient for formation of association between position of the to-be-avoided sector and surrounding distal unstable cues.

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D12-2

DORSAL STRIATAL NEURONAL ACTIVITY IN GOAL-DIRECTED SPATIAL BEHAVIOR

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Several authors have demonstrated a specific involvement of the dorsomedial striatum (DMS) and dorsolateral striatum (DLS) in the acquisition of instrumental action-outcome associations and habit formation, respectively. However, the functional properties of neuronal activity in each striatal subregion have been poorly investigated in relation to goal-directed spatial learning. The aim of this study is to compare DMS and DLS cells activity in a continuous T-maze alternation task, in which rats were required to run up the central stem of the maze and enter the left and right choice arm in alternance to obtain a reward. Rats were implanted with a movable bundle of 4 tetrodes and single unit activity from DMS or DLS was recorded from the first acquisition session. Putative medium spiny projection neurons (MSN) and fast-spiking GABA-ergic interneurons (FSI) were discriminated according to their waveforms and firing frequency. The results showed that a quarter of the total number of neurons recorded in DMS and DLS displayed task-related responses (correct vs errors) and spatial responses (left vs right). However, DMS neurons showed a higher degree of specificity, compared to DLS cells. Indeed, DMS neurons fired differentially at reward locations according to either left or right correct responses, whereas DLS neurons preferentially activated either for correct or incorrect responses irrespective of the reward position. Task-related responses and spatial responses were predominant in FSI, compared to MSN, in both striatal areas. These results suggest that the activity of FSI more than the activity of MSN is modulated by learning processes, and indicate that the DMS and DLS may support in different ways the acquisition and performance of a spatial goal-directed behaviour.

D12-3

GENETIC AND CORRELATION ANALYSIS OF SPATIAL LEARNING OF THE RAT HXB/BXH RECOMBINANT INBRED STRAINS IN THE CAROUSEL MAZE, A SPATIAL AVOIDANCE PARADIGM

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This study evaluated hippocampus-dependent learning in active place avoidance, referred here to as Carousel maze, in the HXB/BXH recombinant inbred (RI) strains (N = 30) derived from SHR/Ola and BN-Lx/Cub strains. The Carousel maze involves avoidance of a stable unmarked sector on a slowly rotating circular arena. The test is dependent on hippocampus, and in addition to ongoing locomotor activity, it requires cognitive coordination and also vestibular stimulation induced by arena rotation. Four daily acquisition sessions were pursued, followed by a retrieval session and three sessions with the shock sector reversed. Number of errors, maximum time between two errors, latency to the first entrance and total distance walked served as main measures of performance. Moreover, we recorded the open-field behavior and beam-walking performance in the RI set. Results showed large inter-strain variability in the carousel arena performance and analysis of within/between-strain variances suggested a significant heritability. We have analyzed possible genetic determinants of this parameter using a web-based tool www.genenetwork.org. We detected no significant QTL, suggesting that learning in HXB/BXH RI strains is determined by many loci rather than oligogenetically. From previously published phenotypes, we observed significant correlations of maximum time avoided on the final reversal session with body weights at 12 weeks (r=0.49, P=0.017), liver triglycerides (r=0.55, P=0.012), serum HDL3 cholesterol (r=-0.45, P=0.021), plasma homocysteine (r=-0.48, P=0.049) and adrenal dopamine beta-hydroxylase (r=0.46, P=0.048). Maximum time avoided on the final day of reversal also showed two suggestive QTLs on chromosomes 7 and 16 (LRS scores 9.8 and 10.8, respectively). Several other correlations with cardiovascular traits were detected. A more detailed elaboration of behavioral parameters including further QTL mapping is in progress. In perspective, further analysis of covariance of multiple parameters from the carousel maze and open-field test with physiological traits and gene expression will contribute to understanding of regulatory genetic relationships between these phenotypes.

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D12-4

OBJECT-LOCATION PAIRED-ASSOCIATES LEARNING IN THE RAT: A c-*fos* IMAGING STUDY

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Object-location paired associates learning (PAL) is impaired in schizophrenic patients using the Cambridge Neuropsychological Test Automated Battery. This deficit may model patients' difficulties 'binding' the different elements of an episodic memory, including the spatial context. To implement PAL for preclinical assays into the cognitive deficits of schizophrenia, a touch-screen version for rodents has been developed in our lab. Maintaining performance in the touchscreen-PAL requires both hippocampal and prefrontal cortex activation, but preliminary results from our lab also show that hippocampus lesions *before* acquisition of this task do not impair animals. In addition, the anatomical substrate of binding object and location information is as of yet unknown. The objective of this study was therefore to elucidate brain regions involved in the touchscreen object-location learning task. Brain activation -as measured by expression of the immediate early gene c-*fos*- was analyzed in animals performing the touchscreen-PAL. Animals were trained to associate pictures with locations on the screen by presenting them an S+ (object in its correct location) and an S- (object in an incorrect location) on each trial. Following acquisition, cell-numbers in several brain areas were stereologically quantified and compared to rats that acquired concurrent object discrimination and control rats. Preliminary results show that rats in both the PAL *and* the object discrimination groups had more active neurons in different subregions of the hippocampus, compared to controls, indicating that the hippocampus is involved in both PAL and object discrimination. Further analysis will be presented showing the involvement of other brain regions in object-location paired associates learning.

D12-5

LATERAL ENTORHINAL CORTEX IS ACTIVATED BY MEMORY FOR OBJECT-CONTEXT ASSOCIATIONS

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Place cells in the hippocampus and grid cells in the medial entorhinal cortex are two key components of the system for spatial representation in the mammalian brain. However, human research suggests that the primary role of the hippocampus is in episodic memory – memory for specific events involving spatial and contextual components. Place cells and grid cells likely provide spatial information to this memory network but one question that remains is where in the brain the contextual component of episodic memory is processed. One potential route for contextual information to influence the hippocampus is via the lateral entorhinal cortex (LEC). Little is known about the functional properties of the LEC other than that single neurons in LEC do not show spatial firing patterns. To assess the role of the LEC we measured Fos expression in medial temporal lobe structures following activation of memory for contextual features. The task used was a variant of the object recognition paradigm. The task was modified so that rats received two sample trials. In the first they were presented with 2 identical copies of a novel object in a familiar context. In the second they were presented with 2 copies of a different novel object in a second familiar context. The objects were 3D household objects and the different contexts consisted of different coloured walls and different textured floors within the same square box. In a test phase the rats were placed in one of the contexts with copies of each of the objects they encountered in the samples phases. The rats spent significantly longer exploring the object which they had not previously seen in the current context, demonstrating a memory for the previously seen object-context configuration. Control conditions involved rats experiencing the same contexts and objects but without a novel object-context memory demand in the test phase. Fos expression in the LEC was significantly greater in the condition where rats demonstrated a memory for object-context association than when rats experienced different contexts or different objects separately and with no memory demand. Differential activation in the context memory condition was also seen in different sub regions of the hippocampus, most notably in the dentate gyrus and subiculum.

D12-6

LESIONS OF THE DORSOLATERAL STRIATUM IMPAIR SPATIAL LEARNING BASED ON THE LANDMARK-GOAL VECTOR BUT FACILITATE COGNITIVE MAPPING IN THE RAT

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Animals can navigate using multiple strategies based on different types of information provided by the environment. Pearce, Roberts, and Good (1998) showed that the hippocampus in the rat is not required for finding a submerged platform in the water maze provided its position is always in a constant distance and direction from an intra-maze landmark (i.e. learning based on a vector from the landmark), but it is required for rapidly learning the same platform position with reference to the array of extra-maze cues (i.e. cognitive map-based learning). In the present study, we used the same task and tested whether the dorsolateral striatum (DLS) is responsible for spatial learning based on the landmark-goal vector strategy. Throughout the training phase, the platform was always submerged 30 cm in a fixed direction from an intra-maze landmark. The positions of the platform and the landmark stayed constant for one session of four trials, but they moved together across sessions. On session 15, a landmark probe test was conducted, during which the landmark was placed in a novel location at the centre of the pool and the platform was removed. While sham-lesioned rats searched in the correct location, which was 30 cm away from the landmark in a particular direction, the animals with DLS lesions showed no sign of such learning, indicating that DLS lesions impaired learning based on the vector from the landmark. At the end of session 16, following three trials of retraining with the landmark-platform unit in another novel location, a place probe test was conducted, during which both the landmark and the platform were removed, so that only information available was provided by the extra-maze cues. During this place test, DLS-lesioned rats, but not sham-lesioned rats, searched around the correct place, suggesting that the DLS lesions facilitated the use of the cognitive map-based rapid place learning. These results, together with results from Pearce et al. (1998), suggest that spatial learning based on a cognitive map and on landmark-goal vectors are mediated in separate neural systems, the hippocampus and the DLS, respectively, and further implicate that those learning processes are not entirely independent but are in competition for behavioural output.

D12-7

POSTERIOR PARIETAL CORTEX IN THE RAT AND CONCURRENT USE OF TWO SPATIAL REPRESENTATIONS

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In order to accurately reach a target or locate a goal, a brain must be apparently capable of reciprocal transformation of coordinates related to various frames of reference. Based on neglect patients studies and electrophysiological recordings in monkeys, it is hypothesized that this function is largely subserved by posterior parietal cortex (PPC). Unlike primate PPC, its role in rodents is still poorly understood. To further elaborate its contribution in reference frames processing, we tested Long-Evans male rats in a behavioral task in which they had to concurrently use two spatial representations, each anchored to a distinct reference frame. Rats were at first trained in seven (20 min) sessions on a stable metallic circular arena to avoid a directly impercievable sector. Its location therefore should be encoded relative to intramaze cues (three small flat magnetic inserts) or extramaze landmarks (such as doors, shelves). During this pretraining phase we did not observe any difference between PPC lesioned and sham operated animals. Since session 8, rats underwent 10 minutes of standard pretraining, followed by 10 minutes of test session in which the arena slowly rotated (1 rpm), dissociating the environment into two independent reference frames (rotating arena frame, stable room frame). The rats were required to continue avoiding in both room frame-based sector and arena frame-based sector. Rotation of the arena resulted in substantial increase of number of entrances into the room frame sector and less prominent increase in arena frame. In the following sessions, sham operated rats acquired to avoid a sector in either frame, while PPC lesioned rats maintained poor performance in the room frame. These results support our previous finding that PPC lesion mildly disrupts navigation based on room (distal) reference frame. Here we show that this deficit is even pronounced when an animal must use room and arena frame simultaneously. Altogether, this pattern of results suggest that PPC plays an important role in encoding goals relative to distal visual cues and in synchronizing this representation with other spatial processes.

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D12-8

COMPETITION BETWEEN DORSOMEDIAL AND DORSOLATERAL STRIATUM DURING THE ACQUISITION OF A GOAL-DIRECTED SPATIAL TASK, IN RATS

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The rat dorsomedial (DMS) and the dorsolateral (DLS) striatum, equivalent to the primate caudate nucleus and putamen respectively, have different roles in instrumental conditioning. In particular, DMS activity is necessary to form action-outcome associations, whereas DLS is required for developing habitual behavior. Whether a similar dissociation exists in more complex goal-directed learning processes such as spatial learning, it is still a matter of debate. The present study examined the role of the two structures in goal-directed spatial learning, by analyzing the effects of NMDA lesions of the DMS and the DLS during the acquisition and extinction of a spatial alternation behavior, in a continuous alternation T-maze task. We showed that DMS and DLS lesions have opposite effects, the first impairing and the second improving animal's performance during learning and extinction. The DMS lesions may impair the acquisition of a spatial alternation behavior by disrupting the signal necessary to link a goal with a specific spatial sequence. The DLS lesions may accelerate goal-driven strategies by minimizing the influence of the external stimuli on the response, thus increasing the impact of action-reward contingencies. Taken together, these results suggest that DMS- and DLS-mediated learning strategies develop in parallel and compete for the control of the behavioral response early in learning.

D12-9

EXPOSURE TO RETINOIC ACID DURING HINDBRAIN SEGMENTATION IMPAIRS THE LEARNING ABILITIES IN MICE, BY MODIFYING NORADRENERGIC FUNCTION

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Pontine noradrenergic system activation acts on the elaboration of adaptive and cognitive responses participating in different processes as wakefulness, attention, memory processes and more complex models related to errors predictions, making of decisions and so on (reviewed in Bouret and Sara, 2005). It has also been described the involvement of the alpha-adrenergic system in some motor responses related associated events: pre-pulse inhibition of the startle reflex and also the development of labyrinth tests and social behaviours (Shishkina et al., 2001). During early development central neuronal networks are specified according to a complex genetic programme. Exogenous retinoic acid (RA), which has teratogenic effects on vertebrate embryos, is known to change this organisation by altering gene expression in the embryonic hindbrain through RA Response Elements (RAREs). In a previous study (Guimarães et al., 2007), we observed that non-teratogenic RA doses (0, 5mg/kg) given to pregnant females during early embryonic development, induces an abnormal breathing behaviour including generation of hyperpnoeic episodes, characteristic of some human syndromes (as Cheyne-Stokes, Joubert), carrying also some psychomotor deficits. To investigate whether these low RA doses affects learning abilities in the adult mice, we tested the acquisition of classically conditioned eyelid responses, as well as other motor reflexes and cognitive cues. The results show that non-teratogenic RA doses produce a decrease in the acquisition of conditioned responses, similar to that obtained with postnatal chronic administration of noradrenergic antagonists. Implication of alpha adrenergic receptors in this process is discussed. We conclude that the alteration of the normal gene expression pattern during the embryonic hindbrain development, affects the elaboration and acquisition of motor conditioned responses.

D12-10

AMPA RECEPTOR ACTIVATION AND PHOSPHORYLATION WITHIN THE VENTRAL STRIATUM ARE REQUIRED FOR LONG-TERM SPATIAL MEMORY IN MICE

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We have previously reported that AMPA receptors activation within the ventral striatum (VS) is needed for short-term processing of spatial information, while less clear is their involvement in the long-term stabilization of spatial memories. Recent findings indicate that the regulation of AMPA-R by phosphorylation at its GluR1 Ser845 and Ser831 sites is required for the induction of different forms of synaptic plasticity and in learning processes, however the role of AMPA-R phosphorylation in memory processes is still unknown. The aim of this study was to verify whether AMPA-R activation and its phosphorylation, were required in the ventral striatum for long-term maintenance of spatial information. Pre-training AMPA receptor blockade in the VS significantly impaired performance during the probe test 24 hours later in the spatial version of the Morris Water Maze. Differently, no effect was found in animals trained in the cued version of the task. Western blot analysis demonstrated an increase in the level of phosphorylation in both AMPA GluR1 sites. In particular we found a selective significant enhancement of GluR1 Ser845 and Ser831 phosphorylation, immediately after training only in the spatial procedure. Further we demonstrated that VS pharmacological blockade of PKA and CaMKII kinases, that are associated with AMPA GluR1 Ser 845 and Ser831 phosphorylation, significantly impaired performance in the spatial version of the MWM. To relate this effect with AMPA receptor phosphorylation we used an RNA aptamer that specifically bind and prevent AMPA receptor phosphorylation at Ser845 site in the VS and we found that this treatment was sufficient to induce an impairment in the probe test; the effect of this drug was also confirmed by Western Blot. These data, together with previous evidence in the literature, demonstrate an involvement of AMPA receptors within the VS in the early stages of long-term stabilization of spatial information; further they strongly suggest that such process requires AMPA receptor phosphorylation at both Ser845 and Ser831 GluR1 sites.

D12-11

AMPA RECEPTOR ACTIVATION IN THE VENTRAL STRIATUM IS REQUIRED FOR THE RETRIEVAL OF 24 HOURS AND 7 DAYS BUT NOT FOR 30 DAYS OLD SPATIAL MEMORIES

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It has been suggested that memory is characterized by a transfer of information from sub-cortical to cortical areas. This model is based on evidence demonstrating a progressive disengagement of the hippocampus and a parallel involvement of prefrontal cortical areas in the retrieval of information. Given the anatomical and functional interaction between the hippocampus and the ventral striatum, this latter structure has also been involved in memory stabilization. Indeed, previous studies from our laboratory have demonstrated that ventral striatal manipulations impair mice performance in spatial memory task. Moreover recently we demonstrated the occurrence of plastic changes within this structure after spatial learning. However it has never been investigated whether the storage of information within this structure follows the same dynamic demonstrated in the hippocampus. To investigate this issue we trained mice in the massed version of Morris Water Maze testing them after different time intervals (1, 7 or 30 days). Immediately before testing, animals were focally injected in the ventral striatum with either saline or the AMPA antagonist NBQX. Preliminary results show that mice are able to correctly locate the platform also 30 days after training. Furthermore, we found that AMPA receptor blockade impairs mice performance 24 hours and 7 days but not 30 days after training. This effect is specific for spatial memory since no impairment was observed in animals trained in the cue version of the task. These data demonstrate the role of the AMPA receptor in the ventral striatum in the retrieval of spatial information up to 7 but not 30 days after acquisition. Thus suggesting that such as the hippocampus this structure might be needed in the early stages of memory storage before information transfer and stabilization in cortical areas.

D12-12

EVIDENCE THAT DOPAMINE IS RELEASED IN THE STRIATUM TO PROMOTE AVERSIVE CONDITIONING

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Three hypotheses compete for the role of phasic release of dopamine (DA) in the striatum: (i) encoding the hedonic valence of a stimulus; (ii) encoding the saliency of a stimulus; (iii) promoting learning. The present study aims to test the later hypothesis, which implies that: (i) DA release in the striatum increases in order to promote learning; (ii) such increase occurs only when learning is possible; (iii) after learning, the same stimuli that promoted DA release will no longer do this. These questions were addressed by an *in vivo* microdialysis study in rats trained to perform an action to avoid a footshock that otherwise would follow a warning cue (tone). We observed that striatal dopamine release is important for learning to avoid an aversive stimulus. Release increased only when learning was possible, baselining after learning even when the stimuli that promoted learning were present. Dopamine activity in the first session correlated positively with learning in a subsequent session; and treatments that prevented dopamine release impaired learning. Dopamine is therefore critical for aversive conditioning establishing dopamine's fundamental role in learning rather than just reward processing.

D12-13

AMYGDALAR MODULATION OF A SPATIO-TEMPORAL MEMORY IN RATS

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Interval timing refers to the ability to estimate duration between two events. This aptitude is essential to form associations and memories in the everyday life. Current assumptions in the literature depict the basal ganglia as central structures acting as a cortical inputs coincidence detector during temporal processing. Previous results from our team suggest that plasticity in prefronto-striatal pathway is involved in learning the CS-US interval in an aversive Pavlovian task. This result came along with activation in the Lateral and Basal nucleus (LA and BLA) of the amygdala, in accordance with data in the literature suggesting that the amygdala may detect irregularity in a temporal pattern. In the present work we tested the role of the BLA in the learning of new rules in a spatio-temporal task, using an appetitive instrumental paradigm (5-hole nose-poke). After initial training associating a given location-duration with reinforcement, rats were infused with a GABAa agonist (muscimol) in the BLA 15 minutes before the shift to new location-duration association. The results showed that BLA inactivation delayed the behavioral adaptation to the new spatio-temporal association. Thus, the activation of the amygdala is necessary for the detection of changes in spatio-temporal rules, and its corresponding behavioural adaptation. We suggest that the amygdala may modulate cortico-striatal processing in interval timing.

Support: ANR Memotime, LIA Emotime, PUF Emotion & Time.

D12-14

TRANSFERENCE OF TEMPORAL CONTROL FROM FIXED-TIME TO FIXED-INTERVAL REINFORCEMENT SCHEDULES

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Transference of duration in a Fixed Interval (FI) schedules is a well established finding (Roberts & Church, 1978), but evidence of transference between different temporal procedures is scarce. López & Menez (2010) reported transference from one non contingent periodic schedule, like Fixed Time (FT) to a contingent one (FI), of the same value. In that experiment, the stimulus associated to duration was the same (houselight). In order to determine if transference of temporal learning was related to this variable, in this experiment, Wistar rats were subjected to a Fixed Time (FT) 30s schedule or a Random Time (RT) 30s schedule for 30 sessions (Training phase) signaled by houselight or tone. Then, all subjects received a Fixed Interval (FI) 30s schedule for 30 sessions (Testing phase). In this phase, duration elapsed in the absence of signals (no houselight, no tone). Results indicate transference of duration even when there was not a signal during testing phase. Also, FT exposure speeded up acquisition of temporal learning, in congruence with an adaptive view.

D12-15

USING CIRCULAR STATISTICS TO ANALYZE TIME DISPERSION PATTERNS DURING MOTOR LEARNING

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The cerebellum-red nucleus-facial motoneuron pathway has been reported as being involved in the proper timing of classically conditioned eyelid responses. This special type of associative learning serves as a model task of event timing for studying the role of the cerebellum in dynamic motor control. Here, we have re-analyzed the firing activities of cerebellar posterior interpositus neurons and orbicularis oculi motoneurons in alert behaving cats during classical eyeblink conditioning, using a delay paradigm. We reviewed the hypothesis that the interpositus neurons can be considered as a neuronal phase-modulating device supporting orbicularis oculi motoneurons firing with an emergent timing mechanism and an explicit correlation code during learned eyelid movements. Optimized experimental and computational tools allowed us to determine the different causal relationships (temporal order and correlation code) during and between trials. These intra and inter-trials timing strategies ranging from sub-second range (millisecond timing) to seconds-to-minutes-to-hours range (interval timing) expanded the functional domain of cerebellar timing beyond motor control. Interestingly, the results supported the former hypothesis. The causal inferences were influenced by the precise motor and premotor spike-timing in the cause-effect interval, and in turn, the timing of the learned responses depended on cerebellar-motoneuron network causality. Furthermore, the timing of conditioned responses was influenced by the simulated causal conditions in the cause-effect interval and not the mere duration of the inter-stimulus interval. The idea of to work with different durations of the inter-stimulus interval and to study the different temporal distributions of the response is essential to study the timing behaviors. However, in a first approach it is possible to explore the spatiotemporal patterns of the different data distributions for the same duration of inter-stimulus interval and to simulate the dispersion patterns when the duration of different intervals are adjusted to angular distribution on a circle. Here, we presented some evidence that such spatiotemporal coding and the parametric timing_intensity and time delay_strength dispersion patterns determine a functional neuronal state evoked by learning process. In this work, the close relation between timing and causality was verified. It could thus be concluded that the firing activities of cerebellar posterior interpositus neurons may be related more to the proper timing and performance of ongoing conditioned responses than to their generation and/or initiation.

D12-16

NEUROPHYSIOLOGICAL CORRELATES OF CS-US INTERVAL TIMING IN THE AMYGDALO-PREFRONTO-STRIATAL NETWORK DURING FEAR CONDITIONING IN RATS

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In associative learning paradigms such as Pavlovian conditioning an organism not only learns that stimulus A predicts stimulus B, it also learns when stimulus B is presented. Recent experimental reports indicate that the amygdala might be involved in this kind of temporal encoding. On the other hand, prefrontal cortex and dorsal striatum are thought to be involved are thought to be involved in temporal processing. In the current study we investigated the role of the basal amygdala and its projections to the dorsal striatum and prefrontal cortex in processing the time of arrival of a footshock unconditioned stimulus (US) during auditory fear conditioning in rats. Using a conditioned suppression paradigm (with lever pressing for food as the instrumental basis), rats were trained on a discrimination protocol in which two different tones (1 kHz and 11 kHz) were associated with two different CS-US interval times (10 and 30 sec). Non-reinforced trials (tones without shocks) were introduced to assess the temporal pattern of suppression. After overtraining, when temporal behaviour was observed, local field potentials were recorded simultaneously from amygdala, striatum and prefrontal cortex while the animal was subjected to this protocol. In each of these structures the power spectral density of oscillations in various frequency bands was analyzed in relation to the expected time of the US. Furthermore, we looked for potential time-modulated changes in interactions between structures by analyzing crosscorrelations and coherence. We also tested for the directionality of interactions between structures via Granger analysis. Thus, our study determines whether the basal amygdala, the prefrontal cortex and/or the dorsal striatum show neural correlates of CS-US interval encoding and tests for their functional connectivity in a Pavlovian fear conditioning paradigm.

Support: ANR Memotime, LIA Emotime, PUF Emotion & Timing.

D12-17

HIPPOCAMPAL LESIONS DISRUPT THE TEMPO-CIRCADIAN CONTROL ON THE EFFECT OF LATENT INHIBITION OF TASTE AVERSION LEARNING

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Previous experiments have shown that a tempo-circadian change between the time of taste pre-exposure and conditioning prevents the phenomenon of latent inhibition of taste aversion learning. The effect of this change in tempo-circadian context between pre-exposure and conditioning on the magnitude of the aversion learned appears to be similar to the effect shown on this learning when between pre-exposure and conditioning changes the spatial context. In order to know the brain areas involved in this tempo-circadian dependence of latent inhibition of taste aversion learning, we analyzed the effects of excitotoxic lesions on a region related to the spatial-contextual modulation in this learning process: the hippocampus. The results showed that the selective injury in the dorsal hippocampus eliminates the tempo-circadian specificity of latent inhibition of taste aversion learning. A change in the time of day between taste pre-exposure and conditioning did not prevent the phenomenon of latent inhibition with hippocampal lesions. On the contrary, this change did prevent the latent inhibition in the sham condition. This study may help understand the possible common involvement of the hippocampus in different kinds of contextual control of associative learning.

D12-18

DIFFERENTIAL INVOLVEMENT OF DORSAL STRIATUM IN LATENT INHIBITION LEARNING

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Latent inhibition (LI) is a process whereby pre-exposure to a stimulus without consequence impairs learning about that stimulus at subsequent conditioning. This process too is believed to be under the control of dopaminergic systems. Dorsal striatum is one of the structures that shows changes in dopamine levels during LI process however its role remains unclear. The main proposal of this study was to analyze the role of the nigrostriatal dopaminergic system in the mediation of LI. The dorsolateral striatum have been considered necessary in the habit acquisition, stimulus-response learning, and procedural memory. In this sense, a short or long exposure to will be conditional stimulus (CS) could determine that learning the CS-no event association were controlled by different striatal structures (dorsomedial or dorsolateral striatum). If so, the temporal blocking of these different structures, during test phase, should differentially affect the expression of learning pre-exposure.

D12-19

SCOPOLAMINE AS A COGNITIVE IMPAIRER: ATTEMPTS TO DISTINGUISH COGNITION FROM NON SPECIFIC IMPAIRMENTS

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Scopolamine is a naturally occurring compound found in the nightshade (Solanaceae) plant family that potently blocks cholinergic muscarinic receptors resulting in pronounced, yet reversible cognitive impairments. Due to its procedural simplicity, efforts over the last 50 years have led to a comprehensive characterization of scopolamine's effects on aspects of animal cognition, but surprisingly there is still debate as to whether the impairments are learning and memory related. The aim of these studies was to dissect out the desired cognitive-impairing effects of scopolamine from its non-specific effects including effects on animal behavior (i.e. locomotor activity) using a relatively simple test of fear-based learning and memory. In our hands, prior studies have demonstrated that scopolamine elicits pronounced effects on freezing immediately after the conditioning shock. However, many publications fail to describe these effects on acquisition/conditioning trials, possibly because the data are not collected. Our aim was to try and identify an appropriate point on the pharmacokinetic exposure rise curve that would elicit significant and robust cognitive impairments devoid of non-specific side effects. On day one, male Long Evans rats (Janvier, France, 260-300 grams) were pretreated with scopolamine (0.04, 0.08, 0.12, 0.16 mg/kg; sc; @ 10 ml/kg dose volume) at either 10, 20 or 30 minutes pretreatment times and then "fear-conditioned" using MED Associates conditioning chambers to associate the chamber with a shock (0.7 mA foot shock, 1 sec duration). On day two, animals were then placed back in the test chambers for a total of eight minutes and freezing responses recorded during the whole period. As expected, pre-treatment time dependent effects were observed for both the conditioning and recall effects of scopolamine. At 10 minutes, there were no effects of scopolamine on freezing responses during either conditioning or recall trials. On the contrary, the thirty minute pre-treatment group showed significant effects of scopolamine on both the conditioning and recall trials with no independent effects on either measure. Interestingly, at the twenty minute pretreatment time, there was some conditioning/recall independence, suggestive that non-specific effects could indeed be separated from cognitive impairing effects. These preliminary series of studies indicate that it could be possible to tease out the desired effects of scopolamine by altering pretreatment times depending on the cognitive task.S

D12-20

D-CYCLOSERINE IN PRELIMBIC CORTEX REVERSES SCOPOLAMINE-INDUCED OLFACTORY MEMORY DEFICITS

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D-cycloserine (DCS) is a partial agonist at the glycine binding site of the N-methyl-D-aspartate (NMDA) receptors that has been regarded as a cognitive enhancer. Previous research has demonstrated that injections of DCS, both systemic and intracerebral, enhance acquisition, consolidation, relearning, extinction or reconsolidation of different learning and memory paradigms. Moreover, systemic administration of DCS can reverse mnemonic deficits due to aging, sleep deprivation, stress, brain lesions and pharmacological manipulations. The present study investigates whether DCS infused directly into the prelimbic cortex (PLC) would reverse scopolamine-induced amnesia in two olfactory tasks of different nature that have been previously characterized as sensitive to muscarinic blockade in the PLC. Such tasks are: an associative odor-reward paradigm, the odor discrimination task (ODT; experiment 1), and a paradigm of relational learning, the social transmission of food preference (STFP; experiment 2). The results of experiment 1 showed that bilateral intra-PLC infusions of scopolamine (20µg), administered immediately after ODT acquisition, dramatically impaired a 24-h test. In contrast, intra-PLC infusions of DCS (10µg), injected 20 min before ODT acquisition, improved performance in the 24-h test and also completely reversed the memory deficits induced by scopolamine infusions into the PLC. In the experiment 2, bilateral intra-PLC infusions of scopolamine (20µg) administered immediately after the social interaction (acquisition) also markedly disrupted the expression of memory measured 24-h after acquisition in a food preference test. Infusions of DCS prior to acquisition did not improve STFP performance, although they enhanced the performance of rats injected with scopolamine, compared to scopolamine-injected rats without DCS treatment. These results suggest an interaction between the glutamatergic and the cholinergic systems in the PLC in such a way that positive modulation of the NMDA receptor/channel, through activation of the glycine site, may compensate dysfunction of cholinergic neurotransmission involved in olfactory learning tasks, such as a rapidly acquired odor-reward associative task and a relational learning task. The facilitative effects of DCS in the PLC might to rely on potentiating synaptic plasticity, consistent with the proposed role of the NMDA receptors in learning and memory enhancement. The present findings also suggest that DCS treatment may be effective for alleviation of memory loss associated with dementia or other neurodegenerative or neurologic diseases.

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D12-21

FACILITATION OF A SPATIAL TASK IN THE MORRIS WATER MAZE BY POST-TRAINING INTRACRANIAL SELF-STIMULATION AND STUDY OF NEUROANATOMICAL CHANGES IN BRANCHING AND SPINE DENSITY IN HIPPOCAMPAL NEURONS

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Post-training intracranial self-stimulation (ICSS) has shown facilitative properties in the acquisition and retention of several learning and memory tasks in rats. Although the evidence for this effect has been established mostly in implicit tasks, recent research from our and other laboratories suggest a similar effect on explicit forms of learning and memory. In this study, including two experiments, we confirm this facilitation in the acquisition of a spatial task in the Morris water maze, in two paradigms with different amount of training (two versus six trials per session for five sessions). Furthermore, for the first time in literature, we observed the maintenance of this effect ten days after acquisition in a retention test. ICSS rats also showed a more flexible use of the acquired spatial learning in a three-trial reversal phase. In addition, we are studying possible modifications of branching complexity and spine density in hippocampal neurons (CA1 and gyrus dentatus) injected with Lucifer Yellow and processed for a light-stable DAB reaction product. We already have some data that suggests that changes in dendritic spine density could be related to the observed improvement in memory by ICSS.

D12-22

OPTIMAL STORAGE AND RETRIEVAL WITH METAPLASTIC SYNAPSES: PREDICTING FUNCTIONAL ADAPTATIONS IN CA3

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Although it has long been accepted that memory relies on long-term changes in synaptic efficacy, how this function is implemented in neural circuits remains unclear. In particular, theoretical models have shown poor memory capacity when synaptic efficacies have a limited dynamical range, as is the case for biological circuits (Amit & Fusi, 1994). The memory trace in such synapses decays over time, as information is overwritten by ongoing plasticity. It has recently been suggested that metaplastic synapses, in which activity-induced changes depend on the history of activity at the synapse, can overcome some of these limitations (Fusi et al, 2005). However, although having multiple "hidden" states corresponding to each "visible" synaptic efficacy (e.g. a cascade model) increases the life span of a memory trace, it remains unclear whether neural dynamics can make effective use of this additional information during retrieval. In fact, poor retrieval performance has been reported for such synapses by traditional attractor dynamics (Huang & Amit, 2010). Here we develop a new theoretical framework for the storage and retrieval of synapses with metastates. This framework allows us to optimise the parameters of synaptic plasticity as functions of the statistics of the patterns that need to be stored and of the expected times of recall. Furthermore, we can derive the optimal neural dynamics that maximise the efficiency of autoassociative recall, given pattern statistics and the plasticity rule used for storing the memory. Optimal retrieval in the model translates into simple, biologically-plausible neural dynamics, with characteristics reminiscent of hippocampal circuit dynamics. In particular, for the family of learning rules similar to plasticity in CA3, the optimal dynamics rely on feedback inhibition (Freund & Buzsáki, 1996) and homeostatic regulation of neuronal excitability (Zhang & Linden, 2003) to ensure stability during retrieval. Finally, we show that oscillations modulating the relative contributions of afferent and recurrent synapses (Wyble et al, 2001) further improve recall performance by helping to explore candidate activity patterns more efficiently. These results suggest functional roles for the activity of inhibitory networks during retrieval and for the excitability changes that are known to accompany learning in hippocampal circuits. More generally, our work provides a framework for linking different aspects of neural plasticity and dynamics to the function of CA3, and provides testable hypotheses to guide future experiments.

D12-23

THE NEUROBIOLOGY OF FORGETTING: INTERNALIZATION OF GLUR2 CONTAINING AMPA RECEPTORS MEDIATES DECAY OF LONG-TERM MEMORY IN HIPPOCAMPUS

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Why are many long-term memories lost over time? There is currently no answer to this fundamental question -neither the psychology nor the neuroscience of everyday forgetting yet exists, and overall, our neurobiological understanding of this ubiquitous phenomenon is in its infancy. We used object-location recognition in rats as a model to investigate the molecular mechanisms of forgetting. We have shown previously[1] that long-term memory for object location resides in dorsal hippocampus (dHCP), that it lasts (given a certain training paradigm) for at least 7 days, but no longer than 34 days, and that it is maintained by the atypical PKC kinase M zeta (PKMzeta). We have also shown[2] that PKMzeta maintains memory by regulating trafficking of GluR2-containing AMPA receptors (GluR2-AMPAR), and that memory strength of auditory fear positively correlates with GluR2-AMPAR levels in amygdala neurons. On the basis of these findings, we hypothesized that internalization of GlUR2-AMPAR over time mediates forgetting of object location memory in dHCP. We used GluR23Y, an interference peptide comprising a binding motif of the GluR2 carboxyl tail, to competitively block internalization of GluR2-AMPAR. We trained rats in the object location task, and infused GluR23Y daily into dHCP for 13 days. When tested the day after the last infusion (14d after training) animals infused with GluR23y remembered the object location, while those infused with the scrambled control peptide did not. We then found that GluR23Y did not prevent memory loss by blocking acquisition of possibly interfering memories, as GluR23Y did not impair new learning, but in fact potentiated it. These findings categorically rule out interference-based accounts of this forgetting, which most resembles decay over time. Finally, we showed that blocking NMDA receptors with AP5 in dHCP also prevented forgetting, which suggests that internalization of GluR2-AMPAR might be induced by NMDAR activation. To our knowledge this is the first study showing internalization of GlUR2-AMPAR as the molecular substrate of everyday forgetting, linking the decay concept to a neurobiological mechanism, while unambiguously demonstration that memory decay exists as a process distinct from interference. The theoretical as well as clinical implications of our findings will be discussed.

-[1] Hardt et al (2010) *Hippocampus 20*: 691-5.
-[2] Migues et al (2010) *Nat Neurosci 13*:630-4.

D12-24

CHOLECYSTOKININ-POSITIVE INTERNEURONS MAY CONTRIBUTE TO THE LEARNING-DEPENDENT CHANGES IN THE BARREL CORTEX OF ADULT MICE

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Although CCK-containing basket cells, which receive abundant subcortical input, are implicated in anxiety, mediating motivational and emotional impacts, little is known about their linking to aversive learning. To understand this population possible contribution in the learning-dependent plasticity, the distribution of CCK-positive interneurons should be established at the site of action, i.e. in the first somatosensory cortex (SI) representation of the mystacial vibrissae after short-time whisker-shock conditioning. During a training session vibrissal rows B of the left snout were stimulated (conditioned stimulus, CS) and immediately after a single tail shock was apply to the tail (unconditioned stimulus). Pairings whisker-shock (CS+UCS) were repeated (4/min) for 10 min daily for 3 days. The control groups received pseudoconditioning, whisker stimulation alone (CS only), and tail shock alone (UCS only). Whisker-shock conditioning has produced an expansion of the cortical representation of the activated vibrissae. This was demonstrated by 2-DG mapping of functional activity in layer IIIb and layer IV of the SI cortex, and accompanied by increased density of GABAergic interneurons. On the other hand, the density of parvalbumin-positive (PV-positive), in most GABA containing inteurons of the mice cerebral cortex, does not alter after whisker-shock conditioning. This suggested that same PV-negative population/s of GABA interneurons are involved in the learning-dependent plasticity of the barrel cortex. Here I will present recent data from multiple immunolabeling for PV-positive and CCK-positive interneurons in the barrel hollow of trained and control group of animals to ensure their proper allocation of specific layer IV of the SI cortex. The most notable observation was that following aversive training CCK-positive cells presented an increased density in the barrel hollows compared with all controls, and therefore, may contribute to the learning-dependent changes in the barrel cortex of adult mice.

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D12-25

THE NICOTINIC AGONIST RJR-2403 COMPENSATES THE IMPAIRMENT OF EYEBLINK CONDITIONING PRODUCED BY THE NONCOMPETITIVE NMDA-RECEPTOR ANTAGONIST MK-801

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The classical conditioning of eyelid responses using trace paradigms is a hippocampal-related model of associative learning, involving the activation of N-methyl-D-aspartate (NMDA) receptors. We have evaluated here the effects of NMDA-receptor blockage with the selective noncompetitive antagonist (5R,10S)-(+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine hydrogen maleate (dizocilpine, MK-801). Mice were implanted with stimulating electrodes on the supraorbitary nerve and with recording electrodes in the ipsilateral orbicularis oculi muscle. Animals were conditioned with a trace shock-SHOCK paradigm. MK-801-injected animals (0.02 mg/kg) seemed unable to acquire this type of associative learning task, but the latency and amplitude of their unconditioned eyelid responses was not affected by drug administration. The administration of the nicotinic agonist (E)-N-methyl-4-(3-pyridinyl)-3-buten-1-amine (RJR-2403; 2 mg/kg) was able to restore completely the acquisition of the conditioned response when administered both before and after MK-801. In vitro recordings of field excitatory postsynaptic potentials (fEPSPs) evoked in the hippocampal CA1 area by the electrical stimulation of the Schaffer collateral pathway indicates that RJR-2403 application to the bath enhance the release of glutamate by a presynaptic mechanism. These findings reveal that nicotinic acetylcholine receptors enhance glutamatergic transmission in hippocampal circuits involved in the acquisition of associative learning

D12-26

THE INTERACTION BETWEEN GLUR2 AND N-ETHYLMALEIMIDE-SENSITIVE FACTOR IS CRUCIAL FOR MEMORY MAINTENANCE IN THE HIPPOCAMPUS

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The formation of long-term memory relies on multiple signaling pathways that in an orchestrated way bring about changes in synaptic strength and modification of synaptic connections. Once memory has been stored/consolidated, however, most of the signaling processes that were initially involved no longer appear necessary for memory persistence. The maintenance of established memories in the dorsal hippocampus and amygdala has recently been shown to involve the stabilization of GluR2-containing AMPA receptors (GluR2/AMPARs) at postsynaptic membranes, which depends on the continuous activity of an autonomously active isoform of protein kinase C, protein kinase M_ (PKM_) (Migues, 2010). We now focus on identifying which signaling pathways PKM_ regulates to maintain a stable pool of GluR2/AMPARs at the synaptic membranes, so that memories can persist. The insertion and removal of GluR2/AMPARs at the synaptic membrane relies on interactions between intracellular proteins and specific regions of the intracellular carboxyl terminus of the GluR2 subunit. In particular, the interaction between N-ethylmaleimide-sensitive factor (NSF) and GluR2 seems to be crucial for the stabilization of AMPAR at the synaptic membrane. In vitro studies have suggested that NSF disrupts the binding of GluR2 to molecules that lead to receptor endocytosis, thereby stabilizing AMPARs at the synaptic membrane. We therefore disrupted the interaction between GluR2 and NSF in the dorsal hippocampus and examined its effect on the maintenance of memory for object location. We used the intereference peptides pep2m, which comprise the NSF binding site on GluR2, and pep-R845A, a modified version of pep2m. Both peptides have been shown to block the binding of NSF to GluR2. Two days after rats were trained, we infused pep2m or pep2R845A or their inactive scrambled version bilaterally into dorsal hippocampus. We found that rats that received pep-R845A or pep2m had impaired object location memory when tested 1 or 5 days after infusion. This result indicates that the interaction between GluR2 and NSF is required for memory maintenance in dorsal hippocampus. Our study thus identified GluR2-NSF binding as a critical component of the signaling process that maintains memory.

-Migues et al (2010) Nat Neurosci 13:630-4.

D12-27

BETA-ADRENOCEPTORS MEDIATE RECONSOLIDATION OF SOCIAL REWARD-RELATED MEMORIES

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Memory reconsolidation studies are often based on memories of negative emotions, such as fear, whereas the dynamics of memories of positive events have been less well studied. Social play is the most characteristic social behavior displayed by young mammals, it is important for social and cognitive development and it is highly rewarding. Indeed, it can be used to induce conditioned place preference (CPP) in adolescent rats. We examined the neural mechanism of the storage and stability of social reward-related memories. We evaluated the effect of propranolol (PROP), a beta-adrenergic antagonist known to impair several memory processes, including reconsolidation of fear-, drug- and food-related memories, on acquisition, consolidation, retrieval and reconsolidation of social play-induced CPP in adolescent rats. Systemic treatment with PROP, administered immediately after a retrieval-session, attenuated CPP 24h later. Following extinction, CPP was reinstated in saline- but not in PROP-treated rats. PROP did not affect social play-induced CPP in the absence of memory retrieval or when administered 1h or 6h after retrieval. Furthermore, PROP did not affect acquisition, consolidation or retrieval of social play-induced CPP. Our results demonstrate that PROP selectively blocks the reconsolidation, but not other processes involved in the storage and stability of social reward-related memories in adolescent rats. Furthermore, we found that the reconsolidation-window for social reward-related memories is quite brief. Together, our findings suggest that beta-noradrenergic neurotransmission, involved in memory reconsolidation for drug and food rewards, is also involved in reconsolidation of social reward-related memories. In addition, these data support the notion that memory consolidation and reconsolidation rely on distinct neural mechanisms.

D12-28

A NOREPINEPHRINE-MEDIATED ACTION ON $_{-2}$-AUTORECEPTORS IS MODULATING THE CONSOLIDATION OF INHIBITORY AVOIDANCE IN THE RAT

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The consolidation of inhibitory avoidance learning (IA) has been shown to be under the control of the α_1 and α noradrenergic system in the basolateral amygdala (BLA) Recently, post-training microinfusions of the selective α_2-adrenoceptor antagonist (Idazoxan) or agonist (UK 14,304) in the BLA were found to enhance or impair, respectively, IA performance, suggesting that the memory-modulating role of norepinephrine (NE) also involves the activation of the α_2-receptors. In reference to the preferentially presynaptic location of the α_2-receptors and their inhibitory control upon NE release in the central nervous system, the present experiment tested the effect of a local manipulation of α_2-receptors on the dynamic of NE release in the BLA during IA learning. To this aim, selective α_2-drugs Idazoxan or UK 14,304 were infused using *in vivo* intracerebral retrodialysis during IA learning. Male Long-Evans rats equipped with a dialysis probe aimed at the right BLA were perfused with Ringer solution for 2 hours before the start of the IA learning. Starting one hour before training, samples were collected every 15 minutes throughout the experiment duration. The infusions of 10 mM of Idazoxan or UK 14,304 started 15 minutes before the administration of the electric footshock and lasted for 45 minutes. Retention latencies were measured 24h later. Results showed that i) the administration of the footshock during IA learning induced a significant increase in NE release in control animals, ii) the infusions of Idazoxan and UK 14,304 induced a significant increase and decrease, respectively, of NE release, iii) the footshock-induced release of NE was significantly potentiated by Idazoxan infusion, an effect that was correlated with an enhancement of IA retention latencies. In contrast, the decrease of NE release induced by UK infusion was too dramatic to reveal any footshock effect and no decrease in the retention latencies was found in this group, revealing the behavioral limits of unilateral infusion technique. These data show that the presynaptic α_2-adrenoceptors in the BLA contribute to the modulation of NE release in the BLA and strongly suggest that the memory-modulated role of NE on IA consolidation is mediated, at least in part, by pre-synaptic α_2-adrenoceptors in the BLA.

D12-29

THE *EUCHROMATIN HISTONE METHYLTRANSFERASE 1* (Ehmt1) HETEROZYGOUS KNOCKOUT MICE AS A MODEL FOR THE KLEEFSTRA SYNDROME OF INTELLECTUAL DISABILITY: DELAYED PUP DEVELOPMENT, HYPOTONIA, AND REDUCED EXPLORATION, SOCIAL INTERACTION AND FEAR-CONDITIONED LEARNING ARE ASSOCIATED WITH DIMINISHED DENDRITE MORPHOLOGY

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Patients with the Kleefstra syndrome (also known as the chromosome 9q34.3 subtelomeric deletion syndrome) have severe intellectual disability with little speech, postnatal developmental delay, hypotonia, congenital heart problems, facial abnormalities, autistic-like behavioral problems and diminished learning. This syndrome is caused by haplo-insufficiency of the *euchromatin histone methyltransferase 1* (*EHMT1*) gene, which is involved in euchromatic gene silencing. In mice, *Ehmt1* is highly expressed during (brain) embryonic development. Male and female heterozygous *Ehmt1* knockout mice (*Ehmt1*$^{+/-}$, kept on a C57BL/6J background), were compared to wildtype littermates and showed delayed postnatal development features and early hypotonia. The *Ehmt1*$^{+/-}$ adult mice revealed reduced activity and exploration, with increased anxiety, when exposed to novel environments in the open field, object exploration, marble burying, light-dark box, mirrored chamber and t-maze tests. *Ehmt1*$^{+/-}$ mice also demonstrated diminished social play when encountering a mouse from a different litter, and a delayed or absent response to social novelty when exposed to a stranger mouse. However, phenotyper-box locomotor activity or rotarod motor function were not affected in *Ehmt1*$^{+/-}$ mice. Interestingly, cognitive functions were impaired as measured in the object recognition task and during fear-conditioned learning in adult *Ehmt1*$^{+/-}$ mice. This has been correlated with affected dendrite morphology, demonstrating a reduced number of branches and endings, a diminished total dendrite length and thickness of the apical dendrites of CA1 hippocampal neurons, and a significant reduction in the number of spines per 30 um dendrite length in *Ehmt1*$^{+/-}$ brain. *Ehmt1* appears to be important for proper brain development and function.

D12-30

INVOLVEMENT OF miRNA IN DIFFERENT BRAIN STRUCTURES AFTER SPATIAL LEARNING IN MICE

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Formation of long-term memories (LTM) is accomplished through structural changes of neurons leading to a rearrangement of the neural networks requiring gene expression and protein synthesis. Evidence for local mRNAs and translational machineries at dendrites has suggested that post-transcriptional regulatory mechanisms at this level might also be crucial in stabilization of LTM. In particular microRNAs (miRs), small noncoding molecules, have been demonstrated a role in post-transcriptional gene regulation. However, experimental evidence in vivo is not available on their possible involvement in learning and memory. The hippocampus and the ventral striatum are considered as key structures in the stabilization of spatial memories. In order to shade light on molecular processes underlying such stabilization in this study we performed a large scale screening of miR expression in these two brain regions after spatial learning. CD1 mice were trained with a massed procedure in the spatial version of the Morris water maze. 1 hour after training, the hippocampus and the VS were dissected and RNA extracted. To study the spatial learning component, we compared miR expression profiles of mice submitted to the spatial procedure with those of mice exposed to the same context but without require the application of a spatial strategy.Our study demonstrated specific alterations in miR expression levels within both brain structures after learning: both increases and decreases. Interestingly, the learning induced profile of miR expression varied between the two structures thus suggesting that different mechanisms might underlie learning induced plasticity in different brain areas. Microarray analysis showed only one miR varied in the both. In order to verify whether it is down regulation had role in memory process we performed ICV administration of the mimic before training. Treated mice did not show any deficit during training but were impaired in the ability to locate the correct quadrant on the probe test 24h after training. This is the first evidence that demonstrates in vivo the involvement of only one miR variation which avoids long term memory process.

D12-31

NEURAL NETWORKS AND RELATED MONOAMINERGIC FUNCTIONS INVOLVED IN GOOD AND POOR DECISION-MAKING IN THE RAT

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Decision-making is profoundly impaired in several psychiatric disorders such as addiction, but also in some healthy individuals. Although it is well-known that the fronto-striatal circuit modulated by monoaminergic systems is critical for decision-making performance, the precise neural networks and related monoaminergic modulation underlying adapted and maladapted decision-making are largely unknown. We have previously demonstrated variability in decision-making abilities across healthy individuals using the Rat Gambling Task (Rivalan et al., Biol. Psychiat. 2009) similar to the Iowa Gambling Task in human. Good decision-makers prefer advantageous options that offer low immediate rewards but are followed by short and unpredictable penalties (time-out). By contrast, poor decision-makers remain on disadvantageous options that are more immediately rewarding, but associated with longer penalties. The present study was designed to explore (1) brain activity within the fronto-striatal network according to decision-making performance using immunodetection of Fos protein and (2) related dopaminergic, noradrenergic and serotoninergic basal functions by a sensitive HPLC/electrochemistry system. We show that the fronto-striatal circuit is selectively and highly recruited during good compared to poor decision-making, with a distinct involvement of several fronto-striatal structures according to the performance and to the readiness to choose advantageously. Moreover, these behavioral differences are associated with distinct monoamine functions within the fronto-striatal network. Thus, different brain activities and neurochemical patterns in the fronto-striatal circuit underly the ability to make good decisions across individuals. These characteristics will be discussed in relation to the interaction between motivational (reward-based behavior) and high-order cognitive processes (most notably outcomes evaluation and flexibility) that differentiate poor and good performers.

D12-32

REDUCTION OF NEURAL METABOLIC ACTIVITY IN CA1 AND SUPRAMAMMILLARY NUCLEUS DURING SPATIAL WORKING MEMORY IN AGED RATS

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Spatial working memory is a short term memory that is related to the ability to prevent interference. Aging results in an increase of interference of information. We aimed to study the effects of aging on retention processes and proactive interference. Our objective was also to know which brain circuits were related to these processes in aged rats. For this purpose, we used aged (18 month old) male Wistar rats and adult rats (3 month old). Spatial working memory was tested in a Morris Water Maze. In order to assess working memory with low interference, rats performed a delayed matched to sample spatial memory task during four consecutive days. Spatial learning with high interference was assessed in a multisession task that lasted 3 consecutive days. In this task, rats performed three sessions each day with an intersession interval of 5 minutes. Each session was composed, as in the case of the other task, by one sample and one retention trials. The following groups (each n=10) were used: G1 (old rats trained in a delayed matching to sample task); G2 (old rats trained in a multisession task); G3 (adult rats trained in a delayed matching to sample task); G4 (adult rats trained in a multisession task). Neural metabolic activity was studied in the hippocampus, prefrontal cortex and mammillary region by means of the cytochrome c-oxidase histochemistry (COX). Once learning tasks were concluded, brain were extracted and frozen. Histochemical staining of COX was done. Regarding behavioral results, old rats showed more problems than adult rats in retention trials ($p=0.02$). Old rats presented longer latencies and more distance traveled during retention trials than adult rats. During multisession task, old rats were severely affected by interference of information, especially in the first training day ($p=0.001$). This worse performance in old rats was related to a significant lower COX activity in CA1 and supramammillary nucleus ($p=0.04$ and $p=0.001$). In multisession task, we found higher COX activity in medial mammillary nucleus and infralimbic cortex of the old group comparing to the adult group ($p=0.01$ and $p=0.002$). This could be related to the effects of interference of spatial information.

D12-33

THE ROLE OF INTRINSIC EXCITABILITY IN MEMORY ALLOCATION

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Memory allocation is the process by which neurons are selected to encode a specific memory episode. Previous results have shown that increasing the levels of the transcription factor CREB using viral vectors in a subpopulation of neurons in the lateral amygdala increases the possibility that these neurons will encode a fear memory episode, during which an auditory stimulus is associated with a fearful event (i.e. electric shock) (Han *et al.*, *Science* 316, 457, 2007). Increased excitability could serve as a mechanism by which CREB might favor recruitment of neurons in the fear memory trace, since CREB-transfected neurons have increased levels of excitability (Zhou *et al.*, *Nat Neurosci* 12, 1438, 2009). Since CREB can bias and facilitate neuronal selection in a fear memory trace, we hypothesized that formation of a specific memory, which is known to increase CREB levels in a subset of neurons, would increase neuronal excitability and facilitate recruitment of the same neurons to a second memory trace, within a specific temporal window (because CREB increases for a specific time after memory formation). In order to test our hypothesis, we trained mice in auditory fear conditioning and performed patch-clamp recordings at different time points (1-3hrs or >4hrs) following training from amygdala pyramidal neurons. We measured properties of intrinsic excitability (input resistance, number of spikes, action potential properties) and found that neuronal excitability was increased 1-3 hours post-training and returned to baseline levels after 4hrs. In addition, we performed behavioral tests in order to test whether this increase in excitability could modulate memory performance on a different task, in this case conditioned taste aversion (CTA). We found that CTA training 3hrs (but not 5hrs) following initial fear conditioning training enhanced memory performance. Finally, we used a computational modeling approach that allows us to test possible mechanisms by which the increased excitability in pyramidal neurons could enhance memory, when a second training follows within a specific time window. Our model suggests that changes in excitability could modify the size of memory traces, which is also dependent on a balance of excitatory and inhibitory connection strength. Collectively, our results show that both neuronal excitability as well as population dynamics could interact to facilitate the process of memory allocation and enhance memory performance.

D12-35

LACK OF CYCLIN D2 IMPAIRING ADULT BRAIN NEUROGENESIS ALTERS HIPPOCAMPAL-DEPENDENT BEHAVIORAL TASKS WITHOUT REDUCING LEARNING ABILITY

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The exact function of adult hippocampal neurogenesis remains elusive, although it has been suggested to play a role in learning and memory processes. In our studies, we employed cyclin D2 gene knock-out (cD2 KO) mice with almost complete deficiency of newborn neurons in the adult brain (Kowalczyk et al., J. Cell Biol., 2004). These mice have also slight morphological abnormalities of the brain, including the hippocampal formation. Previously, we have shown for cD2 KO mice that new hippocampal neurons are not obligatory for memory formation (Jaholkowski et al., Learn. Mem., 2009). In the present study, the animals were subjected to hippocampus-dependant behavioural tests requiring and non-requiring learning component. cD2 KO mice showed significant impairment in such species-typical behaviours as nest construction, digging, and marble burying. They were building none or poorer nests, digging less robustly, and burying fewer marbles than WTs. Moreover, cD2 KO mice showed normal sucrose preference, however, in contrary to the controls, preceded by neophobia phase. cD2 KO animals were more active in the open field and automated motility chamber, and showed increased explorative behaviour in IntelliCage. On the other hand D2 KO mice performed normally in the cue and context fear conditioning tasks. Presented results suggest that either morphological abnormalities of the hippocampal formation or adult brain neurogenesis impairment (or both) alter hippocampal-dependant behaviours without influencing learning abilities.

D12-35

EARLY CONSUMPTION OF HIGH-FAT DIET IS MORE DETRIMENTAL THAN ADULT CONSUMPTION FOR SPATIAL RELATIONAL MEMORY AND HIPPOCAMPAL NEUROGENESIS IN MICE

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Increased consumption of energy-dense food, especially high-fat diets (HFD), participates to the new obesity pandemic. In addition to metabolic and cardiovascular disorders, obesity is associated with adverse cognitive outcomes. This can be particularly problematic during childhood and adolescence as these periods shape the neurobehavioural processes required for life-long cognitive function. In adult rodents, long lasting consumption of HFD induces obesity and neurocognitive impairments. However, the existence of critical periods of development that differ in terms of sensitivity to the detrimental effects of HFD remains unexplored. We thus compare the consequences of early HFD exposure (starting at weaning and covering late infancy and adolescence) and adult HFD exposure on hippocampal-dependent memory and hippocampal plasticity. After 8 weeks of HFD, we assessed relational memory in C57/BL6 mice using radial maze. All animals achieved concurrent spatial discrimination of pairs of arms, except half of early HFD exposed mice. Mice performing this discrimination were then exposed to a recombined pair (made of previously discriminated pairs) to evaluate their relational memory, i.e. their ability to use previously acquired spatial memory in a flexible manner. Again, early HFD exposed mice were specifically impaired: they responded at chance level whereas controls and adult HFD exposed mice responded well above chance. One month after behavioural assessment, mice were euthanized and blood and brains were collected in order to evaluate metabolic status and hippocampal plasticity, respectively. HFD consumption enhances plasma leptin, insulin, cholesterol and triglycerides whenever the diet exposure starts, indicating that metabolic changes cannot be related to specific early HFD effect on cognition. As the level of hippocampal neurogenesis (i.e. persistent formation of newborn neurons in the dentate gyrus) has been linked to hippocampal plasticity and cognition, we labelled immature neurons using doublecortin immunohistochemistry. Early HFD exposure significantly decreases the number of doublecortin-positive neurons in the hippocampus compared to age-matched control mice whereas adult HFD exposure did not induce any effect. Our results identify a critical period of development (late infancy and adolescence) with higher sensitivity to HFD-induced impairment on both hippocampal plasticity and hippocampal-dependent memory.

D12-36

KNOCKDOWN OF THE GLUCOCORTICOID RECEPTOR ACCELERATES FUNCTIONAL INTEGRATION OF NEWBORN NEURONS IN THE ADULT HIPPOCAMPUS

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Stress is well known to reduce adult hippocampal neurogenesis, a process implicated in cognition and psychopathology. Yet, the exact role of the glucocorticoid receptor (GR), one of the major mediators of the stress response, in regulating adult neurogenesis is largely unknown. Here, we show that selective GR knockdown in cells of the hippocampal neurogenic niche, accelerates their neuronal differentiation and migration. Strikingly, this selective GR knockdown induces mispositioning of new granule cells, alters their dendritic arborization and increases the number of mature dendritic spines and mossy fiber boutons. Consistent with the increase in synaptic contacts, cells with GR knockdown exhibit increased basal excitability. Finally, GR knockdown in animals results in impaired contextual freezing during fear conditioning. Together, our data show a key role for GR protein not only in synaptic connectivity but also in the correct integration of newborn granule cells into existing hippocampal circuits involved in memory consolidation.

D12-37

OLFACTORY BULBECTOMY, BUT NOT ODOR CONDITIONED AVERSION, INDUCES THE DIFFERENTIATION OF IMMATURE NEURONS IN THE ADULT RAT PIRIFORM CORTEX

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The piriform cortex layer II of young-adult rats presents a population of prenatally generated cells, which express immature neuronal markers, such as the polysialylated form of the neural cell adhesion molecule (PSA-NCAM) or doublecortin (DCX), and display structural characteristics of immature neurons. The number of PSA-NCAM/DCX expressing cells in this region decreases markedly as age progresses, suggesting that these cells differentiate or die. Since the piriform cortex receives a major input from the olfactory bulb and participates in olfactory information processing, it is possible that the immature neurons in layer II are affected by manipulations of the olfactory bulb or olfactory learning. It is not known whether these cells can be induced to differentiate and, if so, what would be their fate. In order to address these questions, we have performed unilateral olfactory bulbectomy (OBX) and an olfactory learning paradigm (taste-potentiated odor aversion, TPOA), in young-adult rats and have studied the expression of different mature and immature neuronal markers, as well as the presence of cell death. We have found that 14 h after OBX there was a dramatic decrease in the number of both PSA-NCAM and DCX expressing cells in piriform cortex layer II, whereas that of cells expressing NeuN, a mature neuronal marker, increased. By contrast, the number of cells expressing glutamate decarboxylase, isoform 67 (GAD67), a marker for interneurons, decreased slightly. Additionally, we have not found evidence of numbers of dying cells high enough to justify the disappearance of immature neurons. Analysis of animals subjected to TPOA revealed that this paradigm does not affect PSA-NCAM expressing cells. Our results strongly suggest that OBX can induce the maturation of immature neurons in the piriform cortex layer II and that these cells do not become interneurons. By contrast, these cells do not seem to play a crucial role in olfactory memory.

D12-38

D-CYCLOSERINE IN THE PRELIMBIC CORTEX REVERSES THE IMPAIRING EFFECTS OF PARAFASCICULAR THALAMIC LESIONS ON AN ODOR-REWARD ASSOCIATIVE TASK

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The parafascicular nucleus (Pf), a posterior intralaminar nucleus of the thalamus, has been involved in cognitive processes since detrimental effects of Pf lesions have been reported on different learning and memory paradigms. One example is the odor-reward task (ODT), which requires discrimination of three odors, one of which associated with an edible reward. ODT learning has also been related to the prelimbic cortex (PLC), as infusion of antagonists of the NMDA receptors (NMDArs) prevents early ODT consolidation. In contrast, intracerebral and systemic injections of NMDArs agonists, such as d-cycloserine (DCS), a partial agonist at the glycine site of NMDArs, have been shown to enhance ODT in normal rats and to reverse learning deficits in several paradigms due to aging, sleep deprivation, stress, pharmacological manipulations or brain damage. To examine whether the cognitive deficits occurring after Pf lesions in ODT may be reverted by enhancing glutamatergic transmission in the PLC, in the present experiment infusions of DCS were administered directly into the PLC. Thus, the Pf of Wistar rats were bilaterally lesioned (excitotoxic lesions with NMDA: 0.15M, 1.2 microl/side) during stereotaxic surgery, and then DCS (10 µg/side) was bilaterally infused in the PLC before ODT training. Rats underwent an ODT acquisition session and a 24-h test and latency before making a correct response and total number of errors were scored during both sessions. To rule out olfactory alterations due to the Pf lesions, an additional olfactory test was conducted at the end of the behavioral tests. The results showed that the Pf integrity seems to be indispensable for the acquisition and retention of ODT, consistent with previous reports. In contrast, Pf-lesioned rats infused with DCS in PLC prior to training, exhibited a significant enhancement of performance in the 24-h ODT test. Consistent with anatomical and functional data, the Pf contribution to olfactory learning and memory may possibly be linked to its role in the modulation of glutamatergic PLC activity. Therefore, DCS infusions may have reversed the Pf lesion-induced memory deficit enhancing glutamatergic activity in this area of the medial prefrontal cortex

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D12-39

EFFECTS OF ANOSMIN-1 OVER-EXPRESSION ON *IN VIVO* HIPPOCAMPAL LONG-TERM POTENTIATION AND OLFACTORY MEMORY

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Anosmin-1 is an extracellular matrix glycoprotein encoded by the *KAL1* gene, which is responsible for the X-linked form of Kallmann syndrome in humans. During CNS development, Anosmin-1 participates in the migration of immortalised GnRH neurons, neuronal precursors, as well as of oligodendrocyte precursors. It also has a role in axon guidance, neurite outgrowth and the formation of axon collaterals from neurons of the olfactory system and proyection neurons of the cerebellum. Although to date, the mechanism of action of Anosmin-1 it is not completely understood, it has been proposed that Anosmin-1 could regulate the signalling of FGF2/FGFR1 and other receptors and ECM molecules. We have generated a transgenic mouse line that over-expresses Anosmin-1 under the control of the beta-actin promoter. Histological examination of adult transgenic mice did not reveal seeming neuroanatomical alterations, compared with control mice. So far, we have studied the effect of Anosmin-1 overexpression in adult neurogenesis and the distribution of several neuronal markers in the hippocampus. Adult transgenic mice show defects in olfactory function in an olfactory memory test, since a significant increase in the investigacion time during the second presentation, 15 or 30 minutes after the first exposure, indicates these mice were not able to recognize an odorant previously presented. We monitored the physiological properties of the CA3-CA1 synapse in adult mice *in vivo* under specific experimental conditions, which included input/output curves, paired-pulse facilitation, and electrically-evoked LTP. Field excitatory postsynaptic potential (fEPSPs) evoked at the CA1 area by stimulation of Schaffer collaterals in Anosmin-1 transgenic mice for input/output curves and the paired-pulse test presented values similar to those reached by controls. Induction of long-term potentiation (LTP) in alert-behaving mice showed that Anosmin-1 overexpression prevented evoking an LTP response. Present results suggest the involvement of Anosmin-1 in synaptic plasticity in adult mice.

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D12-40

NOT ONLY NOVELTY, BUT ALSO RECONSOLIDATION, CAN PROMOTE THE BEHAVIORAL TAGGING PHENOMENON

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Introduction: Based on synaptic tagging theory, new behavioral studies showed that a novel experience, but not a familiar one, can provide plasticity-related proteins (PRPs) for the consolidation of another memory, by an analogous behavioral tagging process. However, upon certain situations a familiar experience can induce reconsolidation of the memory trace, what also requires PRPs synthesis. Thinking that way, we evaluated whether reconsolidation of a previous memory could promote the behavioral tagging phenomenon even not being a novel experience. Methods and Results: Male Wistar rats were trained in a weak protocol of object recognition (OR) that only induces short term memory (STM), and four or one hour, before or after that, they were reexposed to a context where they were previously fear conditioned (CFC) for 3 min (what is known to induce memory reconsolidation). Twenty-four hours later OR test was performed to evaluate long term memory (LTM). Only the groups that reconsolidated CFC's memory one hour before or after OR training showed LTM memory, suggesting a behavioral tagging phenomenon. To be sure that it was behavioral tagging and not "emotional tagging", the same experiment was performed with the subcutaneous injection of Nimodipine before the CFC context reexposition. This drug only prevents the reactivation/destabilization process, not having any effect upon memory retrieval or storage. As memory is not destabilized its do not need to be reconsolidated and new PRPs are not synthesized. Upon these conditions, the reexposion to CFC context did not promoted LTM formation of OR memory. Conclusions: We show that in rats subjected to weak training protocol that induce solely STM, LTM is promoted and formed only if training sessions took place in contingence with reconsolidation, but not just retrieval, of another memory occurring during a critical time window around training. These findings represent the first evidence indicating that not only novelty, but also reconsolidation, can promote the behavioral tagging phenomenon, and triggers new insights for this process that is Just beginning to be understood.

D12-41

BRAIN-BEHAVIOURAL LATERALIZATION IN HONEYBEES: ODOUR DEPENDENT ASYMMETRY AND A FIRST MORPHOLOGICAL COMPARISON OF THE PRIMARY OLFACTORY CENTRE

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Recently, a striking lateralization in the recall of odour memories was revealed in the honeybee, Apis mellifera, showing a right side dominance in short-term retrieval. Further asymmetries were demonstrated at the antennal level, with a higher number of olfactory sensilla, the locations of olfactory receptor neurons on the right antenna and in odour reception where the right antenna showed a higher level of overall neuronal depolarization after odour presentations. Here we investigated whether a morphological asymmetry can be observed in the volume of the primary olfactory centres of the central nervous system, the antennal lobes (ALs). A subset of ALs functional units, the glomeruli, has been imaged using two-photon microscopy and the volume of these glomeruli have been reconstructed and compared between the right and the left side of the ALs. Those glomeruli were chosen which showed the highest morphological plasticity after long-term odour conditioning. Furthermore, single-antenna olfactory recall experiments were performed, conditioning the proboscis extension reflex for the odours that provoke functional responses mostly in the selected subset of glomeruli. Anatomical analysis did not reveal significant differences between the sides. The behavioural test instead showed strong odour dependence of the degree of response lateralization. While floral key compounds triggered a highly asymmetric response, the effect vanished for more ubiquitous volatiles. These data provide new evidence of the odour effect on behavioural asymmetries in honeybees and new upper limits for an anatomical asymmetry beyond the lateralized behaviour.

D12-42

SPATIAL MEMORY AND EARLY METABOLIC BRAIN CHANGES IN A MODEL OF HEPATIC ENCEPHALOPATHY

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Portal hypertension is a major complication of cirrhosis that frequently leads to a neuropsychiatric disorder that affects cognition. The present study was undertaken in order to compare the performance of sham-operated rats (SHAM) and portal hypertension rats (PH) at early evolutive phase of PH in reference memory tasks in the Morris water maze (MWM). Our work shows that spatial learning in the MWM is not impaired in PH group ($p=0.007$) although it showed a one-day delay in the task acquisition respect to the SHAM group ($p=0.006$). We assessed the brain metabolic activity of the animals by means of cytochrome c-oxidase (COx) histochemistry. We found no differences between groups in metabolic activity in infralimbic cortex, prelimbic cortex, the cingulate cortex and CA1 subfield of the dorsal hippocampus. However, significative changes were found in the CA3 ($U = 166.000$, $n_1 = 11$ $n_2 = 12$; $p = 0.039$), dentate gyrus ($U = 171.000$, $n_1 = 11$ $n_2 = 12$; $p = 0.018$), basolateral ($U = 165.000$, $n_1 = 11$ $n_2 = 12$; $p = 0.045$), medial ($U = 173.000$, $n_1 = 11$ $n_2 = 12$; $p = 0.013$), lateral ($U = 165.000$, $n_1 = 11$ $n_2 = 12$; $p = 0.045$) and central ($U = 168.000$, $n_1 = 11$ $n_2 = 12$; $p = 0.029$) amygdala showing lower COx activity in the PH group as compared to the SHAM group in all cases. In fact, different neural networks were established to performance the task. The present study extends previous findings on the brain metabolic activity changes without alteration of spatial memory at early evolutive phases of PH

D12-43

STRIVING FOR SURVIVAL: IS FEAR-REACTION TO RAT URINE PRESENT IN ALL STRAINS OF MICE?

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After studying the neurobiology of attraction to sexual pheromones in mice, we are interested in another innate emotional response to another vomeronasal stimulus, fear to predator "odorants" (acting as *kayromones*). It has recently been shown that mice detect proteins in rat urine and cat saliva to which they react with fear and anxiety (Papes et al. 2010, Cell 141:192-703). Therefore, we tried to characterise the defensive reactions of our CD1 mice to rat urine and cotton fabrics rubbed onto cat's fur. After habituation to the test cage and experimenter, female mice were introduced in a 13.5x44 cm test cage with "safe" (13.5x14.6cm) and "dangerous" compartments (13.5x29.2 cm). Animals were introduced in the safe compartment and the stimulus (or blank) was adhered to the floor in the opposite side of the cage (within the dangerous compartment). The behaviour was videotracked for 5 minutes for analysis. Three groups of animals (n=10 per group) received three tests each: control (blank-blank-blank), rat urine (blank-rat urine-blank) and cat (blank-cat odour-blank). An ANOVA comparing the mean time spent in the safe compartment revealed a significant effect of the TEST, but no effect of GROUP nor TESTxGROUP interaction ($p>0.1$). This suggests that CD1 mice show no fear to either cat or rat chemosignals. Since Papes et al. (2010) used C57BL/6J mice, our negative data might reflect strain differences. Therefore, we run tests of defensive reactions to rat urine in CD1 (n=6) and C57BL (n=6) female mice. The results indicate a clear effect of the strain on the investigation of the stimulus zone (CD1>C57BL, $p<0,001$) throughout the experiment. In addition, C57BL mice show a trend ($p=0,056$) to remain in the safe area during the stimulus test, as compared to CD1 mice in the same test. These data strongly suggest inter-strain differences in the fear responses to rat urine maybe due to C57BL mice showing generally fearful reactions to novelty, whereas CD1 mice displaying active, fearless investigation of new stimuli.

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D12-44

BEHAVIORAL AND ENDOCRINE CONSEQUENCES OF SIMULTANEOUS EXPOSURE TO TWO DIFFERENT STRESSORS IN RATS: INTERACTION OR INDEPENDENCE?

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There is little experimental research on how simultaneous exposure to two stressors interacts to induce short-term and long-term physiological and behavioral effects, including activation of the HPA axis. In the present experiment, adult male rats were exposed to two stressors well-characterized in our lab, immobilization on wooden boards (IMO) and cat fur odor, which greatly differ in a wide range of properties. We reasoned that the detection of the odor while the animals are immobilized, and therefore with no opportunity to escape, may markedly enhance the stressfulness of the situation. We then expected that simultaneous exposure to both stressors may potentiate their acute HPA activation and enhance their long-term consequences as compare to the exposure to only one of the stressors. Cat fur odor-exposed animals showed a marked inhibition of activity and avoidance of the area where the impregnated cloth was located. In addition, cat odor elicited a modest activation of the HPA axis, whereas IMO elicited a much stronger response that did not further increase by simultaneous exposure to both stressors. Cat fur odor, in contrast to IMO, induced a long-lasting increase in anxiety-like behaviour evaluated in the elevated plus maze (EPM) 7 days after the stressors, with no evidence of enhanced HPA activation. Moreover, cat fur odor caused strong long-lasting (8 days later) fear conditioning to the stress-paired context. Thus, cat odor exposed groups showed hypoactivity, avoidance of the cloth area and enhanced HPA activation. We found no differences between rats only exposed to cat odor and that exposed to both cat odor and IMO. In rats only exposed to IMO, only some weak behavioral signs of fear conditioning were found, but HPA activation in response to the context paired to IMO was enhanced to the same extent as in cat odor-exposed animals, supporting a certain degree of endocrine conditioning. Apparently, in contradiction with our initial hypotheses, there appears to be little interaction between the two stressors regarding their behavioral and physiological consequences.

D12-45

PERFORMANCE OF INBRED ROMAN HIGH- (RHA-I) AND ROMAN LOW- (RLA-I) AVOIDANCE RATS IN THE FORCED SWIM TEST: BEHAVIOURAL DIFFERENCES AND EFFECTS ON VOLUNTARY ETHANOL INTAKE

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The outbred sublines of Roman High-Avoidance (RHA) and Roman Low-Avoidance (RLA) rats were initially selected and bred for their good (RHA) vs. poor (RLA) acquisition of the two-way active (shuttle box) avoidance response. Two inbred strains (RHA-I and RLA-I, respectively), derived from the Swiss outbred rat lines, are maintained at the Autonomous University of Barcelona laboratory since 1997. This psychogenetic selection procedure led to stable strain divergences in behavioural traits such as emotional reactivity, coping style, impulsivity, novelty seeking and vulnerability to addiction. Recent studies have evaluated the performance of the outbred Roman lines in the forced swim test, a procedure extensively used to reproduce in rodents passive coping responses to stress. Experiment 1 investigated the performance of male inbred RHA-I and RLA-I rats in the forced swim test, whereas Experiment 2 evaluated the impact of forced swimming on voluntary ethanol intake in a preference test (water vs. a 4% ethanol solution). Immobility, mild swimming and struggling were used as dependent variables in the forced swim test, whereas water and alcohol consumption, and ethanol preference were registered before and after the forced swim experience. The results obtained in Experiment 1 showed significant RHA-I/RLA-I performance differences in the forced swim test, being discussed on the basis of the repeatedly observed strain divergences in coping styles and fearfulness. Experiment 2 showed that forced swimming stress abolished the pre-test strain differences observed in voluntary ethanol intake (higher values of alcohol consumption and preference in RHA-I rats as compared to RLA-I rats). These data suggest that the effects of stress on alcohol preference depend on genetically determined differences in emotional reactivity.

D12-46

CANNABINOIDS PREVENT THE DEVELOPMENT OF STRESS-INDUCED ALTERATIONS IN A RAT MODEL OF TRAUMA

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Cannabinoids have recently emerged as a possible treatment of stress- and anxiety-related disorders such as post-traumatic stress disorder (PTSD). Here we examined whether cannabinoid receptor activation could prevent the effects of traumatic stress on the development of behavioral and neuroendocrine measures in a rat model of trauma, the single-prolonged stress (SPS) model. Rats were injected with the CB1/CB2 receptor agonist WIN55,212-2 (WIN) into the basolateral amygdala (BLA) following SPS exposure and were tested one week later for inhibitory avoidance (IA) conditioning and extinction, acoustic startle response (ASR) and hypothalamic-pituitary-adrenal (HPA) axis function. Exposure to SPS enhanced conditioned avoidance and impaired extinction while enhancing ASR and negative feedback on the HPA axis**.** WIN microinjected into the BLA (5 µg/side**)** prevented SPS-induced alterations in IA and ASR. These effects were blocked by intra-BLA co-administration of the CB1 receptor antagonist AM251 (0.3 ng/side), suggesting the involvement of CB1 receptors. Furthermore, WIN (0.5 mg/kg) administered intraperitoneally after SPS prevented the trauma-induced alterations in HPA axis inhibition. Our findings suggest that cannabinoids could serve as a pharmacological treatment for stress- and trauma-related disorders. Although the precise mechanism by which cannabinoid receptor activation prevents the stress-induced behavioral modifications remains to be clarified, our findings suggest a crucial contribution of CB1 receptors in the BLA.

D12-47

THE SEROTONERGIC SYSTEM IN THE BRAIN OF FEMALE RATS EXPOSED TO NEONATAL, ADOLESCENT AND ADULT STRESS

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The serotonergic system is known as an important modulator of emotional balance in both normal and pathological states such as depression and anxiety for which females are more vulnerable. Adverse experiences during critical periods such as the neonatal and adolescence are aetiopathogenetic factors for adult psychopathologies. Based on the above we determined 5-HT, 5-HIAA and 5HT1A receptor levels in the PFC, the AMY, and in the HIPP of adult females exposed to a neonatal experience and either stressed or not as adolescents. During the neonatal period (PND 10-13) rat pus were exposed to a T-maze one arm of which lead to the mother. One group of animals was allowed the contact with the mother (rewarded) while the other was denied (the expected reward-DER). HPLC analysis revealed that in both the PFC and in AMY, neonatally rewarded animals had higher basal 5-HT levels. Furthermore, in the AMY of this group of animals, higher levels of 5HTIA receptors were detected by western blot analysis. Another cohort of animals exposed to the neonatal experience was either subjected or not during adolescence (days 30-38) daily to 1 hour of isolation and cage partner stress. In adulthood rats were exposed to Forced Swimming Stress (FSS). Following the adult stress neonatally frustrated animals had higher 5HT in the AMY, and lower 5HIAA in the PFC and HIPP when not stressed in adolescence than when stressed. The adult FSS resulted in increased 5HT- compared to basal levels - in the AMY in animals not subjected to any neonatal experience. In contrast in the PFC the adult FSS resulted in decreased (compared to basal levels) 5HT in all animal groups. 5HT1A receptor levels in the AMY of the neonatally rewarded animals were decreased following FSS in adulthood compared to the basal condition. Since the serotonergic system is intimately involved in the control of HPA axis reactivity, which is determined by early experiences we also measured basal plasma corticosterone and following the FSS. Neonatally DER animals who had also been exposed to the adolescent stress exhibited the most effective stress response, lowering the stress induced corticosterone levels faster.

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D12-48

THE MULTIPLE-HIT HYPOTHESIS OF PSYCHOPATHOLOGY: ENHANCED STRESS REACTIVITY AND SCHIZOPHRENIA ENDOPHENOTYPES CO-PRECIPITATE FOLLOWING ADVERSE LIFE EVENTS IN GENETICALLY SUSCEPTIBLE RATS

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Purpose: Schizophrenia is a complex mental disorder driven by genetic and environmental risk factors. This study sought to test, in rodents, the “multiple-hit hypothesis” of schizophrenia by examining the interaction between predisposing genes, adverse early-life experience, and exposure to a stressful condition during adolescence. Methods: Genetic predisposition: we used the pharmaco-genetically selected apomorphine-susceptible (APOSUS) line, which is characterized by schizophrenia-like phenotypes. Wild-type Wistars (parental strain of APOSUS) were used as controls. Adverse early-life experience: poor mother-pup interaction (i.e. low licking & grooming) was used as a marker of early-life adversity causing epigenetically driven stress hyper-responsiveness. Isolation-rearing: post-weaning isolation rearing was used as unfavourable environment for late brain maturation, a condition known to produce sensorimotor-gating deficits. Adult phenotypes: animals were tested on apomorphine-induced gnawing for dopamine sensitivity, pre-pulse inhibition (PPI) of the acoustic startle for sensorimotor-gating, spontaneous alternation for working memory and conditioned emotional response for ACTH, prolactin and corticosterone (CORT) stress-reactivity. Results: 1. APOSUS individuals are, in contrast to controls, CORT resistant. Additionally, apart from their high gnawing behaviour, they display normal PPI and working memory, but reduced acoustic startle and fear acquisition. Their endocrine response to fear-context revealed a blunted prolactin release, enhanced ACTH, but normal CORT (adrenal hyporesponsiveness). 2. Adult AS rats having experienced as pups poor maternal care develop a baseline PPI-deficit, and show enhanced working memory. Their stress-induced CORT secretion is enhanced together with an enhanced prolactin release and a dramatically enhanced ACTH release. 3. Additional isolation rearing abolished baseline PPI in the low maternal care AS offspring, increased gnawing and impaired their working memory. 4. The enhanced stress reactivity found in the adult APOSUS animals exposed to early-life adversity is already present from the first week of life and corresponds to priming of the amygdala circuitry. Conclusion: Our data support the multiple-hit hypothesis of psychopathology: early-life adversity enhances susceptibility of the genetically predisposed individuals to a later psycho-social stressor precipitating a severe schizophrenia-like phenotype.

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D12-49

STRESS AND DECISION-MAKING IN RATS: EFFECTS OF CORTICOSTERONE

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In several domains of the society, such as in the military, financial business and health care, decisions have to be made under highly stressful conditions. Recently we showed that male subjects performed poorly under acute stress in the Iowa Gambling Task (IGT), which measures decision-making performance under uncertainty (Van den Bos et al., 2009, Psychoneuroendocrinology 34). This effect was dependent on stress-induced cortisol levels: high-responders performed poorly, while low-responders did not. Here we studied the effect of corticosterone (CORT) on decision-making performance of male rats in a rodent version of the IGT (rIGT; Van den Bos et al., 2006, Behav. Res. Meth. 38). Male Wistar rats, kept on a reversed day-night cycle under mild food-restriction (90-95% of free feeding weight), were tested in the rIGT (120 trials in total). CORT-injections (1mg/kg s.c., HBC-complex, Sigma) were given in the second half of the task (3 days, 20 trials/day), 30min prior to testing, 2h after dark onset. Compared to saline controls, CORT-injections led to strongly increased plasma CORT levels 30min after administration. Behavioural data showed that CORT-injections were followed by a poor rIGT performance: CORT-treated rats made more choices for the long-term disadvantageous option than saline-treated controls. Currently we are analysing c-Fos expression in prefrontal, striatal and amygdalar areas to unravel the underlying neural mechanisms. Thus, high levels of corticosterone may disrupt decision-making performance in male rats. The observed effect of CORT 30min after administration might be due to non-genomic effects, which is subject of further study.

D12-50

ANTINOCICEPTIVE EFFECTS INDUCED BY GRAVITY STRESS IN RATS: SEX DIFFERENCES

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Objective: A number of studies have shown that sex is one of the major variables that confer differential sensitivity to stress. Therefore, it is interesting whether sex-related differences exist in gravity-induced analgesia. Methods: In the present study, we investigated the analgesic effects induced by high-gravity loading (1.5G and 2.0G for 10 min) and compared the pattern of the stress-induced analgesia (SIA) between male and female rats. In each rat, eight sites (nose, both forepaws, upper and lower back, both hindpaws and tail) were selected to apply noxious stimuli using a von Frey-type needle stimulator. The threshold values of the withdrawal responses were measured. In order to confirm whether the endogeneous opioids are concerned with the gravity-induced antinociceptive effects, naloxone-HCl was used. Results: In case of weak stress (1.5G), analgesic effects were scarcely observed both in males and females. Effective analgesic effects could be induced by stronger (2.0G) gravity-loading and clear sex differences were observed. Gravity-induced analgesic effects were more effective in males than in females, indicating that males are more sensitive to stress than females judging from nociceptive modulation. The ratio of naloxone-reversibility against the gravity-induced analgesia is clearer in males than in females. Conclusion: In rats, SIA was more effective in males than in females and antagonizing effects of naloxone against SIA were stronger in males than in females. The present results suggest that non-opioid SIA system evoked by gravity-loading may be more actively present in females than in males.

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D12-51

COMPARISON OF STRESS-INDUCED MODULATION OF SMOOTH MUSCLE ACTIVITIES BETWEEN SMALL AND LARGE INTESTINE IN ADULT RATS

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Objective: One of the possible mechanisms of feeding disorder induced by stress may be linked to changes in the intestinal movements. Therefore, we investigated and compared the gravity (G) stress-induced changes in small and large intestinal movement, *in vitro*. Methods: Rats (Wistar male, SPF, 7 week old) were divided into Control (1G) and 3G groups. 3G-stress (every day for 10 min) was loaded by a centrifugal apparatus for 1 to 30 days. Under barbiturate anesthesia, a 1 cm-long section of the ileum or the colon was isolated and fixed in a conventional chamber filled with Tyrode solution. Intestinal movements were evoked by applying acetylcholine (Ach, 10^{-2} to 10^{-8} g/ml). Antagonistic effects of adrenalin (Adr, 10^{-4} g/ml) on the Ach-evoked movements were also observed. Results: The movement pattern induced by Ach application was phasic (early) and tonic (late). Peak amplitude of the phasic wave was dose-dependent on the Ach concentration. No significant differences in the peak amplitude between control and 3G groups were observed in the ileum; by contrast, significant differences were detected at 6 and 30 days in the colon. The peak amplitude was decreased by Adr application in both control and 3G groups. The decrease in movement amplitude was significantly different in the colon, but not in the ileum at 6 days after stress loading. Conclusion: The present study indicates that G-stress modified ileal and colonal movement. Basic intestinal movements by Ach were influenced in the colon, but not in the ileum. However, stress-induced movements were more clearly antagonized by Adr in the ileum than the colon. The present results suggest that stress-induced modulation of intestinal movements varies among the different sections of the digestive tract.

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D12-52

BILATERAL DISTRIBUTION OF NEUROPEPTIDASE ACTIVITIES IN THE FRONTAL CORTEX OF SPONTANEOUSLY HYPERTENSIVE RATS AFTER BETA-NORADRENERGIC RECEPTOR BLOCKADE

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The brain function is virtually asymmetric. Indeed, this asymmetry is not static but rather is a dynamic concept. The lipophilic beta-noradrenergic receptor blocker propranolol has been extensively used in hypertensive therapies. It readily crosses the blood-brain barrier being able to influence brain function, including the emotional processing. Several angiotensins, cholecystokinin, oxytocin, vasopressin and enkephalins are neuropeptides involved in diverse anxiety-related behaviours, being their function regulated in part by the neuropeptidases oxytocinase (OX), aminopeptidase A (AP A) and enkephalinase (ENK). The emotional processing, in which the frontal cortex is directly involved, is lateralized in basal conditions. Since changes in this basal brain bilateral pattern may reflect modifications in that processing, we analyzed the bilateral response of OX, AP A and ENK, in the left and right frontal cortex of spontaneously hypertensive rats, after treatment with propranolol, administered in drinking water. Enzymatic activities were measured fluorometrically, using arylamide derivatives as substrates. The bilateral response to propranolol treatment differed depending on the enzyme analyzed, but always changed significantly after treatment. Propranolol increased significantly all the enzymatic activities determined in frontal cortex, the degree of increase depending on the considered hemisphere.

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D12-53

LONG-TERM MODERATE EXERCISE IN FEMALE RATS

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Exercise has been reported to enhance cognitive performance, to reduce stress and anxiety, and to obtain cardiac benefits; however, the exercise protocols in terms of amount and intensity that produce better and specific benefits are poorly known. In humans, the recent recommendation of physical activity to improve and maintain health consists of moderate-intensity aerobic physical activity for a minimum of 30min each day, five days/week (Haskell et al. 2007). The present experiments were aimed to evaluate the long term effects of that moderate training procedure (treadmill running, 12m/m, 30min/d, 5d/week) in female rats as a lifestyle factor. A group of animals initiated the exercise protocol at youth (3-month-old) and a second group at adulthood (9-month-old), they were tested for heart rate and HRV over training, for emotional behaviour and HPA axis stress response at the age of one year, and for cognitive behaviour at the age of 18 months. Control groups receiving treadmill handling (CON) or no manipulation (SED) were also tested. HRV was measured monthly by telemetric devises implanted in the abdominal cavity, the analysis is currently under progress. The behavioral tests administered were: Hole-Board, Elevated Plus Maze, Forced Swimming, Shuttle-Box and Barnes Maze. ACTH and corticosterone were measured after hole-board and shuttle-box sessions. Moderate treadmill training improved early shuttle-box acquisition and slightly increased Barnes Maze learning. Trained rats decreased behavioral despair in the FST, but no effects appeared in exploration of the hole-board or anxiety in the elevated plus maze. However, treadmill training and handling showed a similar and more adaptive response than sedentary rats, but only when training and handling started at youth. Thus, the forced long term moderate treadmill training procedure used in the present study was not stressful, improved mood and the coping response to conflict situations, as well as maze performance in the elder female rats.

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D12-54

NECTIN-3 IN CA1 HIPPOCAMPUS AS A TARGET FOR THE PREVENTION OF CHRONIC STRESS-INDUCED ASOCIAL BEHAVIOR AND COGNITIVE DYSFUNCTION

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Chronic stress is a vulnerability factor for the development of psychopathologies often characterized by both cognitive dysfunction and asocial behaviour. Previous work showed that chronic stress evokes profound structural and molecular rearrangements in the hippocampus, including a structural remodelling of excitatory axo-spinous synaptic connectivity and a decrease in CA1 spine density. Existing evidence has implicated cell adhesion molecules (as shown for the neural cell adhesion molecule .NCAM- and L1) in the effects of stress on hippocampal remodeling and cognition. In this study, we assessed the role of the cell adhesion molecules Nectin-1 and Nectin-3, which are also widely expressed in the brain, in the social and cognitive abnormalities induced by chronic restraint stress in the rat. Nectin-1 (N1), is preferentially localized in axons, while its heterophilic partner, Nectin-3 (N3), is present in both axons and dendrites. In the CA3 area of the hippocampus, N1-N3 interactions at puncta adherentia junctions were shown to provide axodendritic adhesion, a process that is implicated in spine formation, and necessary to maintain proper mossy fiber trajectory. We found that 21 days of exposure to chronic restraint stress reduced N3 protein levels in CA1, but not in CA3, synaptoneurosomes. Bilateral infusion of N3 overexpressing adeno-associated viral vector into the hippocampus while not affecting anxiety-like and exploratory behaviors or corticosterone responses to stress, it prevented stress-induced reduction in social exploration and abnormalities in a CA1-dependent task. These results highlight the 21-days chronic restraint stress regimen as a valuable tool to model stress-induced asocial behaviors. In addition, they point out at the disruption of N3-mediated adhesion as a mechanism contributing to the observed stress-induced and CA1-related alterations in behaviour and cognition.

D12-55

VARIATIONS IN MATERNAL REINFORCEMENT EARLY IN LIFE ARE ASSOCIATED WITH DIFFERENTIAL BEHAVIORAL APPROACHES IN SOCIAL ENCOUNTERS: THE ROLE OF THE SEROTONERGIC SYSTEM

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Several different approaches in developmental research converge on the notion that manipulations of the early environment are linked to long-lasting alterations of emotional regulation. We have developed a paradigm in the rat in which mother contact is used as either a positive or negative reinforcer in a T-maze, during postnatal days 10-13. The serotonergic system, which develops early in life and is distributed widely in the brain, is one of the main players in maturational processes associated with emotional challenges later in life. The present study was based on the hypothesis that this early life manipulation of the primary social factor i.e. mother-infant interaction may affect social interactions in adolescence, and social conflict in adulthood and alter components of serotonergic function. Results showed that male rats trained under negative reinforcement (denied expected reward-DER) as neonates exhibited more aggressive-like behaviors during social play in adolescence and more proactive coping behaviors during social defeat in adulthood. HPLC analysis of biogenic amines from various brain regions of adult animals showed that rats trained as neonates under negative reinforcement had lower serotonin (5-HT) levels in both the prefrontal cortex and the amygdala. Social defeat resulted in increased serotonin levels in the prefrontal cortex and amygdala of these animals. 5HT1A receptor distribution measured immunohistochemically in the hippocampi of adult animals, with or without early life experience revealed that denial of expected reward is linked to a lower number of immunopositive cells in the CA1 area. Western blot detection of 5HTT protein levels in various brain areas showed that adult animals trained as neonates under negative reinforcement had higher levels of 5HTT in their amygdala and lower in the prefrontal cortex, when compared to naïve. These data suggest that a challenging early life experience shapes components of the serotonergic system in a direction that promotes a proactive coping style and aggressive-like phenotype in social confrontations, supporting further its role in aggression and coping strategies, as well as its susceptibility to the specific conditions of the early environment.

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D12-56

NEUROPATHIC PAIN INFLUENCES NEGATIVELY HIPPOCAMPAL NEUROGENESIS OF ADULT RAT BRAIN

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Chronic pain is a debilitating disease state characterized by complex alterations in both peripheral and central nociceptive pathways affecting brain structure and function. The hippocampus is implicated in the modulation of pain and is one of the few brain regions where production of neurons occurs throughout the lifetime of animals, including humans. The effect of neuropathic pain on the proliferation, survival and maturation of new neurons in the hippocampus is an almost unknown field of study. In the present study, we evaluated the effect of chronic constriction injury (CCI) of sciatic nerve on proliferation and survival of new cells by adminstration of bromodeoxyuridine (BrdU), immunohistochemistry for Ki67 and other markers of neuroblasts and mature neurons. We studied the presence in plasma corticosterone and TNF as well as the expression of BDNF and TNF in the hippocampus by Western blot. In our experiments, CCI animals showed mechanical hyperalgesia and mechanical allodynia in the first week after injury. In animals with chronic pain had a lower number of proliferating cells and also was less than the total number of neuroblasts. Moreover, CCI animals showed a reduction in the pool of new mature neurons in the granular layer of the hippocampus one month after the injury. Taken together, our results demonstrate that neuropathic pain influences negatively on hippocampal neurogenesis. In plasma, the amount of corticosterone increased non-significantly. However, TNF increased significantly in plasma but not hippocampus tissue of animals with neuropathy. There were also no changes in the expression of BDNF.

D12-57

THE EFFECT OF A FRUSTRATIVE EXPERIENCE OF REWARD DEVALUATION ON HIPPOCAMPAL GENE EXPRESSION IN INBRED ROMAN HIGH- (RHA-I) AND LOW- (RLA-I) AVOIDANCE RATS

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A recent microarray and qRT-PCR study conducted under basal conditions has showed that inbred Roman High- (RHA-I, low emotional reactivity) and Low- (RLA-I, high emotional reactivity) Avoidance rats (derived from outbred rats and selected and bred on the basis of their extreme divergences in two-way avoidance acquisition/performance) significantly differ in the whole brain expression of genes related to emotion, stress, aversive learning, drug seeking behaviour and neuropsychiatric disorders (EPHX2, PRL, CaMKII, CRHBP and HOMER3). In the present experiment we extended this study by analyzing strain differences in hippocampal gene expression after an aversive experience of reward-loss (instrumental successive negative contrast, iSNC). This effect was induced by exposing food-deprived RHA-I and RLA-I male rats to the sudden reduction in the amount of solid food presented in the goal of a straight alley (from 12 pellets –preshift phase- to 2 pellets -postshift phase-). iSNC effect appeared only in the more emotional RLA- I rats (higher response latencies in the 12-2 group as compared to the 2-2 control group in the postshift phase), supporting those theories that account for this effect on the basis of emotional mechanisms. Two hours and a half after this behavioural test, the hippocampus were removed and adequately prepared for the microarray study. After RNA extraction, the samples were hybridized onto the Whole Rat Genome Codelink Bioarray (Amershan Biosciences) and data processed following conventional statistical and computational studies for microarray analysis. The comparative analysis of hippocampal gene expression profiles in RHA-I and RLA-I animals enabled us to explore the role of this brain structure in the modulation of instrumental responses linked to frustrative non-reward, and lend support to the usefulness of Roman rats for neurogenetic research of anxiety/frustration- related behavioural traits.

D12-58

TIME-OF-DAY EFFECTS ON EMOTIONAL BEHAVIOUR IN RATS EXPOSED TO ONE SINGLE TRIAL INTEGRATED TEST

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The integration of anxiety tests formed by a light-dark box, an elevated-plus maze and an open field (Ramos et all, Behav. Brain Res, 193:277-288; 2008) provides a wide vision of animal´s emotionality. The aim of present study was to evaluate the effect of time-of-day on the performance of this integrative anxiety test. With this purpose, three months aged male Wistar rats were divided into three groups: morning (8:00-10:00), early afternoon (12:00-14:00) and late afternoon (18:00-20:00) and exposed to the integrated maze for 30 minutes. In all the tasks, anxiety-related exploratory behavior, general exploratory activity, grooming activity and elimination behavior, were measured. The results of the present study showed that animals tested in the early afternoon explored the open field and light part of the light-dark box more frequently than the morning period group. Moreover, the early afternoon group significantly spent more time exploring the open arms of the elevated-plus maze than the groups in the morning and late afternoon. In conclusion, the time of the day has significant influence on emotionality, in rats tested in an integrative anxiety test, appearing the lowest anxiety level in the early afternoon period.

D12-59

THE EXTRA-ADRENAL ORGAN OF ZUCKERKANDL MODULATES ANXIETY-LIKE RESPONSES AFTER IMMOBILIZATION IN RATS

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The organ of Zuckerkandl (OZ) is an abdominal paraganglion located on the aorta near the bifurcation of iliac arteries. It contains chromaffin cells arranged in cell nests, and these extra-adrenal chromaffin cells belong to the sympathoadrenal lineage like adrenal medulla ones. This extra-adrenal tissue is known to be involved in the development of cardiovascular system, and adaptive respiratory changes during birth. As a chromaffin tissue, it could be involved in stress responses like the adrenal medulla. The objective was to discern the role of this organ, after its extirpation, in stress and anxiety-like responses of rats subjected to immobilization. Animals were subjected to chronic immobilization by using a restraint tube during 5 days, and then blood levels of catecholamines and behavioral responses in the open-field, elevated plus-maze and dark-light box tests were evaluated. The findings revealed that the OZ induces a dimorphic effect on blood adrenaline levels, because male rats release lower levels of this catecholamine after OZ extirpation relative to female animals. Responses in the open field test were not modified by removing the OZ, indicating that response to a low stressful situation is not modified after OZ extirpation in immobilized rats. However, anxiety-like responses were modified. In fact, the presence of OZ modulates anxiety-like responses in a dimorphic way and in different behavioral situations. Thus it enhances anxiety-like responses in male rats placed on the elevated plus maze, because the time spent on open arms is enhanced after OZ extirpation. In the dark-light box, it reduces anxiety-like responses in female rats, because time spent on the dark side is enhanced after OZ extirpation only in female animals. These differences could be related to dimorphic effects on adrenaline release.

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D12-60

PERIPUBERTAL STRESS YIELDS REDUCED ADULT LATERAL SEPTUM GABA AND A CUE INTERPRETATION BIAS THAT CAN BE PHARMACOLOGICALLY ALLEVIATED IN RATS

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In order to better understand the mechanisms implicated in the long-lasting emotional effects of stress during adolescence, an animal model was used to examine the impact of stress on a brain region associated with emotionality and implicated in stress-induced activation of the hypothalamus-pituitary-adrenal axis (HPA) function, the lateral septum.
Short, unpredictable episodes of stress were applied peripubertally in male rats, from perinatal day 28 to 42. In adulthood, these peripubertally stressed rats exhibited more aggression than control rats when faced with an intruding, unfamiliar male (resident-intruder test). Next, non-invasive, *in vivo* magnetic resonance spectroscopy analyses were conducted in the lateral septum. Notable amongst the various metabolites found to be altered was the neurotransmitter GABA, exhibiting a reduction in the peripubertally stressed gorup. Follow-up *post-mortem* immunohistochemical analyses also revealed a reduction of the GABA-synthesizing enzyme gad67, highlighting a potential role for GABAergic mechanisms in the lateral septum in the emotionality exhibited by the peripubertally stressed rats. In support of this possibility, GABA levels in the Stress, but not Control group were negatively correlated with adult aggression challenge-associated plasma corticosterone concentration. Next, aiming to test the hypothesis that increased aggression in peripubertally stressed rats was associated with an increased negative reaction to aversive stimuli, instrumental learning tests were conducted using operant boxes. The results suggested that peripubertally stressed rats were more likely than controls to exhibit auditory stimulus generalization to unconditioned probe cues when associated with a negative (shock) but not a positive (food pellet) valence, particularly under high effort conditions (progressive ratio). Finally, the observed negative interpretation bias in the operant boxes was alleviated by intra-dorsolateral septum infusions of the GABAergic agonist muscimol. This finding highlights a potential role in cue interpretation and consequent behavioural implications of the GABAergic function reduction in the lateral septum, which was suggested from the converging evidence from magnetic resonance spectroscopy and immunohistochemistry. The present results suggest the notion that lateral septum GABAergic function may be implicated in brain and neuroendocrine programming via a mediating role in the translation of peripuberty stress effects into adult psychopathologica behavior.

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D12-61

FOUR DISTINCT BEHAVIORAL PROFILES OBSERVED IN MALE MONKEY RHESUS IN RESPONSE TO STRESSFUL HOUSING CONDITIONS

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Investigations of the pathophysiology of mental disorders have dramatically increased in the last decade. Such studies have almost exclusively been performed in rodents submitted to environmental, pharmacological, surgical or genetic manipulations. Those models can be seen as induced as opposed to spontaneously occurring disorders, therefore carrying poor construct validity. Moreover, the diversity of behavioral changes induced is quite limited, conferring poor face validity. Finally, mimicking such complex disorders in species phylogenetically and behaviourally closer to Humans seems more appropriate. Thus, we investigated the existence of spontaneous atypical behaviors displayed by non-human primates (NHP) housed in stressful conditions and their possible similarity with symptoms of human mental disorders. Stressful conditions, imposed by the breeding process, are defined by a peer-rearing from 5-months to 3-years old followed by housing in single cages; as opposed to large wild-like enclosure in social group. Forty males *Macaca mulatta* housed in single cage were observed using a scan sampling method, commonly used in Ethology. The parameters assessed were behaviors, body posture and orientation, gaze- direction and location in cage. Factor and cluster analysis were used to study inter-individual differences and revealed 4 distinct profiles. The inactive “depressive-like” profile contains males displaying mainly inactivity, a few changes of behaviors between the scans, a body facing the wall and located at the upper back corners of the cage. The self-centered “anxious-like” profile contains males displaying the higher levels of itching, yawning and selfgrooming. The “active-cautious” profile contains males quite active, exploring the cage and handling the feeding tray a lot, facing the wall as much as the front of the cage but standing at the back down corners of their cage. Finally the “active-aggressive” profile contains males very active but displaying a lot of threatening faces and vocalizations toward the observer and standing at the front of the cage. Motor stereotypic behaviors were observed among the 3 last profiles. These results suggest that NHP differ in their ways of coping with stress. As Humans, some individuals seem to be more severely affected by stressful events than others. The use of behavioral observations might allow us to find spontaneous model animals and forecast new perspectives in the study of mental disorders.

D12-62

CONTRIBUTION OF THE AMYGDALA AND DEEP LAYERS OF SUPERIOR COLLICULUS TO SOCIAL BEHAVIOR IN MACAQUES

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In the present study, we investigated the contribution of the amygdala and deep layers of superior colliculus (DLSC) to defensive behavior and social interactions in rhesus macaques, with relevance to anxiety disorders. Previously, we found that disinhibition of DLSC, a midbrain structure, by the GABA-A antagonist bicuculline methiodide (BIC) evoked defensive behaviors in the monkey. Here, we used reversible intracerebral drug infusions of GABA agonists and antagonists to investigate the interaction between DLSC and the amygdala in social behavior. Social interactions were observed in five dyads; in each, one subject received intracerebral drug infusions, via a removable cannula, and was paired with a familiar non-treated partner. The pair was videotaped for 2hrs. Drug sessions were compared with intervening saline or no-drug baseline sessions. We found that bilateral inactivation of the basolateral amygdala (BLA) by focal infusions of the GABA-A agonist muscimol (MUS) resulted in a significant increase in social contact (body contact + proximity) and grooming (all ps<0.05). These findings were consistent with our previous results in pigtail macaques (Lower et al., 2002). Unilateral disinhibition of DLSC by infusions of BIC evoked various defensive behaviors, not observed during baselines, including vocalization, escape, and exaggerated startle (all ps < 0.05). There was also a significant decrease in social contact from an average of 786 s (per 15-minute time segment) to 519 s and grooming from the baseline level of 441 s to 0 as compared with baseline. Finally, we investigated whether the defensive behaviors and socioemotional effects evoked by disinhibition of DLSC can be attenuated by a pre-treatment of BLA with MUS. These combined drug infusions attenuated both the defensive behaviors and the decreased social interactions evoked by the BIC infusions in DLSC in the following way. Defensive behaviors were markedly decreased during the first 30 min after treatment, and completely absent thereafter; exaggerated startle was completely blocked throughout the session, whereas cowering remained evident. Grooming, not observed under BIC in DLSC, increased significantly (p<0.05). The amount of social contact also increased, but the change did not reach the level of significance. These results indicate that BLA and DLSC interact to modulate emotional and social behaviors, either via direct reciprocal connections, or via independent regulation converging on a final common output.

D12-63

DISSOCIABLE EFFECTS OF REWARD ON ATTENTIONAL LEARNING: FROM PASSIVE ASSOCIATIONS TO ACTIVE MONITORING

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Visual selective attention (VSA) is the cognitive function that regulates ongoing processing of retinal input in order for selected representations to gain privileged access to perceptual awareness and to behavioural control mechanisms, facilitating analysis of currently relevant information while suppressing the less relevant input. Recent findings (Della Libera & Chelazzi, 2006, 2009) indicate that the deployment of VSA is shaped according to past outcomes. Targets whose selection has led to rewarding outcomes become relatively easier to select in the future, and distracters that have been ignored with higher gains are more easily discarded. Although outcomes (monetary rewards) were completely predetermined in our prior studies, participants were told that higher rewards would follow more efficient responses. Therefore, owing to this deception, it is conceivable that participants monitored rewards earned on individual trials as feedbacks of their performance. In a new experiment we have eliminated the illusory link between performance and outcomes by informing subjects that rewards were randomly assigned. This trivial yet crucial manipulation led to strikingly different results. Items that were associated more frequently with higher gains became more difficult to ignore, regardless of the role (target or distracter) they played when differential rewards were delivered, as if they had acquired greater perceptual salience as a result of the consistent association with reward. Therefore, VSA is shaped by two distinct reward-related learning mechanisms: one requiring active monitoring of performance and outcome, and a second one detecting the sheer association between objects in the environment (whether attended or ignored) and the more-or-less rewarding events that accompany them.

D12-64

PROCESSING OF PROSODIC CHANGES IN NATURAL SPEECH STIMULI IN SCHOOL-AGE CHILDREN

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Prosodic features of the speech (e.g. intensity, pitch, duration) convey information about two important aspects of communication: the meaning of the sentence and the emotional state of the speaker. In this experiment, processing of prosodic changes in natural speech stimuli was studied in school-age children using the electroencephalogram (EEG) and facial electromyography (EMG). The rapid facial reactions, reflecting autonomic nervous-system responses, will be later further analyzed. 18 healthy children (mean age 10 years) participated the experiment. The stimulus was a Finnish word (female name “Saara”) uttered by a female speaker with four different emotional connotations: neutral, commanding, sad, and scornful. During the EEG and EMG recordings the children were presented with frequent standard stimulus (79%) that was occasionally replaced with commanding (7%), sad (7%) or scornful (7%) deviants while watching self-chosen soundless video. Behavioural sound-discrimination abilities were evaluated by presenting the children stimulus pairs in which the stimuli were either identical (two standards) or different (a standard stimuli followed by any of deviant sounds). The children’s task was to press the response button according to whether the sounds were the same or different. The reaction times were fastest for the commanding stimulus and longest for the scornful stimulus, whereas no differences in reaction times between neutral and sad stimuli were observed. There were no significant differences in the hit rates. All deviant stimuli elicited a negative-going, fronto-centrally distributed neural response peaking at about 500 ms from the onset of the deviant stimulus. It was followed by a fronto-central positive deflection; peaking at about 740 ms. The results show that prosodic changes in natural speech stimuli activate pre-attentive neural change-detection mechanisms in school-age children.

D12-65

AUTISTIC TRAITS AND BRAIN ACTIVATION DURING FACE-TO-FACE CONVERSATIONS IN TYPICALLY DEVELOPED ADULTS

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Autism spectrum disorders (ASD) are characterized by impaired social interaction and communication, restricted interests, and repetitive behaviours. The severity of these characteristics is posited to lie on a continuum that extends into the general population. Brain substrates underlying ASD have been investigated through functional neuroimaging studies using functional magnetic resonance imaging (fMRI). However, fMRI has methodological constraints for studying brain mechanisms during social interactions (for example, noise, lying on a gantry during the procedure, etc.). In this study, we investigated whether variations in autism spectrum traits are associated with changes in patterns of brain activation in typically developed adults. We used near-infrared spectroscopy (NIRS), a recently developed functional neuroimaging technique that uses near-infrared light, to monitor brain activation in a natural setting that is suitable for studying brain functions during social interactions.

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D12-66

COMPUTATIONAL MODELING OF VISUAL SELECTIVE ATTENTION

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A neurocomputational model of visual selective attention was implemented in the MATLAB/SIMULINK environment and was used to account for a variety of empirical findings in the field of attention. The model is based on what is currently known about the neural basis of attention and involves two stages of processing realized as spiking neural networks (SNN). The first stage simulates the initial bottom-up competitive neural interactions among visual stimuli, while the second stage involves modulations of neural activity based on the semantic properties of the stimuli. During the progression of the neural activity in the two stages of processing, the encoded stimuli compete for access to working memory (WM) through forward, backward and lateral inhibitory interactions, which influence the strength of their neural response. At the same time, top down interactions may influence the overall processing in both stages. The basic functionality of the model relies on the assumption that an incoming visual stimulus is processed based on the rate and temporal coding of its associated neural activity. Thus, a saliency map algorithm is used in the model to set neural activity at the early stages of processing. In the second stage of processing, neural activity passes through a correlation control system comprised of coincidence detector neurons. These neurons measure the degree of semantic correlation between endogenous goals and the neural representation of the visual stimuli and may increase the synchronization between the brain areas involved in vision and goal maintenance. The developed model was used to simulate the findings from several behavioral experiments on the Attentional-Blink Phenomenon, the Perceptual Load theory of attention, and the relation between attention and consciousness.

D12-67

COGNITIVE CORRELATES OF CHOLINERGIC FOREBRAIN ATROPHY IN AGING AND ALZHEIMER´S DISEASE

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Introduction: The basal forebrain cholinergic system (BFCS) is known to undergo moderate neurodegenerative changes during normal aging as well as severe atrophy in Alzheimer´s disease (AD). Based on experiments with animal models, declining functional and structural integrity of the BFCS is hypothesized to be a major contributor to age- and AD-related impairments in attention and memory function. However, little is known about the role of the BFCS in human cognition, and the specific effects of BFCS atrophy on age- and AD-related cognitive impairments remain to be elucidated. Methods: We used neuropsychological test scores across a wide range of cognitive domains in combination with automated morphometry techniques on high-resolution 3T-MRI scans to examine associations between reduced volumes of the BFCS and impaired cognitive function in 28 patients with Alzheimer´s Disease and 31 healthy older adults. Location and individual volumes of the basal forebrain region of interest (BF-ROI) were determined based on a cytoarchitectonic map of basal forebrain cholinergic nuclei in MNI standard space. Results: When controlling for global cognitive impairment (MMSE), individual volumes of the BF-ROI correlated strongly with measurements of episodic memory (delayed verbal and constructional recall) and set-shifting (Trail-Making Test B) across age and AD groups. Weaker associations with BF volume were found for visual attention (Trail-Making Test A) and semantic fluency. No associations were found between BF volume and test scores of phonemic fluency (S-Words), confrontation naming (Boston Naming Test) and constructional praxis (Drawing Test). Complementary voxel-wise volumetric analyses restricted to the BF-ROI revealed different foci for associations with episodic memory, semantic fluency, visual attention and set-shifting, indicating lateralization and functional specialization among BF subregions. Conclusion: Our findings demonstrate the utility of morphometric in-vivo analyses to unveil specific cognitive correlates of age- and AD-related atrophy of the cholinergic BF. If reproduced in a bigger sample and complemented with functional imaging experiments, these findings may further our understanding of the role of the BFCS in specific cognitive impairments associated with normal and pathological aging.

D12-68

ATTENTION ALLOCATION TO 3D EMOTIONAL VISUAL SCENES AS REVEALED BY AUDITORY P3 AMPLITUDE AND POWER SPECTRAL ANALYSIS

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The present study aimed at comparing the effects of two-dimensional (2D) and three-dimensional (3D) visualization techniques in the modulation of attention by peripheral emotional visual information, as indexed by the amplitude of the P3 event-related component. We recorded the EEG signal (32 channels) of 30 healthy male subjects while they performed and active auditory oddball task. While performing the task, participants were presented with affective and neutral visual scenes, composed by computer-generated stimuli, in two visualization modes, 2D and 3D. We analyzed the effects of emotional valence and visualization mode in the amplitude and peak latency of the P3 component for the midline electrodes (Fz, Cz and Pz). The results revealed an effect for visualization mode in P3 mean and peak amplitudes at Pz, with lower amplitudes when the visualization of 3D scenarios was concurrent with the target detection task. Also, we found a trend for longer P300 latencies to targets in 3D conditions. No emotional modulation of P3 amplitude was found. However, we observed an emotional modulation in the frequency domain, namely in the theta and alpha bands. Overall, these results suggest that more attentional resources are allocated to 3D than to 2D visual scenes. It is discussed how virtual reality techniques may be more efficient to study attention modulation effects and emotion in experimental settings.

D12-69

2D:4D RATIO AND ITS RELATIONSHIP WITH OTHER ANDROGENIZATION PARAMETERS IN PARENTS OF PEOPLE WITH AUTISM SPECTRUM DISORDERS

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Introduction: The 2D:4D ratio is the quotient between the index and middle finger lengths and is a non-direct indicator of androgenization. If prenatal testosterone levels exceed the level of estrogens in the amniotic fluid then the probability increases of developing lower ratio values. It has been suggested that people with autism spectrum disorders (ASD) and their parents may have highly androgenized brains, and for this reason the D2:D4 ratio is used as a marker of such idiosyncrasies. Objectives and aims: To analyse if parents of people with ASD differ from the general population in several parameters of androgenisation related to the 2D:4D ratio. Methods: The sample was composed of parents of both genders of people with (n=43) or without (n=42) ASDs. The ratio was calculated as the average of three measurements: two were executed directly by two different researchers, whereas the third was a hand scan measured after printing. Furthermore we use trait questionnaires to measure: empathy (IRI); autism (AQ adults); anger (STAXY-2); and cooperative (TCI-R) behaviours. Two samples of saliva were collected to determine hormonal levels. Testosterone was analysed by LIA and cortisol by radioimmunoassay. Results: Although no differences were obtained between groups in the 2D:4D ratio, the ratio of the left hand of ASD parents showed greater predictive ability to explain the autism quotient, cooperative behaviour, and cortisol levels. In addition, only in male parents, the ratio D2:D4 predicted the severity of the symptomathology of their offspring. Conclusions: The results indicate that the 2D:4D ratio could be used together with other parameters as an indicator of the likelihood of developing autistic traits in offspring. However the participants analysed in the present study are first-degree relatives of adolescents with ASD, and so these differences in androgenisation are subtle and require further analysis.

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D12-70

EFFECTS OF PERIPUBERTY STRESS ON COGNITIVE PERFORMANCE IN ADULTHOOD

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Stress during early life in humans has been shown to increase the risk for developing psychopathologies in adulthood, including aggression and impaired decision-making related disorders. Adolescence is a particularly critical period for the development of key brain regions involved in cognitive and emotional processes. Importantly, stress does not affect all individuals in the same way, some being more vulnerable than others. In our lab, a protocol has been developed in which male Wistar rats are subjected to unpredictable stress during peripuberty (P28-42). Data from previous experiments showed that peripubertally stressed animals (PPS) display increased aggression accompanied by altered activation of the prefrontal cortex (PFC) and the amygdala. Altered activation of the PFC and of its interactions with limbic structures has been implicated in impaired decision-making, attention, impulsivity and aggression in humans. In order to assess the attention performance and impulsive behaviour of CTRL (control) and PPS rats a continuous performance task was utilized, namely the 5-Choice Serial Reaction Time Task (5-CSRTT). The cognitive performance of the PPS animals in this task was suboptimal concerning key parameters of the task such as accuracy and latency to respond. Additionally, Principal Components Analysis (PCA) and correlations were performed between key parameters of the 5-CSRTT and other non-cognitive tasks to which the same individuals have been subjected to. With this experimental design, we aim here to examine the role of personality-like differences in predicting impulsivity/compulsivity and decision-making. Our principal goal is to investigate how stress during peripuberty can affect vulnerable individuals in adulthood in different domains and whether there are behavioural markers of vulnerability and resilience.

D12-71

YOUR FLAWS ARE MY PAIN: NEURAL BASIS OF VICARIOUS EMBARRASSMENT

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TV shows such as "America's Next Top Model" have reached high levels of popularity across the globe. In part, they capitalize on the feeling humans experience while witnessing others' public norm violations - a feeling best described as vicarious embarrassment. Cognitive neuroscience has distinguished two networks involved in empathically representing another person's inner state. Cognitive inferences of another's perspective are associated with activations in the mPFC and the STS. The anterior insula and the ACC respond to sharing another person's feeling state and have been most frequently examined in response to another person's pain. The present study aimed to identify the neural substrates involved in processing others' public norm violations and the corresponding vicarious emotional reaction. We hypothesized observers to feel for another person's inappropriate condition in an embodied manner and the intensity of this vicarious experience to be linked to the activation in associated areas. Thirty-two subjects participated in the fMRI study. Forty validated sketches displayed protagonists during public norm violations in every-day life situations. The situations varied concerning the intentionality of the protagonist's behavior and his/hers awareness about the inappropriate situation, resulting in four different scenarios. Ten sketches displayed non-norm-violating control scenarios. A conjunction analysis contrasting the four modeled situations to neutral scenarios revealed stronger BOLD signals in the left anterior insula and ACC, as well as in the left mPFC and temporal poles. Similar activations were observed in the thalamus/brainstem, and cerebellum. Contrasting situations showing another person while being embarrassed to situations when the observed person did not experience any emotion revealed stronger activations in the TPJ. The average effect of the parametric modulations indicated significant associations of hemodynamic responses with self-reported vicarious embarrassment experiences within the ACC, anterior insulae, secondary somatosensory cortices, and the left amygdala. The present results support the hypothesis that empathic processes are involved in vicarious embarrassment experiences on the neural systems' level. Well subscribed networks typically associated with different empathic processes are simultaneously involved in the experience of this complex vicarious emotion. The unique response of the TPJ is best explained by its role in distinguishing self- and other's emotions. Further prove is provided by linking activation in areas associated with emotion/homeostatic regulation to the intensity of the self-reported vicarious emotions for other's norm violations.

D12-72

TEST-RETEST RELIABILITY OF ATTENTION NETWORK TEST MEASURES IN SCHIZOPHRENIA

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The Attention Network Test (ANT) is a well established behavioral measure in neuropsychological research to assess three different facets of selective attention, i.e., alerting, orienting, and conflict processing. The ANT has been widely used in healthy individuals and various clinical populations. However, data on re-test reliability are still scarce in healthy samples and lacking for clinical populations. To fill this gap, we assessed reaction times and error rates of ANT network measures in 55 healthy controls and 45 schizophrenic patients in a longitudinal design with an average interval of 7.4 months between the two test sessions. Test-retest reliability was analyzed with Pearson and Intra-class correlations. Healthy controls revealed moderate to high test-retest correlations for mean reaction time (Pearson's r= .776, ICC r= .749; p< .001), mean accuracy (Pearson's r= .558, ICC r= .553; p< .001), conflict effect (Pearson's r= .610, ICC r= .504; p< .001), and conflict error rates (Pearson r= .748, ICC r= .750; p< .001). Schizophrenia patients showed moderate test-retest correlations for mean reaction time (Pearson's r= .674, ICC r= .663; p< .001), orienting effect condition (Pearson's r= .548, ICC r= .532; p< .001) and conflict effect (Pearson's r= .530, ICC r= .522; p< .001). The analysis of error rates in schizophrenic patients revealed very low retest correlations. In summary, these findings support the notion that only mean reaction time and the conflict portion of ANT reveals acceptable test-retest reliability when schizophrenic populations are investigated in a case-control design. Usage of error rates may need to be restricted to the conflict effect in healthy controls and may not be encouraged for studies on schizophrenia. Future case-control studies involving schizophrenia patients should carefully evaluate significant reaction time differences in the alerting and orienting conditions, and caution should be taken when evaluating error rate differences assessed by the ANT.

D12-73

TRANSCRANIAL DIRECT CURRENT STIMULATION AND CONJUNCTION SEARCH: AN INTERACTION BETWEEN STIMULATION TYPE AND BRAIN AREA

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The right posterior parietal cortex (rPPC) and the right frontal eye fields (rFEF) are both involved in conjunction visual search, as evidenced by a deterioration in performance with the application of TMS (Lane, Smith, Schenk, & Ellison, in press, Brain Stimulation). However, we have been unable to establish contingency between these areas in the processing of such tasks. To understand the temporal dynamics of how neurodisruption affects these areas, we sought to investigate the effects of longer term neuronal modulation to these areas using anodal and cathodal transcranial direct current stimulation (tDCS). Participants completed four blocks of conjunction search trials. After completing block 1, participants received 15 minutes of tDCS at a current intensity of 1.0mA. After 5 minutes of stimulation, they completed block 2. After the 15 minutes of stimulation participants did block 3, followed, after a delay, by block 4. There were three stimulation conditions: Cathodal, Anodal, and Sham, and two stimulation sites: rFEF and rPPC. Participants only completed one condition. Overall, there was a significant interaction between block and stimulation condition, indicating that tDCS effects were modulated by site (rFEF or rPPC) and type of stimulation (Cathodal, Anodal, or Sham). For cathodal stimulation, there was a significant reduction in search times across the four blocks in the Sham and rFEF conditions but no change in search times in the rPPC condition. Moreover, there was a trend for an increase in search times in the rPPC condition between the first two blocks, while in the other two conditions search times became faster across these two blocks. For anodal stimulation there was no interaction between block and site: participants became faster across the four blocks in all stimulation conditions. Therefore, only cathodal tDCS to rPPC overrides improvements normally seen with practice, while search times decreased to the same degree in the Sham and rFEF conditions. The effects of tDCS to rPPC and rFEF do not mirror those of TMS, suggesting that rFEF has a more transient role in the processing of this task that is robust to longer term methods of neurodisruption. The question of contingency between rFEF and rPPC will now be investigated using fMRI with tDCS over rPPC to investigate any modulatory effects this has on rFEF activity.

D12-74

THE EVALUATION OF MEMORY FUNCTION IN APHASIC PATIENTS

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Introduction and aims: Memory can be defined as the process of storing and retrieving mental products and actions for use after different period of retention. While considerable body of knowledge exists, describing various aspects of memory and disorders of memory specific to the amnesic syndromes, relatively few investigations have been concerned with the memory deficits in aphasia. The aims of this study were the assessment of verbal and visual memory in aphasic patients. Methods: The sample was consisted of 30 adult subjects with aphasia following a stroke. According to fluency of spontaneous speech, the subjects were divided in to the two groups. The first group was consisted of 15 patients with fluent aphasias (Wernicke's aphasia, transcortical sensory aphasia and anomic aphasia), and second group included 15 patients with non-fluent forms of aphasias (Broca's aphasia and transcortical motor aphasia). The control group was consisted of 15 healthy adult subjects. Diagnosis of aphasia was done according to Boston Diagnostic Aphasia Examination. Memory assessment included Rey Auditory-Verbal Learning Test and Rey-Osterrieth Complex Figure Test. Results: Memory testing revealed significant differences in the short-term and long-term verbal memory ability in aphasic patients compared to the control group of subjects. The differences in short-term and long-term visual memory were found only between fluent aphasics and control group of subjects. The significant differences of memory ability were also noticed between fluent and non-fluent aphasics. Conclusions: Memory analysis in aphasic patients can provide additional information in understanding of the nature of aphasia, and can assist in patient management.

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D12-75

EFFECTS OF CHRONIC OVEREXPRESSION OF ERYTHROPOIETIN IN THE BRAIN ON COGNITIVE FUNCTIONS AND PHYSICAL PERFORMANCE

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The renal cytokine erythropoietin (Epo) has been suggested to improve memory, attention, and mood and to have antidepressant-like properties in patients subjected to a prolonged (repeated injections) or acute (single injection) Epo treatment. In healthy subjects, a single injection of Epo leads to mood improvement and enhances the processing of emotions, but not cognitive performance. Furthermore, experiments in animal models suggest that Epo improves learning and memory. However, very little is known about the effects of chronically elevated levels of Epo in the brain on cognitive functions. Thus, the main aim of the present study was to investigate how Epo affects cognitive performance using a transgenic mouse line (Tg21) that chronically overexpresses Epo in the brain (4-fold times more than wild-type), without any changes in blood parameters. We also checked for possible effects of Epo on physical performance. We used a battery of behavioral tests followed by the application of several test protocols in the IntelliCage. We did not found any difference between wild-type (Wt) and Tg21 in working memory, spatial recognition memory or short and long-term memory tasks. However, Tg21 animals showed an increased anxiety-like behavior in the emergence and open field tests with a stronger preference for the protected and safer areas. They also exhibited an increased reactivity in fear conditioning, startle response as well as in the extinction phase of the nose-poke suppression protocol in the IntelliCage. When cognitive and motor impulsivity where tested in the IntelliCage (by applying a delay discounting and reaction time tasks, respectively), Tg21 showed a greater tolerance to delay, therefore, making fewer impulsive choices. However, no difference in motor impulsivity between Tg21 and Wt mice could be found. Moreover, Tg21 kept balance for longer periods in the rotarod and swam faster in the water maze, thus showing a better motor coordination and physical performance than Wt mice. In conclusion, our data suggest that chronic endogenous overexpression of Epo may affect anxiety-like behavior, cognitive impulsivity and physical performance but may not play a major role in memory processes.

D12-76

EFFECTIVENESS OF A STANDARDISED COGNITIVE TRAINING IN DEPRESSION AND THE INTERACTION WITH HPA-AXIS REGULATION

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Cognitive impairments are frequently observed among depressed patients. Cognitive dysfunction in depression, however, is not an epiphenomenon of the disorder, but seems to be a result of affected functional networks in the brain. Recent studies have shown that these impairments often persist after recovery from mood symptoms, suggesting dissociation between mood and cognition in depression. These results indicate that the classical psychopharmacological approach can improve psychopathology but does not likewise improve cognitive dysfunction. Impaired regulation of the hypothalamus-pituitary-adrenocortical (HPA) system during an acute episode is the most consistent laboratory finding in depression and cognitive dysfunction in depression has been linked to hypercortisolism as a result of impaired HPA axis regulation. The association between hypercortisolism and cognitive dysfunction is explained by the fact that excess of corticosteroids can damage the brain or impede its function either directly or by increasing its susceptibility to other coincident damaging agents. In a subproject of the Munich-Antidepressant-Response-Signature (MARS) study we evaluated the effect of standardised attention training on cognitive functions in depressed patients and examined whether cognitive improvement depends on HPA-axis regulation. Training effects were evaluated with a comprehensive neuropsychological test battery administered before and after training. We found a significant improvement of attention and transfer effects to the domains of learning and executive functions, but no effect on long term verbal memory. There was no influence of HPA-axis regulation on cognitive deficits or improvement to the training. Systematic cognitive training seems to be an effective intervention strategy to improve in particular attention in depressed patients and should therefore be integrated in the treatment regimen. HPA-axis regulation was not associated with cognitive deficits in general or with the effectiveness of the training procedure.

D12-77

LANGUAGE LATERALISATION IN LATE PROFICIENT BILINGUALS: A LEXICAL DECISION fMRI STUDY

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Approximately half the world's population can now speak more than one language. Understanding the neural basis of language organisation in bilinguals, and whether the cortical networks involved during language processing differ from that of monolinguals, is therefore an important area of research. A main issue concerns whether L2 (second language) is processed using the same neural mechanisms that mediate L1 (first language) processing. Moderating factors include the age of L2 acquisition and the level of proficiency. Here we used a lexical decision task with five conditions during functional magnetic resonance imaging (fMRI) to investigate language processing in eight late proficient bilinguals when using Macedonian (L1) and English (L2). Bilinguals had greater bilateral activation during both L1 and L2 processing, and therefore weaker language lateralisation, compared to matched control English monolinguals. A greater amount of overall activation was also seen in bilinguals, especially during L2 conditions. Late proficient bilinguals living in their L2 environment employ a more extensive neural network than monolinguals when processing their second language.

D12-78

BRAIN AND BEHAVIOR MODULATIONS AFTER REHABILITATION THERAPY IN MULTIPLE SCLEROSIS PATIENTS

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Background: The objective observation of the benefits of neuropsychological rehabilitation programs through neurophysiological techniques has been scarcely applied. In this study, an attentional and mnesic rehabilitation program was applied in a sample of patients with multiple sclerosis (MS) and evaluated with behavioral measures and ERPs (event-related potentials). Material and methods: EEG from 10 subjects with MS was recorded in 16 channels when a paradigm of spatial attention (Posner paradigm with central cues) was displayed. A control group (N=10) matched in age, gender, handedness and scholar level was also registered under the same conditions. Results: Neuropsychological follow up showed that rehabilitation program improved Buschke Test scores (free recall, $p<0.01$) and PASAT scores (interference, $p<0.047$). Behavioural responses (reaction times) were faster after neuropsychological rehabilitation for MS patients ($p<0.001$). Control group did not improve behavioral responses in the longitudinal measure ($p<0.05$). Respect to ERP components, N450 ($p<0.001$) showed higher amplitude in post-rehabilitation measure. Other ERP components were not modulated by the application of the neuropsychological treatment. Conclusions: Neuropsychological rehabilitation improved attentional and mnesic scores in this sample of MS patients. Behavioral responses were also better for the treatment group evaluated with a millisecond resolution. ERP modulation (higher amplitude in N450) showed that the improvement in the cognitive impairment was due to better engage of the attentional system. This study clearly demonstrated that neuropsychological rehabilitation is linked to physiological parameters and it is possible the identification of possible mechanisms for these changes by ERP analysis.

D12-79

COGNITIVE FUNCTION AND VITAMIN D IN ADULTS AND OLDER ADULTS IN LEBANON: A PILOT STUDY

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Age-related cognitive decline is positively correlated with low Vitamin D levels. This pilot descriptive study aimed to investigate vitamin D level and cognitive function in adults and older adults in Lebanon using the Montreal Cognitive Assessment (MoCA) Arabic version and Rey-Osterrieth Complex Figure (ROCF). Cognitive function and vitamin D levels were examined between randomly selected adults (≥ 30) and older adults (≥ 60) groups. To ensure eligibility, all participants' medical and lifestyle history were collected and screened for depression, and then cognitive assessment and serum vitamin D measured. Data collection on 98 eligible participants was completed; of these 98 participants 61 (62.2%) had abnormal (< 30 ng /ml) vitamin D level; 32 (37.8 %) had below normal cognitive score (< 26) on the Montreal cognitive assessment; 22 (22.4%) scored below the 5th percentile on the Rey immediate recall, 27 (27.6%) scored below the 5th percentile on Rey delayed recall and 28 (28.6%) scored below the 5th percentile on the Rey recognition memory subtest. The correlation between abnormal vitamin D level and cognitive function was positive for both adult and older adults groups, but it did not reach statistical significance in the adult group (N=81). However, as expected, in the older adults group (N=17) the correlation between vitamin D and the total MoCA score was positive and statistically significant (rho = .467; $p \leq 0.029$). Similarly, the correlation between the vitamin D level and the Rey subtests was positive and as follow; on the Rey Immediate recall the correlation rho= .330 ($p<0.09$); on the Rey delayed recall rho = .494, ($p<0.022$); yet, the Rey recognition subtest did not reach statistical significance. Given promising preliminary results, recruitment will continue until a sample size of 260 participants is reached and total of 100 older adults are gathered to ensure a larger sample from population of interest. Also, more work is being done to establish these cognitive tests' normative values in Lebanon using the adult group for comparison. The symbol digit modalities test will be added as well to examine other cognitive function subtypes. Identifying early cognitive impairment and exploring its' modifiable risk factors will lead to the development of more targeted interventions to prevent further progression.

D12-80

THE DISENGAGE DEFICIT IN VISUAL NEGLECT IS ASSOCIATED WITH INVOLUNTARY BUT NOT VOLUNTARY ORIENTING OF ATTENTION

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Patients with left spatial neglect are particularly slow to respond to visual targets on their left when attention is first engaged to their right. This deficit is referred to as the disengage deficit (DD). Studies investigating the DD typically employ nonpredictive peripheral onset cues to measure involuntary orienting and predictive central arrow cues to measure voluntary orienting. A DD has been observed with both types of cues, suggesting that a DD occurs for involuntary and for voluntary orienting. Recent evidence questions this conclusion. It has been observed that nonpredictive central arrow cues trigger involuntary orienting, which implies that predictive central arrows also involve involuntary orienting and hence do not measure only voluntary attention. This new knowledge suggests a new conceptualization of the DD. While it is undisputed that a DD occurs when attention is shifted involuntarily, it is uncertain whether a DD is produced by voluntary orienting because most previous cueing studies of the DD have involved shifts of involuntary attention. To address this critical question, we tested neglect and control patients with nonpredictive and predictive peripheral onset cues (Experiment 1), nonpredictive and predictive central arrow cues (Experiment 2), and predictive central number cues (Experiment 3). The experiments provide three lines of converging evidence that voluntary orienting does not contribute to a DD. First, the DD was the same whether attention was engaged involuntarily by nonpredictive peripheral cues or engaged involuntarily and voluntarily by predictive peripheral cues (Experiment 1), indicating that voluntary orienting does not modulate the DD. Second, the DD was the same whether attention was engaged involuntarily by nonpredictive central arrow cues or engaged involuntarily and voluntarily by predictive central arrow cues (Experiment 2), replicating the finding of Experiment 1 with very different cues. Third, the DD was not present when attention was only engaged voluntarily by central predictive number cues (Experiment 3). This new knowledge has an impact on theories of neglect as well as of normal attention.

D12-81

BETA BAND POWER CORRELATED WITH HUMAN ALERTNESS

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Scarce observations in human EEG indicated that enhanced beta activity which accompany certain experimental tasks may be used as an arousal index. In our cat studies (Wróbel 2000, Wróbel et al. 2007) we have found that local field potential oscillations in beta band (12-29 Hz) might serve as a carrier for attentional activation within the visual system. Here we have adopted the animal paradigm for evoking anticipatory attention to study alertness-related changes of beta activity in human subjects. Results indicated that increased alertness - manifested by faster responses to target visual stimuli - is accompanied by higher EEG activation in beta band.

-Wróbel A (2000) Acta Neurobiol Exp 60: 247-260.
-Wróbel A, Ghazaryan A, Bekisz M, Bogdan W, Kami□ski J (2007) *J Neurosci 27*: 2230-2240.

D12-82

NEURAL DIFFERENCES REVEALED BY fMRI DURING A TEMPORAL DISCRIMINATION PROCEDURE IN CHILDREN WITH AUTISM

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There is a relatively small, but growing body of evidence that aspects of temporal information processing, in the seconds-to-minutes (so-called interval) range, may be anomalous in individuals with autistic disorder. Although there are somewhat inconsistent results (and the population is itself heterogeneous), it is generally found that those affected with autism reveal particular difficulty (i.e., less precision, more variability) in their temporal estimations for relatively longer durations (over several seconds). This is potentially relevant to our understanding of autism as it may be suggestive of disordered temporal integration processes that correspond to problems linking sensory information over time. In the first assessment of time estimation in this population using fMRI (to our knowledge), a duration estimation (ordinality comparison) procedure was administered to children (aged 8-13 years) with and without a diagnosis of autism. Each child completed two versions of the task (the standard duration was either 2.2-s or 8.2-s). In each version, the presentation of the standard stimulus duration (e.g., 2.2-s) was followed in quick succession by a comparison stimulus duration that was a percentage deviant (+/-) of the standard, and participants were required to classify whether it was 'shorter' or 'longer' than the standard. During fMRI analysis, neural activation during the standard and comparison duration presentations (likely reflecting different cognitive processes) could be dissociated. Results revealed quantifiable group differences in brain regions recruited to perform each version of the task: In particular, comparison participants revealed greater activation in the cerebellum when timing the 2.2-s standard and the caudate-putamen when timing the 8.2-s standard (as expected); but in contrast, those with autism recruited the caudate-putamen to a greater extent when timing the 2.2-s standard. These results lend support to existing behavioral evidence that individuals affected with autism may subjectively experience durations as 'longer' and have particular problems with durations several seconds long. The implications of these results to our understanding of autism will be outlined.

D12-83

INCREASED SALIVARY CORTISOL LEVELS IN ELDERLY SUBJECTS WITH NON-AMNESTIC AND MULTIDOMAIN MILD COGNITIVE IMPAIRMENT

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Animal and human studies have shown that cumulative exposure to elevated glucocorticoid levels can have a detrimental impact on several brain structures and affect age-related cognitive decline. Although previous studies have already examined whether salivary cortisol secretion is related to mild cognitive impairment at aging, most of them focused on the relationship between saliva cortisol secretion and memory function. However, little attention has been paid to examine whether salivary cortisol levels are altered in the non-amnestic subtype of mild cognitive impairment. In the present study, we investigated the cognitive state of 246 elderly subjects (aged 66-95). Cognitive profile of individuals was evaluated using an extensive neuropsychological battery including episodic memory and learning, language, attention, executive function, constructive and ideomotor praxis. All subjects were classified as cognitively healthy, amnestic, non-amnestic or multidomain. After this period, we selected people of the four subgroups that matched in age and years of education, in order to obtain salivary cortisol samples at awakening, evening and bedtime. Here, we report that subjects with a non-amnestic or a multidomain mild cognitive impairment profile showed increased salivary cortisol levels immediately after awakening, but not in the evening of at bedtime, compared to stable cognitively normal controls. Individuals with an amnestic mild cognitive impairment did not show significant differences in salivary cortisol levels compared to unimpaired subjects. These data indicates that elevated salivary cortisol levels in the morning are associated with a non-amnestic and a multidomain profile of mild cognitive impairment in elderly subjects.

D12-84

SPATIAL ORIENTATION DEFICIT IN CHILDREN DUE TO CEREBELLUM ASTROCITOMA PEDIATRIC TUMOR BY MEANS OF ATTENTIONAL NETWORK TEST

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Cerebellum astrocitomas are the most typical nervous system tumors in children. Several cognitive deficits have been previously described. These deficits are probably produced by cerebellar connections and gray matter damage. Current study examines attentional deficits in children operated from cerebellum astrocitomas using an attentional paradigm with theoretical and clinical bases: the Attentional Network Test (ANT). This test has been designed considering the attentional network theory proposed by Posner and it has been demonstrated its usefulness in clinical settings. The attentional networks scores obtained from the ANT were compared between Control (29 subjects, 19 females) and astrocitoma children (11 subjects, 8 females). In order to demonstrate the possible influence of the astrocytoma resection on the values of the attentional networks, controlling the age, a multiple regression analysis of the attentional network scores was computed. RT (or accuracy) was the dependent variable, with group (clinical and astrocitoma) and age being the independent variables. Children operated from cerebellar astrocitoma showed a mild attentional deficit in the orientation network. The results indicate an involvement of the cerebellum in attentional functions independently of the visual and motor performance.

D12-85

ANTI-TOBACCO ADVERTISING THROUGH THE LENS OF ADDICTION: EVIDENCE FROM EEG GAMMA AND ALPHA BAND ACTIVITY

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Chronic consumption of nicotine generates neuroadaptations in cortico-limbic circuits, altering cognitive function (Koob, 2009) and behavioral regulation (Chanon et al., 2010). Nevertheless evidence regarding how chronic tobacco consumption biases attention, perception and decisions requires further research. 15 smokers and 18 non-smokers were exposed to anti-tobacco advertisement. Brain activity was measured using a 14 electrode EEG; power spectrum density of alpha and gamma bands was performed. Fixation frequency and duration were measured using a Tobi X120 Eye Tracker. In both intragroup and intergroup comparisons, higher gamma power was found in smoker's right frontal and temporal lobes, and higher alpha power was found in smoker's right frontal lobe. These findings suggest that smokers presented relative higher levels of arousal, anxiety (Oathes et al., 2008), positive valence emotions (Müller et al., 1999; Coan & Allen, 2003) and approach behavior tendencies. Simultaneously, gamma power was significantly lower in smoker's right occipital lobe compared to non-smokers. This suggests that there are differences in the way in which visual information is processed in smokers and non-smokers (Jensen et al., 2007). No differences were found in occulomotor behavior which raises questions about whether addicts, while watching anti-tobacco advertisement, are employing top-down strategies that do not affect visual exploration or if there are alterations in attention regarding information processing which are not related to visual exploration. The neurobiology of addiction should be considered in the development of anti-tobacco campaigns.

-Chanon, V.W., Sours, C.R., Boettiger, C.A. (2010). Attentional bias toward cigarette cues in active smokers. *Psychopharmacology, 212,* 309–320.
-Coan, J.A. & Allen, J.J. (2004). Frontal EEG assymetry and the behavioral activation and inhibition system. *Psychophysiology, 40,* 106-114.
-Jensen, O., Kaiser, J., Lachaux, J.P. (2007). Human gamma-frequency oscillations associated with attention and memory. *Trends in Neurosciences, 30(7),* 317-324.
-Koob, G.F. (2009). Neurobiological substrates for the dark side of compulsivity in addiction. *Neuropharmacology, 56 (1)*, 18–31.
-Müller, M., Keil, A., Gruber, T., Elbert, T. (1999). Processing of affective pictures modulates right hemispheric gamma band EEG activity. *Clinical Neurophysiology, 110,* 1913-1920.
-Oathes, D., Ray, J., Yamasaki, A., Borkovec T., Castonguay L., Newman M., & Nitschke, J. (2008). -Worry, generalized anxiety disorder, and emotion: Evidence from EEG gamma band. *Biological Psychology, 79*, 165-170.

D12-86

THE VIRTUAL HAND ILLUSION ENHANCES AUDITORY MEMORY

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It has been demonstrated that multisensory integration of synchronous visuo-tactile stimulation can evoke an illusion of ownership over external body parts as well as of whole bodies. Nevertheless, it is not known whether altering the body scheme or owning a virtual body affects the cognitive processing of incoming external stimuli through different sensory streams. Here we examine the possible effects of lateral virtual body ownership in auditory memory recognition and recall. Twenty four healthy right-handed female subjects participated in the study. A head-mounted display allowed participants to see the whole virtual environment and their own virtual body from a first-person perspective. The participants could see in particular both their virtual arms projecting out from their shoulders in a feasible position. The virtual hand illusion (VHI) experiment was carried out as in (Slater et al., Frontiers in Human Neuroscience, 2008) on the left arm, where an experimenter tapped and stroked both the real and virtual hands in the same position. Visual stimulation of the virtual arm and tactile stimulation of the real arm were given synchronous or asynchronously according to the condition. During the visuo-tactile stimulation a list of words was randomly presented via headphones to the left or right side. At the end of each block, participants were asked to retrieve all the words they remembered (recall task) and then to recognize them from a list of words (recognition task). Then, a 4-item questionnaire was given to evaluate the strength of the body illusion. As reported in previous studies (Slater et al., 2008) the questionnaire results revealed a statistically significant difference between the two conditions, such that the strength of the reported body illusion was significantly higher in the left (stimulated) hand during the synchronous condition as compared to the asynchronous stimulation and to the right (non-stimulated) hand. Regarding the non-stimulated right hand, there was no change in the illusion score depending on the synchronous/asynchronous stimulation of the left hand. The number of recalled words in the left side was significantly higher during the synchronous condition compared to the asynchronous one. We speculate that induction of ownership of a virtual body part impacts the stimulus processing and memory stimuli received ipsilaterally. In particular, we detected a better retrieval of the stimuli presented on the "owned" side. Differences were not due to lateralized attention or ipsilateral stimulation, since they occurred between synchronous and asynchronous stimulation of the same side.

D12-87

SENTENCE COMPREHENSION IN GERMAN KINDERGARTEN CHILDREN – ON THE NEUROPHYSIOLOGICAL LEVEL

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The ELAN-component, an early left-frontal negativity, is an EEG-correlate of the recognition of morpho-syntactic mistakes. Question: Does ELAN in kindergarten children correlate with phrase-understanding? Study-Group: 69 children, mean age 55.6 (SD 10.2) months, 75% multilingual. Method: Correct and incorrect phrases are presented under standardized conditions via loudspeaker: 32-channel-EEG-measurement. Phrase-understanding was assessed via SETK 3-5 (Subtest SV); auditory memory-span via WET-Subtest. Results: Incorrect phrases activated early (270-390 ms, ELAN1; Electrode F7) and late (500-1000 ms, ELAN2; AFz) ELAN component parts. A negative correlation between SV and ELAN (higher negativity significance with improved SV) was not verifiable (ELAN1: r= -.15, p= .22; ELAN2: r= -.12, p= .32). However, a positive relationship between memory-span and ELAN1 was found; no positive correlation for ELAN2 (r= .18, p=.14). After partialing-out of the relatively language-unspecific memory-span parameter, the correlations between SV and ELAN1 (r= -.22, p= .07) as well as of SV and ELAN2 (r= -.19, p= .13) increased. Because the age correlated (r =.31, p= .012) significantly with the memory-span, correlations between ELAN and SV were calculated separately for younger (n= 35; $\leq$ 55 months) and older children (n=34; > 55 months). Only older children displayed significant memory-span corrected correlations of phrase-understanding of SV and ELAN1 (r= -.34, p= .05) as well as ELAN2 (r= -.37, p= .03). Monolingual, German-speaking children showed significantly higher SV-values than multi-lingual children (11.9 vs 7.3; t[66]=3.6, p= .001); in the memory-span no differences (p= .66) were detected. This language specific performance advantage (grammar competence) was accompanied by significantly higher ELAN1 (t[66]=2.1, p= .04) and ELAN2 (t[66]=2.2, p= .03) components. Conclusion: For children the ELAN-component delivered a specific neurophysiological index of the receptive language development. This index will be used to compare the effects of music and painting training in very young migrant children on a neurophysiological level.

D12-88

PREDATION-DRIVEN BEHAVIOURAL VARIATION IS ASSOCIATED WITH VASOTOCIN SYSTEM CHANGES IN THE GUPPY (*Poecilia reticulate*)

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Social grouping behaviour can provide adaptive benefits such as protection from predators through confusion effects and increased vigilance. We have been examining how high levels of predation produce changes in social behaviour and in associated brain circuitry in the guppy, *Poecilia reticulata*. We compared domesticated guppies with a population of feral guppies taken from Burgers' Zoo (Arnhem, NL), which have experienced extensive daily predation for approximately 20 years. Shoaling and anti-predator behaviours were measured before and after exposure to a predator and these experiments showed that feral guppies spend more time shoaling both when there is no predator present and when then exposed to a predator threat. We then examined candidate neural systems that may regulate such differences in social behaviour. Oxytocin and vasopressin are neuropeptides which play important roles in social behaviour in mammals and their homologues have also been shown to regulate social behaviours in other vertebrates, including fish. In investigations of the teleost homologues isotocin and vasotocin, we found fewer vasotocin neurons in the preoptic area of the brain in feral guppies and also found that feral guppies exhibited greater behavioural sensitivity to pharmacological manipulation of the vasotocin system than domestic guppies. To determine whether these changes are due to direct experience of predation within the Burgers' Zoo environment, we also examined social and anti-predator behaviours in F1 feral guppies reared in the laboratory. Our data suggest that experience of predation has driven changes in social behaviour in feral guppies and that these are associated with changes in brain vasotocin circuits. These results indicate that the vasopressin family of neuropeptides may be involved in adaptive regulation of social behaviours across different vertebrate taxa which have distant evolutionary origins.

D12-89

THE OREXIN1 RECEPTOR ANTAGONIST SB-334877 POTENTIATES THE REWARDING EFFECT OF INTRACRANIAL SELF-STIMULATION IN RATS

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The orexins (also known as hypocretins) comprise two neuropeptides (orxA or hcrt-1 and orxB or hcrt-2) produced in a few thousand neurons localized in the lateral hypothalamus (LH). Orexin producing neurons project locally within the hypothalamus and widely throughout the brain, with prominent input to areas involved in energy homeostasis, arousal and brain reward. The prevailing view of orexin function focused on arousal and maintenance of the waking state, but recent evidences links orexin system with reward and reinforcement. Some experimental data indicate that orexin system cloud play an important role in expression of drug preference and may also be involved in relapse of drug-seeking behavior induced by stress or external triggers, such cues or context associated with drugs.Intracranial self-stimulation (ICSS) has demonstrated an important role of the LH in reward. Compared to other brain regions, LH-ICSS is by far the most potent and it has been demonstrated that LH-ICSS activates orexigenic cells in the perifornical area of the hypothalamus. In addition, orexinA administration caused a clear dose-dependent increase in the reward threshold of ICSS, an effect which is reversed by the antagonist SB 334867, suggesting that orexinergic neurons attenuate the rewarding effect of ICSS. We evaluated the SB-334867 effects upon LH-ICSS behavior. On three consecutive days, the animals were trained in ICSS to establish the individual ICSS optimum current intensity. Seventy-two hours after the last ICSS establishment session, animals were submitted, for two consecutive days, to one daily ICSS session and were pre-treated with Dimethyl sulfoxide (DMSO,3ml/Kg i.p., used as the control) or SB-334867 (3, 6 or 15mg/Kg dissolved in 3ml of DMSO i.p.). Main results showed that only the highest dose, 15mg/kg of SB-334867, decreased the ICSS optimum current intensity, confirming previous results indicating that orexigenic neurons seem to attenuate the rewarding effect of ICSS.

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D12-90

ULTRA FAST OSCILLATIONS IN RAT EEG DURING REM SLEEP

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Since first described in pioneer works by Berger at the beginning of the XX century, electroencephalography (EEG) is one of the main tools for the evaluation of vigilance states. According to this, wakefulness in the rat is identified by low voltage and high frequency EEG up to 40 Hz with a main peak around 6-10 Hz; slow wave sleep (SWS) by a high amplitude of low (0.5-4 Hz) and middle (10-14 Hz) frequency; and, REM sleep by a desynchronized low amplitude and high frequency EEG peaking around 7 and in the 30-60 Hz band. In addition to EEG, it became necessary to record other parameters as electromyography (EMG) and eye movements to clearly distinguish between quiet alertness and REM sleep. Ultra-fast oscillations in the range of 80-200 Hz (ripples) has been described during SWS superimposed to the 6-10 Hz band, but there are no studies that analyse the presence of ultra-fast frequencies during other states. In this work, ultra-fast oscillations in the EEG during the sleep-wake cycle were analyzed in rats. Five animals were chronically implanted with electrodes for the recording of EEG and the EMG, and scleral search coils for eye movements, allowing an accurate identification of sleep states. In these animals, having identified each vigilance state, a precise study of EEG revealed the presence of a previously undescribed high frequency band from 120 to 160 Hz (peaking at 131.7 ± 3.0 Hz) during REM sleep. This frequency band was specific of REM sleep and its mean power was four times higher than that of the corresponding band during wakefulness or slow wave sleep. Additionally, another nine animals were implanted for EEG recording in 18 localizations covering most of the cerebral and cerebellar cortex to identify the areas where ultra fast oscillations were of highest amplitude. Cortical localization analysis revealed a central location around motor and visual cortex. The existence of this REM sleep specific high frequency gives rise to new questions about its generating mechanisms and functional implications, besides of being *per se* a new and precise tool for REM sleep scoring using EEG signal.

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D12-91

ANXIETY TRAIT PREDICTS DOMINANCE STATUS

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Although the organization of individuals in dominance hierarchies occurs readily in many species both in nature and under experimental, the determinants are not fully understood. The outcome of an initial encounter between two or more individuals can have important consequences for future behavioral interactions and fitness. Classically, the factors that influence the organization of individuals that meet for the first time in a dominance structure are classified into two categories, including (i) 'intrinsic' factors or traits, such as sex, age and size that predispose individuals into certain positions, and (ii) 'extrinsic' factors, including animals' former social experience. Using male adult Wistar rats, we have recently identified stress as an important extrinsic factor in the formation of social hierarchies. Under our experimental conditions, given equal opportunities to become either dominant or submissive, stress experienced by one of the individuals during their first encounter determines the long-term establishment of a social hierarchy by 1) influencing the rank achieved after a social encounter; and 2) facilitating and/or promoting a long-term memory for the specific hierarchy. Here, we investigated the role of trait anxiety in the formation of a social hierarchy between two adult male rats equivalent in body weight. Animals were classified as either high (HA), normal (NA) or low (LA) anxious according to their behavior in two anxiety tests (the elevated plus maze and the light-dark box) performed on different days. HA and LA animals were those whose behavior in the anxiety tests fell within either the higher or lower quartile, with NA animals being those in the two intermediate quartiles of the distribution. The type of offensive behaviors in pairs with opposite anxiety levels (i.e., LA vs HA) did not differ from control NA-NA dyads. Dominancy was determined by summarizing the durations of offensive-type behaviors (including lateral threat, offensive upright and keeping down). Importantly, high trait anxiety predicted the outcome of subordinate status in the LA-HA encounters. This predisposition was abolished by administration of the anxiolytic diazepam (1mg/kg, given i.p. 30 min prior to social encounter). Altogether, our results highlight the personality trait of anxiety as a critical factor in the establishment of social hierarchies and suggest that anxiolytic pharmacological treatments might help overcome a predisposition to low status in highly anxious individuals.

D12-92

OXYTOCIN FACILITATES PRO-SOCIAL BEHAVIOR AND PREVENTS SOCIAL AVOIDANCE IN RODENTS

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Social avoidance and social phobia are core symptoms of various psychopathologies but their underlying aetiology remains poorly understood. Therefore, this study aims to reveal pro-social effects of the neuropeptide oxytocin, under both basal and stress-induced social avoidance conditions in rodents using a social-preference paradigm. We initially show that intracerebroventricular (icv) application of an oxytocin receptor antagonist (OTR-A) in naïve male rats (0.75µg/5µl) or mice (20µg/2µl) reduced social exploration of a novel con-specific indicative of attenuated social preference. Prior exposure of male rats to a single social defeat resulted in loss of their social preference and social avoidance, which could be restored by icv infusion of synthetic oxytocin (0.1µg/5µl) 10 min prior to the social preference test. While the amygdala has been implicated in both social and oxytocin-mediated actions, bilateral oxytocin receptor antagonist (0.1 µg/1µl) or oxytocin (0.01 µg/1µl) administration into various subnuclei of the amygdala did not affect basal or stress-induced social preference behavior, respectively. Finally, we demonstrate the social specificity of these oxytocin-mediated effects by showing that neither an arginine vasopressin V1a receptor antagonist (0.75µg/5µl, icv) nor the anxiogenic drug pentylenetetrazol (15mg/kg, i.p.) altered social preference, with oxytocin receptor antagonist not affecting state anxiety. Overall, the data indicate that the basal activity of the endogenous brain oxytocin system is sufficient to promote pro-social behavior in rodents while synthetic oxytocin shows potential to reverse stress-induced social avoidance and might thus be of use for treating social phobia and social dysfunction in humans.

D12-93

MEASUREMENT OF AKINESIA IN RATS: DESIGN AND VALIDATION OF A SIDE EFFECT PARADIGM IN FREELY MOVING RATS

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Antipsychotics are known to potentially induce extra pyrimidal side-effects such as catalepsy, akinesia (the inability of a subject to smoothly initiate a voluntary movement), etc. Drug-induced akinesia can be assessed in rodents in several ways, but is generally based on qualitative behavioural observations. The purpose of this study was to validate a non-invasive set-up to obtain quantitative measures of drug-induced induced akinesia in rats. A circular black platform (ø120 cm) was positioned 75 cm above ground level, in a low light intensity room (1 lux). A 2 cm^2 spot marked the centre. A high resolution video camera (Samsung SDC-435, lens F1.3/12 mm) was mounted 165 cm above the platform. Video images where captured using Ethovision 3.0 (EV) on a PC for off-line analysis. Male Wistar rats (230-260 g) were placed in the centre of the platform facing away from the investigator. The recording automatically started 0.5 sec after the rat was detected, to allow the investigator to withdraw his arm. Recording was programmed to stop when the rat was first detected in the outer area of the platform, or after 30 seconds. Latency to leave the centre area (ø 30 cm) and total distance moved were calculated. Drug or vehicle were administered SC after a baseline recording (T=0 min), and sessions were repeated hourly up to 4h after drug. At baseline (T=0) rats immediately moved away from the centre: latency time = 1.5_1.2 sec (mean_SD), 95th percentile = 4.8 sec (n=562 rats). This remained relatively stable in vehicle treated rats over the 4h observation period: max 3.2_7.2 sec, though the distribution curve became skewed (95th percentile = 22.2 sec, n=50). Lorazepam and alprazolam (0.63-10 mg/kg) dose-dependently increased latency time, which was maintained over the 4h period, but diazepam (0.16-1.25 mg/kg) had only a very mild effect. D2-antagonists haloperidol (0.01-0.63), risperidone and olanzapine (0.08-10) also dose-dependently increased latency time, while amisulpride (0.63-10) showed only a very mild increase. The PDE10-inhibitors papaverine (2.5-40) and MP10 (0.16-10) also increased latency. While D2-antagonists also cause catalepsy in rat, PDE10-inhibitors do not to that extent. The akinesia test therefore identifies a different motor disturbance (inability to initiate movement) than catalepsy caused by PDE10-inhibitors.

D12-95

ROLE OF GLUCOCORTICOIDS IN MEDIATING THE EFFECTS OF PERIPUBERTAL STRESS ON PSYCHOPATHOLOGICAL BEHAVIORS

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Adolescence is an important maturational phase during which substantial remodeling occurs in brain regions associated with learning, motivation, emotion and cognition. The ongoing maturational changes during this stage render the brain more susceptible to the harmful effects of stress. Both human and animal studies show that stress during adolescence enhances the risk of psychopathologies later in life. Our laboratory aims to understand the mechanisms involved in the long lasting impact of stress during peripuberty on brain and behavior. Our stress protocol consists on subjecting male rats to fear-inducing experiences on 7 specific days during the peri-puberty period (from P28 to P42). We have previously shown that animals undergoing stress during the peri-puberty period exhibit increased aggressive and depressive like behaviors in adulthood. Furthermore, we found the existence of significant correlations between corticosterone response to peripubertal stress and the degree of aggression and anxiety displayed later in life. This finding raised the possibility of involvement of corticosterone in mediating the long lasting impact of stress on some of the psychopathological behaviors. Therefore, we examined the consequences of pharmacological blockade of glucocorticoid receptors on the effects of peripubertal stress. The glucocorticoid receptor antagonist (RU38486; 10mg/kg), dissolved in propylene glycol, was administered intraperitoneally and injected on the days of peripubertal stress 30 min prior to stress. We utilized four groups for this study: (1) control + vehicle, (2) control + RU38486, (3) stress + vehicle and (4) stress + RU38486. Our results show that antagonizing the function of glucocorticoid receptor on days of stress abolishes the effects of peripubertal stress on social preference and aggressive like behavior, without affecting anxiety and depressive-like behaviors. Taken together, our findings suggest that increased release of glucocorticoids triggered by stress during the peripuberty period is responsible for mediating the alterations induced by peripubertal stress on subsequent social behaviors.

D12-96

NEONATAL DISTURBED ALLOP LEVELS AFFECT ADULT PERFORMANCE OF THE PASSIVE AVOIDANCE AND ALTER THE ADULT CA1 HIPPOCAMPAL RESPONSE TO NEUROSTEROIDS

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Neurosteroids (NS) are well known to exert modulatory effects on ionotropic receptors. In fact, NS such Allop has been widely related with several psychopatologies and stress responses. In addition, recent finding indicate that NS could also act as an important factors during development. In this sense, Allop altered levels have been demonstrate to cause an alteration of the adult hippocampal response to other GABAA positive modulators such as benzodiazepines and also to alter the morphology of several structures in the brain. Moreover, it has been postulated that alteration of Allop levels during a critical period could also alter the morphology of the hipoccampus. The aim of the present work is to screen whether the alterations of Allop levels alters the adult CA1 hippocampal response to NS. For this purpose, pups were injected with Allop (20mg/kg s.c.), Finasteride (50 mg/kg s.c.) or vehicle from postnatal day 5 (P5) to postnatal day 9 (P9). To test the hippocampal response to NS in adulthood, animals were implanted with a bilateral cannula into the CA1 hippocampus at 80 days old. After recovery from surgery animals were injected with AlloP (0.2_g/0.5_l), PREGS (5 ng/0.5 _l) or vehicle in each hippocampus, immediately after the passive avoidance acquisition training. Retention was tested 24 hour later. Results indicate that neonatal Allop and finasteride administration disrupts the passive avoidance learning in adulthood, and also affect the hippocampal response to NS. This data indicate that the correct maintenance of Allop levels during development is critical for hippocampal maturation and also point out the role of NS in the development of the CNS.

D12-97

EFFECT OF OREXIN-B-SAPORIN INDUCED LESIONS OF THE LATERAL HYPOTHALAMUS ON PERFORMANCE ON A PROGRESSIVE-RATIO SCHEDULE

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Abstract. It has been suggested that a sub-population of orexinergic neurones whose somata lie in the lateral hypothalamic area (LHA) play an important role in regulating the reinforcing value of both food and drugs. This experiment examined the effect of disruption of orexinergic mechanisms in the LHA on performance on the progressive-ratio schedule of reinforcement, in which the response requirement increases progressively for successive reinforcers. The data were analysed using a mathematical model which yields a quantitative index of reinforcer value and dissociates effects of interventions on motor and motivational processes (Killeen, 1994). Rats were trained under a progressive-ratio schedule using food-pellet reinforcement. They received bilateral injections of conjugated orexin-B-saporin (OxSap) into the LHA or sham lesions. Training continued for a further 40 sessions after surgery. Equations were fitted to the response rate data from each rat, and the parameters of the model were derived for successive blocks of 10 sessions. The OxSap lesion reduced the number of orexin-containing neurones in the LHA by approximately 50% compared to the sham-lesioned group. The parameter expressing the incentive value of the reinforcer was not significantly altered by the lesion. However, the parameter related to the maximum response rate was significantly affected, suggesting that that motor capacity was diminished in the OxSap-lesioned group. The results indicate that OxSap lesions of the LHA disrupted food-reinforced responding on the progressive-ratio schedule. It is suggested that this disruption was brought about by a change in non-motivational (motor) processes.

D12-98

DEVELOPMENT OF A TWO-TRIAL SPATIAL RECOGNITION TASK: EFFECTS OF ANIMAL HANDLING, CUES, DELAYS AND PHENCYCLIDINE

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Pharmacological characterization of novel molecules identified during the drug discovery process is critically dependent on data obtained from “disease-relevant” in vivo pharmacodynamic assays. To support a variety of projects targeting cognitive dysfunction in Alzheimer’s disease and schizophrenia, we aimed to develop and pharmacologically validate a semi-automated spatial/visual recognition task that could act as a relatively high-throughput in vivo pharmacodynamic assay. The apparatus was based upon an existing 8-arm radial maze and was constructed by enclosing two arms (70×10×30 cm) to form a V-maze with a centre zone. All walls were constructed with transparent Plexiglas and entry to either of the arms was controlled by guillotine doors. Typically, the experimental protocol comprised of a five minute exploratory trial, in which either one of the two arms were opened. After a defined inter-trial interval, both arms were opened and the animal placed back for a five minute retention trial and we investigate the natural tendency of a rat to explore the new location. Animal exploration/tracking’s were automatically recorded and scored using Ethovision XT. All studies were conducted using male Long Evans rats. The first series of studies aimed to determine whether animals utilize extra-maze cues (room furniture etc) to discriminate between the novel and familiar arm. Interestingly, animals could only significantly discriminate when intra-maze cues were employed and there were clear preferences/biases for particular cue combinations. Prior in-house experience with exploration-based tasks suggested that there may be beneficial effects of prior animal handling and sham dosing on assay robustness and indeed this was also evident in this assay, with three days of prior animal handling/dosing providing the most robust discrimination. The final series of studies aimed to establish significant and reproducible performance deficits amenable for pharmacological reversal studies using extended intra-trial interval delays and phencyclidine (PCP). Use of extended inter-trial interval delays time-dependently reduced discrimination providing a window for reversal studies. Four separate PCP dose-ranging studies generated dose-dependent arm discrimination attenuation with 0.63mg/kg (sc; 30 minutes pre-treatment time) providing the most robust and cleanest cognitive impairing signal. In summary, we have established a robust, high throughput cognitive pharmacodynamic assay that avoids the use of electric shocks or deprivation, capable of screening approximately 40-50 compounds per annum.

D12-99

SOCIAL FEAR CONDITIONING – A NOVEL AND SPECIFIC ANIMAL MODEL OF SOCIAL ANXIETY DISORDER

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Social anxiety disorder (SAD) is a major health concern with a high lifetime prevalence and high degree of co-morbidity with other psychiatric disorders. The current medication is rather unspecific and, despite considerable efforts, their efficacy is still unsatisfactory. A better understanding of the underlying etiology of SAD would provide important information for the development of more specific medication for the disorder. However, at present, there are no appropriate animal models for studying SAD as those used tend to be rather unspecific or directed towards a specific, dominant, con-specific. Social fear was induced in naïve mice by administering an aversive stimulus (electrical foot shock) during the investigation of a con-specific. 24h later, the effect of social fear conditioning on social investigation of unknown con-specifics, as well as other behavioral parameters, such as general anxiety (elevated plus-maze), depressive-like behavior (forced swim test), and home cage locomotion was assessed. The predictive validity of our model was assessed by administering benzodiazepines (acutely) and antidepressants (chronically) before assessment of social investigation. We could demonstrate reduced investigation of different con-specifics in conditioned mice compared to unconditioned mice 24h and 15 days after conditioning, indicating social fear. The induced fear was specific to social stimuli, long-lasting and did not lead to other behavioral alterations that might account for the decreased social investigation, such as anxiety, depression or impaired locomotion. Moreover, the SAD phenotype was reversible with both acute benzodiazepine and chronic antidepressant treatment, currently used for relieving anxiety symptoms in SAD patients. Taken together, these findings demonstrate that we have developed a novel and specific animal model for studying SAD, which will lead to a better understanding of the underlying etiology and, in turn, novel treatment approaches.

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D12-100

PERCEPTUAL SIMULTANEITY IN AUTISM SPECTRUM DISORDERS: A MAGNETOENCEPHALOGRAPHY (MEG) STUDY

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Magnetoencephalography (MEG) is a non-invasive brain imaging technique that records magnetic fields associated with synaptic transmission in the human brain. MEG has good spatial resolution and extremely high temporal resolution. We used event-related MEG to examine the brain correlates of perceptual simultaneity in high-functioning adolescents and adults with autism spectrum disorder (ASD) and chronological and mental age matched healthy controls. Two vertical bars were presented simultaneously (onset and offset), or non-simultaneously employing two different onset asynchrony conditions. The short asynchrony separating the two bars was 17ms, which is below the subjective visual simultaneity threshold (i.e. apparent simultaneity), and the long asynchrony was 117ms, which is well above the threshold (i.e. clearly non-simultaneous). Participant's task was to decide whether the onset of the two bars was simultaneous or not. All measurements were taken using an Elekta-Neuromag VectorView™ system, providing a helmet-shaped array of 102 pairs of gradiometers. The responses were averaged separately for physically simultaneous stimuli and non-simultaneous stimuli in the two asynchrony conditions. Significant differences between the evoked responses associated with the simultaneity (0 ms delay) and the apparent simultaneity (17 ms delay) conditions were sought using a time-dependent measure that takes into account the data from all sensors. Analysis of performance showed that participants with ASD distinguished significantly better between the simultaneity condition and the apparent simultaneity condition. This distinction in the ASD group was reflected in event-related MEG activity and was correlated with the latencies of the strongest brain responses observed over occipital cortices at about 120 ms. No such correlation was found in the control group. Overall, Wilcoxon tests showed earlier and more activity differences between conditions in the ASD group again reflecting stronger distinction between the simultaneity and the apparent simultaneity conditions as compared to the control group. Additionally, the control group showed stronger left hemispheric dominance of responses compared to the ASD group. In summary, our results indicate generalised differences in visual temporal resolution and in processing perceptual simultaneity in the ASD group. Increased temporal resolution in ASD is speculated to be based on superior access to early visual brain activity in making judgments about visual organisation.

D12-101

GENERATION OF MICROSACCADES DURING DIFFERENT VISUOMOTOR TASKS. DIAGNOSTIC VALUE IN PARKINSON'S DISEASE

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Microsaccades are rapid eye movements of small amplitude that seem to occur to avoid image fading. Although their dynamic is quite similar to bigger saccades, they are completely involuntary and so they could have a predictive value in the evaluation of oculomotor processing disturbances. The goal of the present study was to describe the distribution of microsaccades during visuomotor tasks of different complexity in healthy subjects and Parkinson's disease patients. Eye movements were recorded by high definition video-oculography during a mixed-block with three visuomotor tasks which included prosaccadic, antisaccadic and nogo responses. Prosaccadic and antisaccadic tasks were also studied in simple blocks in 10 healthy young subjects, 17 elderly subjects in an early state of the Parkinson's disease and in 7 control subjects matching in age and sex with Parkinson's patients. Subjects seated in front of a display monitor and fixed their gaze on a central color point for a random period from 1900 to 2500 ms. At the end of this period, the color point disappeared for 370 ms and a black peripheral dot appeared 8 degrees left or right at random. In the mixed design, color of the central point (green, red or yellow) indicated the type of task (prosaccadic, antisaccadic and no-go) in each trial. In control subjects, the mean execution probability of microsaccades was lesser in the mixed design, especially in the antisaccadic task. The onset of the peripheral target induced a blockade of microsaccades which was followed by a rebound in the prosaccadic task. Comparatively, the microsaccadic rebound was lesser in antisaccadic and nogo tasks indicating that the saccadic blockade in these tasks is also affecting the production of microsaccades. The distribution of microsaccades after antisaccades also showed a blockade in healthy young and in the Parkinson's disease control group. However, this blockade in Parkinson's disease patients was scarce indicating that the saccadic inhibition was affected by Parkinson's disease and visible through the behaviour of microsaccades.

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D12-102

FATIGUE AND COGNITIVE EFFORT IN MULTIPLE SCLEROSIS: AN fMRI STUDY

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Despite recent advances in therapy and diagnosis, fatigue remains a mayor challenge in multiple sclerosis (MS). To further the understanding of the neural underpinnings of fatigue, we undertook a study using functional magnetic resonance imaging (fMRI) to investigate neural networks that may be affected by MS-related fatigue. Twelve MS patients and 12 age- and sex matched controls were administered the Fatigue Impact Scale (FIS) to assess clinically significant fatigue, and underwent a neuropsychological examination. The participants performed a working memory task (Daneman's 'Reading Span' task) while being monitored by means of a 1.5 T Philips Achieva MR scanner. We have previously shown that this task triggers an executive network comprising frontal and parietal areas typically involved in working memory. In addition, the task engages a core network involving the anterior insula and the anterior cingulate cortex. This latter network may be implicated in allocation of mental resources and monitoring of the present state of the individual. There were two main findings. MS participants evidenced less activation than controls in the anterior cingulate and the left parietal cortex (Brodmann area 7) and more activation in left hemisphere language areas as well as the anterior insula. The second main finding was that clinical ratings of fatigue were strongly correlated with activity in wide areas of the core network, as well as posterior language areas. We take this finding to indicate that fatigue is related to compensatory involvement of the core network, and that excess activity in the core network possibly could be used as an objective marker of fatigue in MS.

D12-103

NEUROPSYCHOLOGICAL PROFILE IN SCHIZOPHRENIA MEASURE WITH THE MATRICS BATTERY. THE RELATIONSHIP WITH THE QUALITY OF LIFE

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Neurocognitive impairments have been documented in schizophrenia. Numerous studies have found comprehensive cognitive deficits in adult schizophrenic patients, encompassing global deficits from early sensory information processing to attention, verbal and visual learning and memory and executive functions. Accordingly, cognitive deficits have also been found to be prevalent in early-onset schizophrenia. However, findings have not been consistent as to whether the cognitive deficits in this group have a global profile, or if there are relatively spared or impaired domains of function. An important step toward developing treatments targeting impaired cognition in schizophrenia came with the successful completion of the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative. Through this MATRICS process, a battery of tasks reflecting seven domains of cognitive functioning was developed. The tasks selected were mostly pen and paper measures widely used in clinical neuropsychology and were selected based on criteria that experts indicated were essential for clinical trials. The purpose of this research was to examine whether the profile of cognitive deficits is global or specific; and if there is relationship with the quality of life. The study included 45 persons with schizophrenia. Diagnosis was based on DSM-IV criteria. Symptom level was assessed using the PANSS. Neuropsychological functioning was assessed with the MATRICS battery, consisting of ten different tests measuring seven cognitive domains: speed of processing, attention/vigilance, verbal and nonverbal working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. The QLS was use to assess quality of life. Data were analyzed to examine the neurocognitive profile of clinically stable schizophrenia patients on the MCCB. We found a generalized deficit in cognitive functioning in patients with schizophrenia-spectrum disorders. This may support previous suggestions of a generalized brain dysfunction in schizophrenia. The results also show that there is not relationship between the neurocognitive profile and the quality of life.

D12-104

MELATONIN CONTROL OF NITRIC OXIDE SYNTHASES IN PARKINSON'S DISEASE

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The 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of Parkinson's disease (PD) constitutes a well-known model for studying the participation of oxidative/nitrosative stress, inflammation, and mitochondrial dysfunction in the pathogenesis of sporadic PD. The active metabolite of MPTP, MPP+, binds to and inhibits mitochondrial complex I activity, increasing the production of reactive oxygen species (ROS). In these conditions, microglia is also activated producing high amounts of NO• through iNOS induction, leading to neuronal cell death. The relative role of iNOS and nNOS on mitochondrial dysfunction under MPTP administration is, however, unclear. Here, the participation of iNOS and nNOS in the mitochondrial impairment of the nigrostriatal pathway of MPTP-treated mice, was assayed. For this study iNOS and nNOS deficient mice and their respective wild-type controls, were used. Complex I activity, nNOS and iNOS activities, respiratory complexes expression, and mitochondrial DNA, were analyzed in s. nigra (SN) and striatum (ST) of vehicle- and MPTP-treated mice. Our results show that complex I activity decreases sharply in SN and, in a lesser extent, in ST of wild-type mice. Interestingly, mice lacking iNOS or nNOS showed a comparable complex I inhibition after MPTP administration, probably due to the presence of MPP+. Moreover, the total NOS activity in SN and ST increased significantly after MPTP, which was mainly due to the iNOS induction. Melatonin administration counteracted the effects of MPTP, recovering the activity of the complex I, an effect unrelated to the mice strain used. Melatonin also counteracted the MPTP-dependent expression of iNOS and prevented the mtDNA depletion induced by MPTP. The results also suggest that the mtDNA damage found after MPTP administration could be caused by iNOS induction. In view of these results, we used melatonin as a template for the synthesis of new molecules, looking for selective antagonists of iNOS. These compounds have been also assayed in the same experimental model of PD. Together, our results suggest that melatonin itself and some of the synthetic analogues assayed behave as a neuroprotective drugs against PD induced by MPTP in mice.

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D12-105

NEAR-INFRARED SPECTROSCOPY STUDY ON FRONTAL AND TEMPORAL LOBE ACTIVATION IN BIPOLAR DISORDER PATIENTS DURING A FACE-TO-FACE CONVERSATION TASK

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Introduction: Bipolar disorder patients show various characteristics of talking which vary greatly from state to state. Only a few studies have investigated the time course of frontal activation, and to our knowledge, frontal activation during face-to-face conversation has not yet been investigated. Near-infrared spectroscopy (NIRS) is a functional brain imaging technique used for monitoring brain activation in a natural setting while using near-infrared light. Our group previously investigated brain activation during face-to-face conversation in healthy subjects and found high cyclical activity in their frontal lobes. Here, we investigated frontal and temporal lobe activation in bipolar disorder patients and healthy subjects during face-to-face conversation. Methods: The study population comprised the bipolar disorder (23 patients) and healthy volunteer groups (24 healthy individuals). Brain activation in the frontal and temporal lobes was measured using NIRS for both groups. We used 2 types of activation tasks: conversation task and control task. In the conversation task, the subjects were instructed to converse with the interviewer during the task period according to 2 criteria: (1) the time course of the conversation was predetermined, i.e., the subject and interviewer were supposed to talk in turn (in this order) every 15 s; and (2) the theme of the conversation was limited to food-related topics. In the control task, the subjects were instructed to repeat meaningless syllables such as "a," "ka," "sa," "ta," and "na" to assess the effect on phonation. We compared the grand average of and the amount of changes in [oxy-Hb] during the talking and listening phases of the conversation task for all the subjects and analyzed the correlation between these results and the clinical variables. Results: In the control task, the grand average of the changes in [oxy-Hb] did not differ for the 2 groups. However, the bipolar disorder group had a decreased grand average of changes in [oxy-Hb] in both orbitofrontal lobes during the conversation task. The [oxy-Hb] changes decreased mainly in the frontopolar region for the bipolar disorder group. The grand average of and the amount of changes in [oxy-Hb] were not significantly correlated with the clinical variables. Conclusions: On investigating frontal lobe activation in bipolar disorder patients and healthy volunteers during face-to-face conversation in situ by using NIRS, we found differences in brain activation in bipolar disorder patients and healthy volunteers. The bipolar disorder patients showed hypoactivation of both orbitofrontal lobes throughout the tasks and impaired flexibility of the frontopolar region.

D12-106

AN IMPAIRED HYPOXIC RESPONSE IN CSB-DEFICIENT NEURAL CELLS SUGGESTS A MOLECULAR MECHANISM FOR NEUROPATHOLOGY IN COCKAYNE SYNDROME

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Cockayne Syndrome (CS) is an autosomal recessive disorder with neurodevelopmental impairment, growth retardation, increased photosensitivity and signs of premature aging. One predominant neurological dysfunction is an impaired motor control due to cerebellar ataxia. Most cases of CS are caused by mutations in the CS group B (CSB) gene. Lack of functional CSB protein results in a lack of the transcription-coupled repair subpathway of nucleotide excision repair. As many symptoms of CS patients like a severe mental retardation and neurodevelopmental impairment cannot simply be explained by a defect in DNA repair, it is assumed that CSB has additional functions in the development of the brain. Recently, it has been reported that human CSB-deficient fibroblasts are incapable of upregulating HIF-1-dependent genes under hypoxia-like conditions. Therefore, we investigated whether the transcriptional response to hypoxic conditions is also dysregulated in neural CSB-deficient cells of the mouse. Analysis of 10 weeks old CSB-deficient mice revealed that they had lower body and brain weights compared to littermates. Histological examination of brain slices and staining for calbindin-positive cells indicated atrophic degeneration of the Purkinje cells of the cerebellum. Furthermore, we found a generally decreased expression of the histone acetyltransferase and HIF-1 cofactor p300 in the cerebellum in mRNA and protein level which appeared to be pronounced in the Purkinje cells. Additionally, CSB-deficient neurospheres, generated by neural stem cells from CSB-deficient mice, showed lower transcription of HIF-1-inducible genes VEGF, GLUT-1 and HMOX and had a reduced viability compared to wildtype-derived neurospheres under hypoxic conditions. These results indicate that the transcriptional response of neural CSB-deficient cells is dysregulated under hypoxic conditions and that the transcriptional dysregulation has implications for the survival of the cells. Moreover, reduced viability of CSB-deficient neurospheres might provide a novel mechanistic link to the neurological defects of CSB-deficient mice and suggest a connection between the neuropathology of CS patients and an improper response to low oxygen concentrations in the brain.

D12-107

EARLY SPONTANEOUS BEHAVIOURAL SIGNS OF ALZHEIMER'S AND HUNTINGTON"S DISEASE IN TRANSGENIC MOUSE MODELS IN A HOME CAGE SITUATION

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Studies of the behaviour of transgenic mice modeling human neurodegenerative diseases such as Alzheimer's disease (AD) and Huntington's disease (HD) have increased our knowledge of the role of specific genes in the development of those diseases. The characterization of the earliest signs of these diseases is particularly important concerning testing of drugs aimed at slowing or stopping the progression of the neurodegeneration or alleviating the symptoms. Traditionally, behavioural studies on these models are conducted by using test batteries (clasping test, rotarod, grip strength test, passive and active avoidance) in order to investigate specific evocated responses separately. As an alternative, we use an integrated system based on video-tracking in a home cage situation in which several aspects of the neurodegeneration and its spontaneous behavioural changes can be simultaneously investigated. The advantages are: i) reduction of the confounding effects of stress, transportation, novelty, handling caused by human interference; and ii) the possibility of investigating longitudinal time course of changes. We studied genetic models for AD (APP85SwePS1dE9 and 3xTg-AD) and HD (R6/2) in the home cage and their spontaneous activity was monitored over a series of days. The 3xTg-AD was developed by harboring $PS1_{M146V}$, APP_{Swe}, tau_{p301L}. The R6/2 were generated that are transgenic for the 5'end of the human HD gene carrying $(CAG)_{188}$-$(CAG)_{222}$ repeat expansions (Mangiarini et al. 1996). Compared to wildtype littermates, female AD-mice of the APP85SwePS1dE9-strain showed a significant increase in activity and changes in the circadian rhythmicity at the age of 4 months, whereas R6/2, due to their fast phenotype, showed a decrease already at the age of 4 weeks. We also show that more comprehensive analysis of the locomotion of the animals aiming at having a complete velocity profile of each animal helps to find significant changes at an earlier stage. These findings will improve the drug testing on animal models of neurodegenerative diseases in which an early intervention is crucial to slow or try to stop the progression of the diseases.

D12-108

THERAPEUTIC EFFECTS OF METHYLENE BLUE ON ALZHEIMER'S DISEASE PATHOLOGY IN A TRANSGENIC MOUSE MODEL

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Methylene blue belongs to phenothiazinium family. It has been used for more than a century in the clinical treatment of a variety of ailments. Recent studies suggest that the drug slowed down cognitive decline in Alzheimer'disease. These promising data lead to the development of new applications. The aim of the present study is to evaluate the therapeutic effects of methylene blue on AD pathology, using a transgenic mouse model. Swedish beta-amyloid precursor protein APPswe/PS1 transgenic mice that develops age-dependent accumulation of beta-amyloid and cognitive decline were used. They were submitted to drinking water or intraperitoneal routes of administration of 2mg/10 ml and 2mg/kg respectfully on a 3-months period. Treatment started when animal already exhibiting behavioural deficits and AD-like pathology. Results showed that administration of methylene blue reversed behavioral deficits, no matter what the treatment route was. This effect was observed in a range of behavioral tests, measuring spatial learning, retention of memory formation, and emotional status. Altogether, methylene blue showed interesting data, suggesting that it could be used as treatment to reverse cognitive decline in mice with installed beta-amyloid deposits.

D12-109

WHAT WE (DON'T) KNOW ABOUT SNPS' EFFECT SIZES IN IMAGING GENETICS

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In recent years, genome wide association studies (GWASs) have identified a series of single nucleotide polymorphisms (SNPs) in various genes being related to psychiatric disorders. Typically, the SNPs' effect associated with the illness is very small and large cohorts of patient studies are thus required to identify genetic risk variants. By combining genetic assessment with multimodal neuroimaging numerous studies revealed specific structural and functional brain systems that mediate genetic vulnerability or liability to psychiatric disorders (O'Donovan, et al. 2008). Owing to the proximity to the genetic level SNPs are supposed to have a higher penetrance on the neural systems level than on emergent mental or behavioral phenomena examined in GWASs (Meyer-Lindenberg 2009). This assumption has been supported by two recent meta-analyses accumulating functional imaging studies on the effects of 5-HTTLPR and COMT revealing specific effects up to $d = .70$ – $d = 1.0$ (Mier, et al. 2010; Munafo, et al. 2008). However, there are several issues related to estimating effect sizes out of thresholded imaging data which may result in overestimation of population parameters even in meta-analyses (Kriegeskorte, et al. 2010). In this work we exemplarily discuss some of these issues and raise concerns about the current estimates which are now often cited in the literature. Our conclusions are that at this time we know close to nothing about SNPs' population effect sizes on brain function. Further, most of the applications of the above-mentioned effects in power analyses for other risk candidates in imaging genetic might not be appropriate and larger cohorts have to be examined to be sensitive for a range of much smaller effects. We propose that greater efforts in sharing unthresholded imaging data or beta maps coding effect sizes rather than statistical significance have to be made in order to accumulate evidence across different samples. This would provide the database required for unbiased estimation of effect sizes and revelation of subtle genetic risk related changes in the neural systems' architecture.

-Kriegeskorte N, Lindquist MA, Nichols TE, Poldrack RA, Vul E. (2010): Everything you never wanted to know about circular analysis, but were afraid to ask. J Cereb Blood Flow Metab 30(9):1551-7.
-Meyer-Lindenberg A. (2009): Neural connectivity as an intermediate phenotype: brain networks under genetic control. Hum Brain Mapp 30(7):1938-46.
-Mier D, Kirsch P, Meyer-Lindenberg A. (2010): Neural substrates of pleiotropic action of genetic variation in COMT: a meta-analysis. Mol Psychiatry 15(9):918-27.
-Munafo MR, Brown SM, Hariri AR. (2008): Serotonin transporter (5-HTTLPR) genotype and amygdala activation: a meta-analysis. Biol Psychiatry 63(9):852-7.
-O'Donovan MC, Craddock N, Owen MJ. (2008): Schizophrenia: complex genetics, not fairy tales. Psychol Med 38(12):1697-9.

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CONSEQUENCES OF A LATE DIAGNOSIS OF PROCEDIMENTAL LEARNING DISORDER

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Introduction. Procedimental learning disorder also known as nonverbal learning disorder is a subtype of learning disorder. It's characterized by difficulties in the acquisition and automation of motor and cognitive routines (procedures), deficits in visuospatial and visual constructional capabilities and motor coordination. Patients have preserved linguistic abilities (except the pragmatic use in many cases) and declarative memory. A case report. A 13 year old boy. He came to the Primary Health Service because of school failure. He has just finished 1st year of high school with 90% of the subjects failed. He also has behavioral problems. His mother came to see me in despair after she received the final report card and after the evaluation from a psychologist with no conclusive answer because of the disparity in the results and very low nonverbal IQ. Results. I performed a neurological examination, neuropsychological evaluation and I analyzed his previous tests. Highlights in the following results: dysgraphia, deficits in spatial orientation and visual-motor integration. Difficulty in contextual understanding. Poor performance in attention and reading comprehension. His behavioral problems are characterized by passivity, limited initiative and amazement at the demands of his parents not only with regard to homework, but also with personal care and hygiene. Discussion. The diagnosis of Procedimental Learning Disorder is based on the analysis of the symptoms. Most of the authors consider that the possible etiology is a posterior attentional system dysfunction. According to studies published by Narbona, Crespo-Eguílaz and Magallón, the evolution is conditioned by the time of diagnosis (age), and may be favorable if a comprehensive treatment program is performed in a timely manner by a specialist in this type of disorder. Conclusions. The reason for presenting this communication is to consider the PLD in every child in whom the ADHD is suspected or who have the following symptom: difficulties in coordination, visual-motor integration, attention, contextual understanding and difficulties in relationships with peers. An early diagnosis can prevent unnecessary suffering for the child and his family and prevent future personality disorder, because the child's repeated experience of personal failure could lead to low self-esteem and symptoms of depression.