



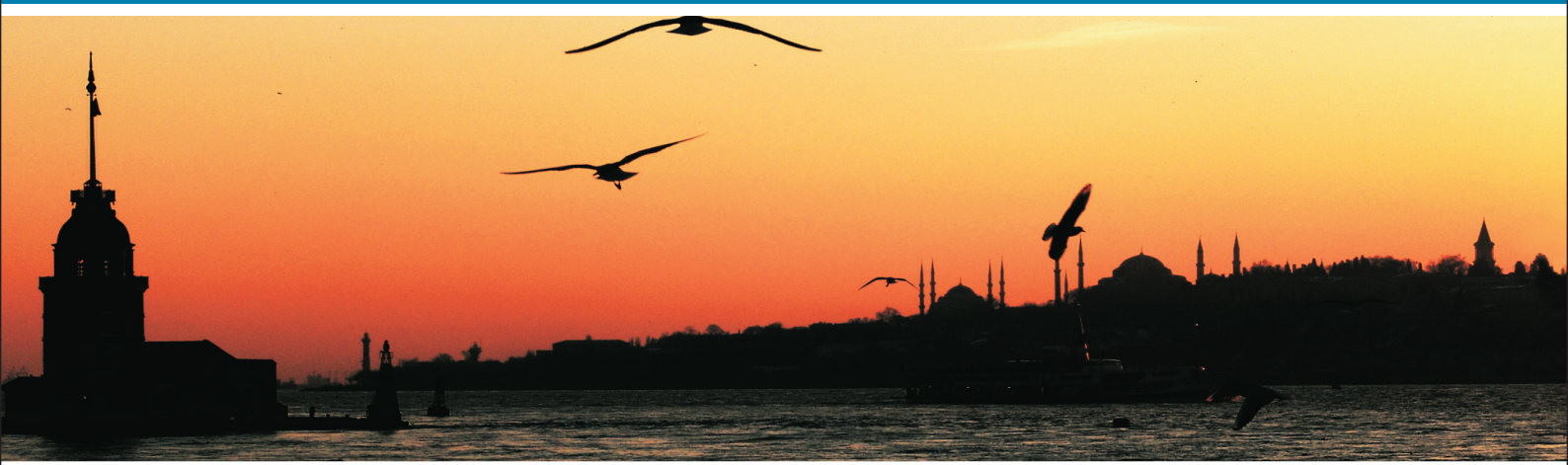
MNS 2012

4th Conference of the Mediterranean Neuroscience Society



Abstract Book

September 30 – October 3, 2012
Military Museum & Cultural Center, Istanbul, TURKEY



www.mns2012.org



MNS 2012

4th Conference of the Mediterranean Neuroscience Society

September 30 – October 3, 2012



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Yasin TEMEL

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Dear colleagues,

It is our pleasure to announce the 4th Conference of the Mediterranean Neuroscience Society, from September 30 – October 3, 2012. As decided in the General Assembly in Alexandria in 2009, this conference will be held in Istanbul, an amazing city covering both sides of the Bosphorus. It is one of the most intriguing cities worldwide, both geographically, connecting Europe with Asia, and historically, since it housed various civilizations. This is evidenced by the many names Istanbul has had in the past, including Lygos, Byzantium, New Rome, and Constantinople.

We have selected the conference venue with special care, the historical Military Museum, located in the heart of Istanbul (Harbiye). Items were collected from the Saint Irene Church by the Armory Marshal Ahmed Fethi Paşa and the museum was opened in 1846. It was the first modern museum building of that time. The Military Museum presents a history of military change and development from the past to the present and showcases a wide-ranging collection of about 55,000 objects. Kindly note that **The MNS, the N€uromed consortium, and the ISIS consortium** will provide stipends for young qualified researchers.

Research on brain function in health and disease is among the priorities for today's societies, and several indicators put the mediterranean research area among strategic issues for the European Union (EU). Many South-North collaborations and networks have emerged in recent years through bilateral and multi-lateral actions, supported by the EU or by international and national actions, both for setting up teaching curricula and for building human potential. Our mission is to support and help strengthen all initiatives that bring together mediterranean neuroscientists. In this conference, we want to gather mediterranean countries and offer a rich program with lectures, symposia, poster sessions and social events. The scientific program will focus on latest advances in Integrative and Clinical Neurosciences, Molecular and Cellular Neurosciences, Neuroendocrinology, Cognitive, Computational and Theoretical Neurosciences. We are convinced that this meeting will be highly beneficial, not only for the scientific exchanges, but also in terms of training opportunities for students and young researchers. We are putting together an appealing programme and invite you cordially to join us at this conference.

Yours Sincerely,

Prof. Yasin TEMEL, MD. PhD.

Conference President

Prof. Abdelhamid BENAZZOUZ, PhD.

Conference Vice-President

Prof. Hagai BERGMAN, MD. PhD.

Conference Vice-President



Sunday, September 30, 2012

- 14:00 – 18:00 **Registration**
- 19:00 – 19:15 **Opening Ceremony**
By Y. TEMEL (Turkey / The Netherlands)
- 19:15 – 20:00 Plenary Lecture 1 **Hall A**
Subconsciousness and basal ganglia
Y. AGID (France)
- 20:30 **Opening Reception**

Monday, October 1, 2012

- 08:30 **Registration**
- 09:00 – 10:00 Plenary Lecture 2 **Hall A**
Cannabinoid signaling in the brain: the where matters
G. MARSICANO (France)

- 10:30 – 12:30 **Symposium 1**
Hall A **Oxytocin and Vasopressin Actions in the Central Nervous System: Control of Social and Feeding Behaviors**
Chaired by: Michel G. Desarménien (France)

The oxytocin receptor in sociability and cognitive flexibility: what do you learn from knockout mice models,
Bice Chini, Italy

Electrophysiological actions of oxytocin and vasopressin in the brain. Vasopressin depresses long term potentiation in the mouse hippocampus,
Michel Desarménien, France

CD38, oxytocin and social cognition in humans,
Richard Ebstein, Israel

Cellular plasticity in the supraoptic and paraventricular nuclei after prolonged dehydration in the desert rodent *Meriones shawi*: Vasopressin and GFAP immunohistochemical study,
Halima Gamrani, Morocco

Studying neurohypophyseal neurons in the zebrafish,
Gil Levkowitz, Rehovot, Israel

Oxytocin, a crucial role at birth in the control of feeding behavior; involvement in the Prader-Willi syndrome,
Françoise Muscatelli, France

- Hall B** **Symposium 2**
Environmental enrichment : a useful paradigm to study brain functioning in physiological and pathological conditions
Chaired by: Marcello Solinas (France) & Claire Rampon (France)

The anxiolytic effect of environmental enrichment,
Alon Chen, Israel



Monday, October 1, 2012

Environmental enrichment as an experimental paradigm to promote stress inoculation-induced resilience or "stress immunization",
Gregorio Segovia, Spain

Prevention and treatment of drug addiction by environmental enrichment, *Marcello Solinas, France*

How environmental enrichment delays the progression of Alzheimer's disease in transgenic mice models,
Claire Rampon, France

Hall C

Symposium 3

Endocannabinoids and the control of memory and emotions

Chaired by: *Liana Fattore (Italy) & Patrizia Campolongo (Italy)*

The endocannabinoid system and the regulation of memory for emotionally arousing experiences
Patrizia Campolongo, Italy

The role of the endocannabinoid system in extinction learning,
Beat Lutz, Germany

Endocannabinoid modulation of learning and emotional processing in the human brain,
Sagnik Bhattacharyya, UK

Homeostatic role of the endocannabinoid system and consequences of its dysregulation on emotional states,
Maria-Paz Viveros, Spain

Sex-dependent differences in the effects of cannabinoids on the emotional brain,
Liana Fattore, Italy

12:30 – 14:30 Lunch with poster sessions

14:30 – 16:30 Symposium 4

Hall A

Basal ganglia physiology: from motor to limbic function

Chaired by: *Izhar Bar-Gad (Israel) & Thomas Boraud (France)*

The subthalamic nucleus and midbrain serotonergic neurons: a novel motor-limbic interface,
Yasin Temel, The Netherlands

Noradrenergic control of the subthalamic nucleus,
Abdelhamid Benazzouz, France

Responses to emotional voices in the right ventral subthalamic nucleus of human patients with Parkinson's disease,
Hagai Bergman, Israel

Role of the striatum in spatial learning: a behavioural and electrophysiological approach in the monkey,
Thomas Boraud, France



Monday, October 1, 2012

Tic-related neuronal activity in the cortico-basal ganglia loop,
Izhar Bar-Gad, Israel

Hall B

Symposium 5

The circadian and seasonal network: a combination of clocks, synchronising inputs and outputs

Chaired by: Paul Pévet (France)

Retinal circadian clocks and non-visual photoreceptors: light input to the circadian system,
Ouria Dkhissi-Benyahya, France

The sympathetic system as an output of the central clock: Its role in metabolic rhythms,
Andries Kalsbeek, The Netherlands

The role of the SCN-endocrine outputs in the circadian and seasonal network,
Paul Pévet, France

Corticosteroids and adaptation to stress,
Mohamed Najimi, Morocco

The arcuate nucleus and neuropeptide systems in the seasonal adaptation of mammals,
Seloua El Ouazzani, Morocco

Hall C

Symposium 6

The Neuronal and Glial Functions of Brain Dystrophins

Chaired by: Alvaro Rendon (France)

DP71- The most abundant non-muscle product of the Dystrophin gene
David Yaffe, Israel

DP71- In the Hypothalamo-Neurohypophysial System of Mice
Latifa Dorbani, Algeria

DP71 and Glial Dystrophin-Associated Proteins in the Blood Brain Barrier of the Dystrophic mdx Mouse,
Beatrice Nico, Italy

Lessons from Renital Dystrophins,
Michel Roux, France

The Molecular, Neurophysiological and Behavioral Profiles of Mice Lacking Brain Dystrophin Products,
Cyrille Vaillend, France

16:30 – 17:00 **Coffee break**

17:00 – 18:00 Plenary Lecture 3 **Hall A**
An update on Alzheimer's disease
M. EMRE (Turkey)

18:00 – 20:00 **General Assembly** **Hall A**



Tuesday, October 2, 2012

09:00 – 10:00 **Plenary Lecture 4** **Hall A**
Neuroendocrine aging: GH/IGF-1 axis, energy balance regulation and cognition
J. EPELBAUM (France)

10:30 – 12:30 **Symposium 7**
Hall A
Neuroglia: the forgotten but emerging player in neurodegeneration
Chaired by: José Julio Rodriguez (Spain)

Neuroglia: from brain homeostasis to Pathophysiology,
Alexei Verkhratsky, U.K.

Astrocyte degeneration in amyotrophic lateral sclerosis: mechanism and rescue,
Daniela Rossi, Italy

Neuroglial alterations in Alzheimer's Disease are concomitant with neurogenic impairments,
José Julio Rodriguez, Spain

NG2-glia: a relevant novel glia with multiple functions in normal brain and neurodegenerative processes,
Arthur Butt, U.K.

Role of glial cells in oxidative stress resistance in neurodegenerative diseases,
Mami Noda, Japan

Hall B
Symposium 8
Adaptive neuroendocrine regulations in stress and food intake control: from molecular to integrated approaches
Chaired by: Youssef Anouar (France) & M.ohammed Errami (Morocco)

Cell plasticity at the splanchnic-adrenal synapse: neuropeptide neurotransmission in stressful experiences,
Lee Eiden, USA

Parvocellular accessory neuropeptides and environmental stressors,
Rabia Magoul, Morocco

Hypothalamic endocannabinoid system and food intake control,
Mohammed Errami, Morocco

Molecular regulation of peptide and neurotransmitter secretion in neuroendocrine cells,
Maria Malagon, Spain

Role of antioxydative enzymes during neuroendocrine and metabolic regulations,
Youssef Anouar, France



Tuesday, October 2, 2012

Hall C

Symposium 9

The Rhythms of life : from bench to bedside

Chaired by: *Nouria Lakhdar-Ghazal (Morocco)*

The daily ambient temperature cycle is a true synchronizer of the camel circadian clock outputs: body temperature and melatonin rhythms,
El Allali Khalid, Morocco

Pineal 5-methoxytryptophol seasonally controls reproductive function in a desert rodent, the jerboa *Jaculus orientalis*,
Nouria Lakhdar-Ghazal, Morocco

Hypothalamic RF-amide neurons are critical for the melatonin control of seasonal reproduction,
Valérie Simonneaux, France

Alteration of circadian rhythms in a non-human primate model of Parkinson's Disease,
Howard Cooper, France

Sleep and infections,
Marina Bentivoglio, Italy

12:30 – 14:30 Lunch with poster sessions

14:30 – 16:30

Symposium 10

Chronic pain mechanisms: from peripheral determinants to spinal cord integration

Chaired by: *Marc Landry (France)*

Hall A

Peripheral pain pathways; Mechanosensory mechanisms and moleculel characterization of mammalian cold thermoreceptors and nociceptors,
Felix Viana, Spain

Functional significance of nociceptive primary sensory neurons diversity,
Aziz Moqrich, France

MiR-134/LIM Kinase1: how far can this duo modulate neuropathic pain?,
Sherine Abdel Salam, Egypt

Calcium-dependent hyperexcitability of spinal neurons,
Marc Landry, France



Tuesday, October 2, 2012

Hall B

Symposium 11

Mapping brain activation by functional MRI and optical neuroimaging: cellular and vascular basis and insights into brain function

Chaired by: *Hiraç Gurden (France) & Ata Akin (Turkey)*

Watching the brain: a brief introduction to issues in functional neuroimaging,
Hiraç Gurden, France

High resolution fMRI & face- and object processing in awake behaving monkeys,
Joziën Goense, Germany

Functional Connectivity of Prefrontal Cortex in Health and Disease: Insights from functional Near-Infrared Spectroscopy,
Ata Akin, Turkey

Functional Imaging of the Vestibular Cortex using Near-Infrared Spectroscopy,
Theodore Huppert, USA

Optical signature of olfactory activation,
Frédéric Pain, France

Hall C

Symposium 12

Serotonin implication in neuropsychiatric disorders: A translational approach

Chaired by: *Giuseppe Di Giovanni (Italy) & Philippe De Deurwaerdère (France)*

Serotonin depletion can promote anxiety and depression in a rat model of Parkinson's disease: an electrophysiological and behavioural study,
Claire Delaville, France

Serotonergic modulation of cognitive flexibility in rodents,
V. Boulougouris, Greece

Serotonin 2 receptor modulation of K⁺ Channels,
M Pessia, Italy

Obsessive-compulsive disorders: Serotonin and Beyond,
J Zohar, Israel

Role of Serotonin 2A/2C in Absence Epilepsy,
G Di Giovanni, Malta

16:30 – 17:00 Coffee break

17:00 – 18:00 Plenary Lecture 5 **Hall A**
Understanding actions, intentions and emotions of others
G. RIZZOLATTI (Italy)



Wednesday, October 3, 2012

9:00 – 10:00 Plenary Lecture 6 **Hall A**
Reward, risk and neuroeconomic decision making
W. SCHULTZ (United Kingdom)

10:30 – 12:30 **Symposium 13**
Hall A **Towards new therapies in stroke rehabilitation**
Chaired by: M. Sahiner (Turkey) & G. Hoogland (The Netherlands)

**Nutraceuticals for stroke protection:
a focus on "alpha"-linolemic omega-3 fatty acid,**
N. Blondeau, France

In vivo brain repair: Electrical fields attract newborn brain cells,
Ali Jahanshivar, The Netherlands

**Stroke awareness in the Saudi community: prompt public health measures must
be implemented,**
Y. Mohammad, Saudi Arabia

Hall B **Symposium 14**
Molecular and behavioral aspects of lead neurotoxicity
Chaired by: Samir Ahboucha (Morocco)

Lead exposure in the environment and human population,
Azeddine Sedki, Morocco

Impact of lead toxicity on recognition memory and motor activity,
Ahmed Omar Touhami AHAMI, Morocco

Genetic mechanisms of developmental Pb neurotoxicity,
Jennifer L. Freeman, USA

Lead neurotoxicity and neurotransmission,
Samir Ahboucha, Morocco

Synaptic mechanisms of lead neurotoxicity,
Dietrich Büsselberg, Qatar

Hall C **Symposium 15**
Alzheimer's disease: shift in focus
Chaired by: Slavica KRANTIC (France)

**Role of cytokines and chimiokines in neuroinflammatory diseases:
possible therapeutic targets,**
Carole Rovère, France

**Amyloid-beta related alterations in hippocampal network activity and
cognitive impairment,**
Patrick Dutar, France



Wednesday, October 3, 2012

Very early changes in hippocampal network rhythms before beta appearance in an Alzheimer mice model,
Sylvain WILLIAMS, Canada

Molecular imaging for amyloid plaques and neuroinflammation,
Denis Guilloteau, France

12:30 – 14:30 Lunch with poster sessions

14:30 – 16:30

Symposium 16

Synaptic plasticity in learning and memory: experimental and computational approaches

Chaired by: Marie Mofteh (Egypt)

Hall A

Spatial distribution of FGFR2 in normal and lesioned CNS of the urodele amphibian *Pleurodeles Waltlii*,
Marie Mofteh, Egypt

Evaluation of lithium chloride treatment on brain and synaptic plasticity,
Marwa Wael, Egypt

A connectionist approach to decision in the basal ganglia,
Radwa Khalil, Egypt

Decision making as a competition mechanism in the cortex-basal ganglia loop circuit: experimental approach,
Camille Piron, France

Hall B

Symposium 17

Neurobiology of stress: new vistas

Chaired by: Emmanuel Moyse (France) & Mohamed Najimi (Morocco)

Mild stress and depression,
Ahmed Abdel Tawab, Egypt

Stress and neurogenesis,
Fatiha Chigr, Morocco

Stress and water restriction,
Hélène Pouzet, France

Stress and addiction,
Sakire Pogun, Turkey

Response to stress: new central pathways,
Valery Grinevich, Germany



Wednesday, October 3, 2012

Hall C

Symposium18
New insights in neuron-glia interactions
Chaired by: Stéphane Oliet (France)

Vesicle dynamics in astrocytes,
Robert Zorec, Slovenia

Astrocytes and neurons, intimate partners during basal synaptic transmission,
Aude Panatier, France

Astrocytes mediate in vivo cholinergic-induced plasticity,
Alfonso Araque, Spain

Astrocytes and epilepsy,
Giorgio Carmignotto, Italy

16:30 – 17:00 **Coffee break**

17:00 – 18:00 **Final remarks**



1 October 2012, Monday / Neurodegenerative Diseases

Poster	Abstract Title	Author Name	Author Last Name
P001	A Review of Biochemical Markers for Early Diagnosis of Alzheimers Disease	Meeha	Aftab
P002	Immunocytochemical Studies of the Neurodegenerative Diseases. The Ubiquitin Proteasome System	Zouambia	Mohamed
P003	Neurotransmitters respecification in Huntington's disease	Ali	Jahanshahi
P004	In vivo efficacy of (CUG) _n oligonucleotides to treat HD	Ali	Jahanshahi
P005	Lesion of dopaminergic terminals in the amygdala produces enhanced locomotor response to D-amphetamine, facilitation of amphetamine self-administration and opposite changes in dopaminergic activity in prefrontal cortex and nucleus accumbens.	Taghzouti	Khalid
P006	Control of the pallido-subthalamic and pallido-nigral pathways by dopamine D2 receptors in the rat	Omar	Mamad
P007	The effects of high frequency stimulation of the subthalamic nucleus on mood: a role for the lateral habenula?	Maartje	Melse
P008	Effect of anti-parkinsonian treatments on motor and non-motor deficits induced by monoaminergic depletions in a bilateral rat model of Parkinsonism	emilie	faggiani
P009	Neuroprotective and Neurotherapeutic Effects of Bee Venom on Neurodegenerative Diseases	Miran	Rakha
P010	Effect of verbal auditory cues on cortical motor excitability in parkinson's disease. Evidence from motor evoked potential	Enas Mohamed	Shahine
P011	Neuronal cell loss in the subthalamic nucleus of experimental Parkinson's disease rats	Frédéric	Schaper
P012	The dopaminergic agonist quinpirole triggers 5-HT _{2C} receptor-dependent controls on both purposeless oral movements and the activity of the hyperdirect pathway in basal ganglia.	Melanie	Lagiere
P013	Effects of tetrabenazine on choreiform movements in the transgenic rat model of Huntington's disease	Dagmar Helena	Zeef
P014	Region-dependent modulation of L-DOPA-induced dopamine release by noradrenergic terminals in the hemiparkinsonian brain	Philippe	De Deurwaerdere
P015	Circadian Alterations in Mouse and Non-Human Primate MPTP Treated Models of Parkinson Disease	Fifel	Karim
P016	Molecular guidance of transplanted embryonic cells in the lesioned substantia nigra in an animal model of Parkinson disease.	Laetitia	Prestoz
P017	Study of brain structures on MRI of Parkinson's	Cherfa	Yazid



1 October 2012, Monday / Psychiatric disorders

Poster	Abstract Title	Author Name	Author Last Name
P018	Suicide and Self-Injury of Offenders in Custody: Assessment, Interventions and Management	Ragaa	Abdelmaaboud
P019	The Effect of Reminiscence on Life Satisfaction among Elderly People	Naglaa	Mostafa
P020	The Impact of an Educational Program about Addictive Behavior on the Performance of Nurses in Mental Hospitals	Nesrine	Hana
P021	Correlates For Self-Injurious Behaviors among Children with Autistic Disorders	Mostafa	Mona Hamdy
P022	Anxiolytic effects of acute administration of Ormenis multicolis in the male Sprague-Dawley rat	Elmahdi	Wakrim
P023	A gender-specific association of interleukin-1 receptor antagonist polymorphism with Schizophrenia susceptibility	Bel Hadj Jrad	Besma
P024	Increased locomotor activity and dopamine release in the nucleus accumbens of adults rats following ketamine administration were observed after neonatal transitory inactivation of the anteromedian prefrontal cortex	Alain	Louilot
P025	Impact of Exposure to a Chronic Social Stress Procedure during Adolescence on the Anxiety Response in NMRI Male Mice	Rosa	Redolat
P026	Epidemiological study of psychiatric disorder in the region of Gharb Cherarda Beni Hsen (Morocco)	Rim	Bousalham
P027	Evaluation of Serum interleukin-23 and interleukin-6 in schizophrenic patients versus healthy control subjects	Ali	Shahraki
P028	Causes of Psychiatric Patients? Aggression and Violence: Nursing Staff and Patients Perspectives	Eman Mohamed Ibrahim	El-Genadi
P029	Prevalence of Epilepsy in Ethiopian Community	Tadesse	Seda
P030	Quantitative Electroencephalographic Monitoring of the Electrical Activity of the Brain in Elderly Demented Patients in Comparison to Normal Aged Subjects	Amani	Elbaz
P031	The Efficacy of "Insight Enhancement Program" on Improving the Perception of Internalized Stigma and Locus of Control Among Schizophrenic Patients	Nashwa	Ibrahim
P032	Analysis of association between Dopamine receptors genes methylation risk of Schizophrenia	Dor Mohammad	Kordi Tamandani
P033	Studies on effect of stress paradigm in Stress-induced behavioral alterations	Mariama	Elouahli
P034	Assessment of Obsessive Compulsive Disorders Before and After Treatment Using Magnetic Resonance Imaging Approach	Saïd	Boujraf
P035	Interleukin-1 beta and microRNA-146a in an immature rat model and children with mesial temporal lobe epilepsy	Ahmed	Galal
P036	Dopamine manipulation limited to pre-exposure session is sufficient to modulate latent inhibition.	Ouhaz	Zakaria



P037	Antidepressant Effect of Barley Grains Incompare with Prozac Drug: Biochemical and Cytological studies on Skeletal Muscles of Mice	Mohamed Ali	Awatef
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1 October 2012, Monday / Neurophysiology

Poster	Abstract Title	Author Name	Author Last Name
P038	Central neuroplasticity and lower limbs functional outcome following repetitive locomotor training in chronic stroke patients	Enas Mohamed	Shahine
P039	Central neuroplasticity and upper limbs functional outcome following repetitive lower limb locomotor training in chronic stroke patients	Enas Mohamed	Shahine
P040	Implication of Calcium-stimulated Adenylate cyclase 1 in the functional recovery of AC1 KO mice injured corticospinal tract.	Nait Taleb Ali	Hanane
P041	Alterations in inhibitory synaptic transmission to lumbar motoneurons after spinal cord injury and stepping recovery in adult rats	Bras	Helene
P042	Neuroglial organization of the hypothalamo-neurohypophysial system of <i>Psammomys obesus</i>	Saliha	Ouali-Hassenaoui
P043	Neuron-Glia interactions in the Hypothalamic Magnocellular Neurosecretory Nuclei An Immunohistochemical Study in the Saharan Lizard, <i>Uromastix acanthinurus</i> Bell, 1825	Barka-Dahane	Zohra
P044	Frontal connections of the medial posterior-parietal cortex in the macaque	Claudio	Galletti
P138	The medial posterior parietal area V6A and the control of arm actions in depth	Patrizia	Fattori
P112	Effect of Haemorrhage on the Catecholindolaminergic Activity of Neurohypophysis in Mal Wistar Rat, <i>Rattus Norvegicus</i> .	Nadia	Rouaiguia

2 October 2012, Tuesday / Neurotoxicity

Poster	Abstract Title	Author Name	Author Last Name
P045	Lead Toxicity And The Hypothalamic - Pituitary - Testicular Axis	Ait Hamadouche	Nadia
P046	Effects of early iron deficiency on catecholaminergic transporters in rat brain	Wael	Mohamed
P047	Behavioral and Neurocognitive Status of Iron Deficient Schoolchildren in Kenitra North West of Morocco	Youssef	Aboussaleh
P048	Neurohepatic toxicity of subacute manganese chloride exposure and potential chemoprotective effects of lycopene	Mohamed	Lebda
P049	Resveratrol attenuates aluminum-induced neuroinflammation: role of apurinic / apyrimidinic endonuclease1 (APE1) and cerebral oxidative stress	Amira	Zaky
P050	The Anti-Nociceptive Activitie and Toxicity of <i>Pistacia Lentiscus</i> of Morocco	Mohamed Yeslem	Ould Mohameden



P051	Potential Neuroprotective Effects Of Hesperidin On 3-Nitropropionic Acid-Induced Neurotoxicity In Rats	Mariane	Tadros
P052	Effects of Nicotine and alkaloids of tobacco plant on extracellular level of dopamine in subcortical regions and behavior	Khalki	Hanane
P053	Protective effect of Artemisia Absinthium L. extract on lead induced neurotoxicity disorder in rats.	Benyamina	Amel
P054	Effect of Acute and Repeated Nicotine Administration on the Electrical Activity of the Lateral Habenular Neurons in Rats	Giuseppe	Di Giovanni
P055	The potential role of Aretemisia absinthium extract after chronic lead toxicity in adult Wistar rats	Sansar	Wafa
P056	Persistence of lead neurotoxicity in male F2 generation Wistar rats: Behavioral and histological aspects	Azzaoui	Fatima-Zahra
P057	Aluminium alters the central nervous system in rat and human: epidemiological and experimental approaches	Wafaa	Laabbar
P058	Impact of exposure to Malathion on locomotor activity in F2 generation of male Wistar rat	Ngo K.	Pakome
P059	Protective effect of Zinc against cadmium cytotoxicity in adult hippocampal neurons of Meriones shawi	Mbarek	Sihem
P060	Toxic effects of Cadmium on retinal neurons of Meriones shawi- a bioindicator of cadmium pollution	Ben Chaouacha Chekir	Rafika
P061	Impact of Lead (Pb) on Cerebral Enzymes and Behavioral Changes in Young Wistar Rats	Missoun	Fatiha
P062	Physiological variations of monoamine tissue content during the reproductive cycle in Perna perna and their outcome in marine polluted sites.	Soumya	Benomar
P063	Beneficial Effects of Pectin against Lead Intoxication	Ouardia	Ouldali
P064	Innate immune responses to African trypanosome brain invasion	Krister	Kristensson
P065	Acute Lead Acetate Administration Affects Motor Coordination in Male Mice	Rabiu Abdussalam	Magaji
P066	Essential Heavy Metals Status in the Brain of Stressed Rats	Zarouk	Kamal
P067	Manganese neurotoxicity induces atypical parkinsonism in the rat	Bouabid	Safa

2 October 2012, Tuesday / Cognitive Sciences

Poster	Abstract Title	Author Name	Author Last Name
P068	Effects of Dates Extracts on Learning and Memory in Mice	Rebai	Ouafa
P069	A New Cognitive Therapeutic Program of Aphasic Impairments In Plurilingual Cases	Nacira	Zellal
P070	The effect of ecstasy in long memory and D1.D4 and D5 dopamine gene expression of hippocampus in male vistar rat	Simin	Mahaki Zadeh
P071	Number processing in Arabic and Hebrew bilinguals: Evidence for the distance and compatibility effect	Deia	Ganayim



P072	Dynamics of decision-related activity in prospective hippocampal place cells	Sidney	Wiener
P073	Study of changes in the neuronal networks responsible for memory in response to stress in different environmental conditions in Rat	Randa	Elshamy
P074	Cross-modal plasticity associated with arg3.1/arc gene expression within the occipital cortex of anophthalmic ZRDCT/An mutant mice following auditory or somatosensory stimulation	Dom	Miceli
P075	Spatial memory and learning deficit following prenatal exposure to fenugreek seeds in adolescent mice	Khalki	Loubna
P076	Right-hemispheric Dominance Of Dentate Granule Cell Activity After Spatial Exploration In Split-brain Mice But Not In Acallosal Mutant Mice	Hassan	Ahmed
P077	Deep brain stimulation of the fornix and entorhinal cortex in an experimental model of memory impairment	Sarah	Hescham
P078	Effects of Cold Exposure on Behavioral and Electrophysiological Parameters Related with Hippocampal Function in Rats	Hajar	El Marzouki
P079	Specific and regionally restricted correlations between monoamine tissue content in cerebral structures involved in cognition	Philippe	De Deurwaerdere
P080	A Comparison between Behavioral Effects of the Cholinergic Agonist PNU282987 in Mice Maintained in Enriched Environments and in Marlow Cages	Rosa	Redolat
P081	Assessment of neuro-cognitive impairments among patients with glioma brain tumors	Afsaneh	Zarghi
P082	Application of cognitive computerized test in assessment of Selective attention	Afsaneh	Zarghi
P083	Rehabilitation with Eye Movement Desensitization and Reprocessing	Afsaneh	Zarghi
P084	Acylation of Ghrelin Ameliorates Learning And Memory Impairments Induced By Transient Global Cerebral Ischemia In Rats	Göksun	Başaranlar Öncel
P085	Melatonin antidepressant effects are regulated by gonadectomy in Wistar rats: a possible implication of sex hormones.	El Mrabet	Fatima Zahra

2 October 2012, Tuesday / Neuroprotection

Poster	Abstract Title	Author Name	Author Last Name
P086	The neuropeptide PCAPA and the gliopeptide ODN prevent 6-hydroxydopamine-induced apoptosis of cerebellar granule neurons	Seyma	Bahdoudi
P087	Neurogenesis Induction by Grape Seed Extract and Its Neuroprotective Activity	Sally	Elkhatib
P088	An evaluation of neuroprotective effects of melatonin, against adverse effects of prenatal exposure to a non-steroidal anti-inflammatory drug, during the peripheral nerve development	İlknur	Keskin



P089	The Effects of Spermine on Neurogenesis and the Passive Avoidance Learning After Transient Cerebral Ischemia in the Chicks	Ebru	Ayrancı
P090	Protective effects of alpha lipoic-acid and n-acetyl cysteine against acrylamide-induced peripheric neuropathy	Meral	Yüksel
P091	Protective effects of Nigella sativa oil control astrogliosis and reduce Haloperidol-induced deficit in rats.	Tafheem	Malik

03 October 2012, Wednesday / Physiology

Poster	Abstract Title	Author Name	Author Last Name
P092	Assessment of the Hemodialysis Impact on Brain Plasticity Using BOLD-fMRI	Said	Boujraf
P093	Cord Blood Brain Derived Neurotrophic Factor: Diagnostic and Prognostic Marker in Fullterm Newborns with Perinatal Asphyxia	Shereen	Atef
P094	Simple Bone Cyst Treated With Aspiration And A Single Bone Marrow Injection. A Case Study.	Mohamed Ramadan	Abdelgawad
P095	Effect of Peripubertal Chronic Stress on Expression of Hypothalamic Kiss-1 mRNA and Histopathological changes of the reproductive tract in female rat.	Nisreen	Omar
P096	Pilot Study: Valproic Acid Effectiveness In Minimizing Incidence Of Seizures In Postoperative Pediatric Brain Tumor Patients	Sherif	Kamal
P097	Effect of long-term noise on food intake and endocrine response (ACTH) in Wistar rats.	Abdelouadoud	Abdelmalek
P098	Assessment of the Role of L-Carnitine in Improving Hepatic Encephalopathy Using MR Spectroscopy	Soliman	Hanan
P099	Type 2 Diabetes Affects M and S Cone Opsin Expression in The Diurnal Sand Rat <i>Psammomys obesus</i>	Saidi	Tounes
P100	Anterior repositioning splint versus laser therapy for treatment TMDs with anterior disc displacement	Mohamed	Elkhodary
P101	The Impact of Expression Profilin Using PCR Technology on Diagnostic and Prognostic Testing in Glioma	Marwa	Elshaer
P102	Modulation of excitatory postsynaptic currents in medium spiny neurons produced by the synaptic activation of cholinergic interneurons in rat nucleus accumbens.	Richard	Warren
P103	Different patterns of dystrophin gene expression in an Egyptian family suffering from muscular dystrophy	Ghada	Abdel Hadi
P104	Kisspeptin-10 Stimulates the Secretion of Testosterone in Prepubertal Male Cattle	Ahmed	Ezzat
P105	Alteration of Dopaminergic Innervation and Voluntary Movements After Long Period of Thirst in a Semi-desert Rodent, <i>Meriones shawi</i> : Behavioral and Immunohistochemical Studies.	Abdeljalil	Elgot



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P106	Chronic Hyperammonemia Induces Tonic Activation of NMDA Receptors in Cerebellum Leading to a Decrease Activity of Neuronal Nitric Oxide Synthase	Nisrin	EI Mili
P107	Nuclear Receptor Rev-Erb Alpha and retinal function	Ouafaa	Ait Hmyed
P108	Stroke Awareness in the Saudi Community: prompt public health measures must be implemented	Yousefmohammad	Professor
P109	Postnatal undernutrition and brain development: Behavioral and Neurochemical study.	Alamy	Meryem
P110	Dysfunction of voltage-gated K ⁺ Channels Kv1.1 in sciatic nerve causes spontaneous and stress-induced neuromuscular hyperexcitability	Mauro	Pessia
P111	Peripheral optic-flow involvement in the multisensory construction of the 3D percept in humans	Alexandra	Séverac Cauquil
P113	Forensically flies detect the nutritional value of corpses through neuro-chemoreceptive cells.	Nagwa	Surour
P114	Comparative study between Moroccan black propolis and French red propolis	Maryam	Mountassir
P115	The rat SCO responsiveness to prolonged water deprivation: Implication of Reissner's fiber and serotonin system	Chatoui	Hicham
P116	L-type channel modulation by CB1 receptors is mediated by PTX-sensitive G proteins and cAMP in hypothalamic immortalized GT1-7 cells	Hanaa	Hoddah
P117	The effect of early age heat conditioning and some feeding programs for heat-stressed broiler chicks on: (3). Immunophysiological Response.	Ahmed	Gouda
P118	Structure and Function of Neurosecretory Cells in the Bivalve Perna perna	Soumya	Benomar
P119	Desynchronized Rhythms and Morphological Changes of the Retina in Ageing: A Study in Crocidura russula	Aicha	Dekar-Madoui
P120	Neuronal nitric oxide synthase expression and activity in supraoptic and paraventricular nuclei of normal and Dp71 deficit mice	Benabdesselam	Roza
P121	Melanopsin expression is altered in a mouse model of diabetic retinopathy	Lahouaoui	Lahouaoui
P122	Effects of High-Fat Diet Induced Obesity on Peripheral Nerve Regeneration in Rats	Ebru	Ayrancı
P123	Neural- Morphological approach for the segmentation of microscopic color images: Provide help to the diagnosis of cancer	Moudache	Said
P124	Loss of analgesic effects of baclofen and galanine in neuropathic rats through interaction of GABAB and Gal1 signaling pathways	Bouali-Benazzouz	Rabia
P125	A Recognition Site for Somatostatin - 14 on the Gabaa Receptor Complex in Rat Mesencephalon?	Mohamed	Najimi



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P126	MRI analysis of the spinal cord by snakes guided by the gradient vector flow (GVF)	Cherfa	Assia
P127	Cortical excitability of Amyotrophic lateral sclerosis:transcranial magnetic stimulation study	Eman M.	Khedr
P128	Ameliorative effect of dexmedetomidine and its combination with tramadol or amitriptyline in rat model of neuropathic pain	Eman M.	Khedr
P129	Functional near-infrared spectroscopy (fNIRS) during vestibulo-ocular and postural challenges	Theodore	Huppert
P130	Effects of Obesity Induced by High-Fat Diet on Peripheral Nerve Regeneration in Rats	Ebru	Ayranci
P131	Functional Mapping of the Bladder Regulatory System: Communication between the Lower Urinary Tract and the Central Nervous System	Céline	Meriaux
P132	Involvement of serotonin and dopamine dysfunction in the pathophysiology of chronic hepatic encephalopathy: the restorative role of dehydroepiandrosterone sulfate	Omar	El Hiba
P133	In vivo brain repair? Electrical fields attract newborn brain cells	Lisa	Schönfeld
P134	Cell cycle aberrations in chordoma: a role for the p53- and RB1-pathway.	Youssef	Yakkioui
P135	Meaglencephaly &white matter disease in infancy and childhood	Iobna	Mansour
P136	Effects of Anti-Inflammatory Drugs on Rabies Encephalitis in Mice	Jahun	Balarabe
P137	Reconstruction of the Nigrostriatal Pathway by Intranigral Transplantation	Gaillard	Afsaneh



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Plenary Lecture 1

Subconsciousness and Basal Ganglia

Y. AGID (France)

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In the human brain, the basal ganglia are considered to play a role in the selection and shaping of sensori-motor programs and the automatic execution of learned motor plans. The anatomo-physiology of the basal ganglia is characterized by four main features: segregation of neuronal circuits ; convergence of informations ; close interrelationships with the cerebral cortex ; complex interactions between the different cortico-subcortico-cortical neuronal loops. They are thus composed not only of sensori-motor territories but also associative and limbic territories, considered to play a role in intellectual and emotional functions. It is, therefore, hypothesized that the basal ganglia are also involved in the control of intellectual and psychic functions underlyed by the associativo-limbic areas within these structures.

There are two ways to study the role of the basal ganglia in the control of intellectual and emotional functions in humans, whether in normal subjects or in patients : one way is to look at the activated or de-activated brain areas using functional neuroimaging in subjects who are confronted with various types of emotions. Another approach is to modify the activity of the basal ganglia neuronal circuits to see if one can reproduce these emotional and intellectual disturbances. Several examples using neuroimaging and deep brain stimulation will be provided to demonstrate that philogenetically ancient structures such as the basal ganglia are directly involved in the subconscious processing of emotions in normal subjects or of psychic disturbances in patients with neuropsychiatric disorders. But, what do we mean by subconsciousness?



Symposium 1

Oxytocin and Vasopressin Actions in the Central Nervous System: Control of Social and Feeding Behaviors.

Michel G. Desarménien (France)

The hypothalamic neuropeptides oxytocin and vasopressin are intensely studied for their roles in social behaviors and their involvement in neurological diseases associated with feeding troubles such as autism and Prader-Willi. In humans, OT and AVP participate in the regulation of emotional and social behaviours, trust, generosity, envy and gloating. In rodents, they contribute to reproductive behaviour, social memory, anxiety and aggression. This symposium will present recent advances in understanding the molecular and cellular mechanisms underlying the central actions of these peptides, approaches will cover the field from experimental approaches on animal models to human genetic studies.

Using OT receptor null mice as a model for autism, B. Chini will present evidence supporting an imbalance between excitation and inhibition in specific brain circuitries as a substrate of neuro-developmental and psychiatric diseases. Using *Magel2* deficient mice, a model for the Prader-Willi syndrome, F. Muscatelli will show that oxytocin supply may constitute a promising treatment of early feeding difficulties and social behaviour troubles. G. Levkowitz uses transgenic zebrafish lines as a valuable vertebrate model for understanding the patterning, specification, morphogenesis and subsequent function of oxytocin neurons at single cell resolution. M.G. Desarménien analyses the electrophysiological actions of vasopressin in the hippocampus, a brain area involved in memory and emotions. H. Gamrani will show how astrocytes and vasopressin neurons display a remarkable plasticity, allowing adaptation to difficult environmental conditions. R.P. Ebstein will describe a neurogenetic strategy unravelling the function of CD38, a coenzyme that mediates the central release of oxytocin, in human behavior.



The oxytocin receptor in sociability and cognitive flexibility: what do you learn from knockout mice models.

Bice Chini

There is a growing interest in oxytocin (OT) and vasopressin (AVP) two neuropeptides widely distributed in the central nervous system. In humans, OT and AVP participate in the regulation of emotional and social behaviours, including facial recognition and mind reading, trust, generosity, envy and gloating (Macdonald 2010 *Harv Rev Psychiatry*). In rodents, a number of studies have reported their activities in maternal care, pair bonding, sexual behaviour, social memory, anxiety and aggression, reward, learning and memory. In knockout mice models for OT/AVP receptors, an impairment in social recognition has been observed, strongly supporting the role of the OT/AVP system in the normal processing of socially relevant cues (Insel 2010 *Neuron*).

Within this line of research, we have recently characterized OT receptor null mice (*Oxtr*^{-/-}) for general health, sociability, social novelty, cognitive flexibility, aggression and seizure susceptibility. We confirmed that the *Oxtr*^{-/-} mice display impaired sociability and increased aggression and we reported two additional, highly relevant, phenotypic characteristics: (i) a resistance to change in a learned pattern of behavior, comparable to restricted interests and behavioral inflexibility, and (ii) an increased susceptibility to seizures. More importantly, we have shown that all these behavioral abnormalities are normalized upon the administration to adult mice of agonists that activate OT/AVP receptors (Sala 2011 *Biol. Psy*).

Very interestingly, the heterozygous *Oxtr*^{+/-} animals, which we found to express 50% of brain OTR, show impaired sociability and a preference for social novelty like *Oxtr*^{-/-} mice, but do not show impaired cognitive flexibility or increased aggression, thus indicating that the *Oxtr* acts as an haploinsufficient gene. The expression level of this gene may thus affect specific behaviors in a dose-dependent manner: social behavior is particularly sensitive to even a partial reduction in *Oxtr* gene expression, whereas the emergence of aggression and cognitive inflexibility requires complete inactivation of the *Oxtr* gene. It is widely recognized that multiple genes and environmental factors interact with each other to produce the different psychiatric phenotypes. Our data suggest that the expression level of the *Oxtr* gene may be among these factors.

Finally, we have shown that *Oxtr*^{-/-} hippocampal neurons display an increased ratio of glutamatergic versus GABAergic synapses (Sala 2011 *Biol. Psy*), an enhanced expression of excitatory, and a decreased expression of inhibitory synaptic proteins, and a parallel increased electrical activity of glutamatergic neurons. This strengthens the hypothesis of an imbalance between excitation and inhibition in specific brain circuitries as the underlying neuro-pathological substrate of neurodevelopmental and psychiatric conditions such as mental retardation, autism and schizophrenia. At present, the neural pathways selectively involved in the emergence of different psychiatric phenotypes are still largely unknown, making the *Oxtr* null mouse an instrumental model to investigate this crucial issue.



Vasopressin depresses long term potentiation in the mouse hippocampus.

Chafai M, Guillon G. and Michel G. Desarménien

Vasopressin, besides its well known endocrine actions, is now recognized as a neurotransmitter in the brain, implicated in the regulation of social and affective behavior. Several recent findings indicate an involvement of the V1a and V1b vasopressin receptors in stress and depression and point out the limbic system as a putative target. The V1a receptor has a wide distribution but the V1b receptor displays a particularly high expression in the CA2 pyramidal area of the hippocampus. Accordingly, we have focused on this region to determine the effect of vasopressin on synaptic activity.

Either whole-cell recording from the soma of pyramidal CA2 neurons or field recording along their dendrites in acute slices from C57Bl6 mice were performed. The synaptic activity in response to stimulation of the LIII entorhinal cortex (EC) afferents was measured. High frequency stimulation (HFS) induced a long term potentiation (LTP) of the excitatory post synaptic potential (EPSP) in the majority of pyramidal cells.

Bath application of vasopressin (1 min., 10-100 nM) transiently decreased the LTP-enhanced EPSP by 15%. Of interest is the fact that the vasopressin-induced EPSP reduction was observed only after LTP establishment. In addition, vasopressin had no effect on the EPSP recorded in CA1 pyramidal cells in response to stimulation of the Schaffer collaterals, even after establishment of a stable LTP.

Our data indicate that vasopressin, by decreasing specifically a synaptic input on CA2 pyramidal cells after LTP, can modulate the recently described (Chevalyere and Siegelbaum, Neuron, 2010) disynaptic pathway involving EC afferents, the CA2 pyramidal cells and their target CA1 neurons. The identity of the vasopressin receptors implicated in this response, and the cognitive consequences of this inhibition, will be the matter of our future studies.

C.M. supported by ANR.



CD38, Oxytocin and Social Cognition in Humans

Richard Ebstein

Social neuroscientists became interested in CD38 following the seminal study of the Higashida group demonstrating that this ectoenzyme mediates the central release of oxytocin (OT) in the brain. Although originally identified as a peptide important in parturition and lactation, accumulating evidence in the past two decades has now revealed OT to be the paramount social hormone in many mammals including our own species, *H. sapiens*. Not only is OT important in contributing to the workings of the social brain in normal subjects but increasing evidence suggests a role for this nonapeptide in disorders of social cognition especially autism. Core deficits in autism include dysfunctional social skills, communication and language that resonate with the recognized role of OT in modulating social cognition. More recently CD38 has also been examined for contributing not only to behavior in socially intact subjects but notably also in autism. Our studies have employed a neurogenetic strategy towards unraveling the function of CD38 in human behavior. The evidence will be presented showing provisional association between CD38 SNPs and autism but notably also in normal human social behavior such as parent-infant bonding. We have furthermore shown reduced CD38 transcription in lymphoblastoid cells (LBC) from autistic patients and that all-trans retinoic acid (ATRA) has an upmodulatory potential on LBC derived from ASD patients as well as from their parents. Intriguingly, CD38 mRNA levels in these LBC is positively correlated with social skills indexed by the Vineland Adaptive Behavioral Scales. In summary, CD38 along with OT are important players in the neurochemical pathways facilitating human social behavior and are potentially important pharmacological targets for therapeutic intervention in diseases of social cognition.



Cellular plasticity in the supraoptic and paraventricular nuclei after prolonged dehydration and rehydration in the desert rodent *Meriones Shawi*: Vasopressin and GFAP immunohistochemical study

Halima Gamrani and Abdeljalil El Got

Supraoptic (SON) and paraventricular (PVN) nuclei are part of the hypothalamic–neurohypophysial system, they constitute the main source for vasopressin and they represent also obvious examples of activity-dependent neuroglial plasticity. Certain physiological conditions such as dehydration are accompanied by a structural remodeling of the neurons, their synaptic inputs and their surrounding glia. In the present work, an adult *Meriones Shawi* (a rodent adapted to desert life) is used as an animal model. Using GFAP and vasopressin expressions as indicators successively of astrocytes and neuronal activations, the effect of a prolonged episode of water deprivation on the SON and PVN, hypothalamus nuclei were examined. In order to evaluate the reversibility of the neuro-astrocytic plasticity in SON and PVN, prolonged episode of water deprivation followed by episode of rehydration were also examined. We studied the immunoreactivity of GFAP and vasopressin in various hydration states (total deprivation of drinking water for 1, 2 and 10 months compared to hydrated animals). Prolonged dehydration produces an important decrease of GFAP immunoreactivity in both SON and PVN after 1, 2 and 10 months of water restriction. This decrease is accompanied by increased vasopressin immunoreactivity following the same periods of water deprivation. These findings may explain a real communication between vasopressin neurons and their surrounding astrocytes, thus the retraction of astrocytes and their processes is accompanied by an enhancement of vasopressin neuron density and their projecting fibers in response to this osmotic stress situation. Conversely, rehydration of animals shows a reversible phenomenon leading a return of vasopressin and GFAP immunoreactivities to the control level. These results show that both astrocytes and vasopressin neurons display a remarkable structural and physiological plasticity, allowing to *M. Shawi*, a great ability to support the hostile conditions in dry environment.



Studying neurohypophyseal neurons in the zebrafish

Amos Gutnick, Janna Blechman and Gil Levkowitz.

Oxytocin-producing neurons are part of a major neuroendocrine interface between axons and the bloodstream through which hypothalamic neuropeptides traverse to control peripheral physiology. The activities of oxytocin in the central nervous system are important for the regulation of stress, feeding and social behaviors. The ontogenesis and physiological activities of these neurons are largely conserved among vertebrates. However, the developmental mechanisms underlying the morphogenesis of the neurohypophysis are poorly understood. The optically transparent zebrafish embryo offers a unique tool to study the development and function of the HNS *in vivo* without the need for surgical intervention. We developed a transgenic system in which both hypothalamic axons and neurohypophyseal vasculature can be analyzed *in vivo* allowing 3D visualization of the zebrafish preoptico-hypophyseal axonal tract analogous to the supraoptico-hypophyseal tract in mammals. Our studies have established that zebrafish is a valuable vertebrate model for understanding the patterning, specification, morphogenesis and subsequent function of oxytocin neurons. I will present recent data concerning the cellular organization of the zebrafish HNS as well as the dynamic processes and key signaling events that contribute to formation of the HNS neuro-vascular interface.

Gutnick A. and G. Levkowitz. 2012. The neurohypophysis – fishing for new insights. *J. Neuroendo.* 24(6):973-974.

Blechman J., A. Gutnick, L. Amir-Zilberstein, S. Ben-Dor and G. Levkowitz. 2011. The metabolic regulator PGC-1 α directly controls the expression of the hypothalamic neuropeptide oxytocin. *J. Neurosci.* 31(42):14835-14840.

Gutnick, A., J. Blechman, J. Kaslin, L. Herwig, H-G. Belting, M. Affolter, J.L. Bonkowsky and G. Levkowitz. 2011. The hypothalamic neuropeptide oxytocin is required for formation of the neuro-vascular interface of the pituitary. *Dev. Cell* 21:642–654.



Oxytocin, a crucial role at birth in the control of feeding behavior; involvement in the Prader-Willi syndrome.

Françoise Muscatelli

Prader-Willi syndrome (PWS) is a complex neurogenetic disorder caused by the alteration of several imprinted contiguous genes including *MAGEL2*. PWS presents with various clinical manifestations, including poor suckling behaviour and feeding problems in neonates. Later, infants develop hyperphagia leading to severe obesity, learning difficulties, hypogonadism, and behaviour problems. Hypothalamic defects have been proposed but the pathophysiological mechanisms remain poorly understood. Previously, we have shown that *Magel2* deficient mouse had an altered onset of suckling activity and subsequent impaired feeding, similar to PW newborns, resulting in 50% neonatal mortality. The hypothalamus of *Magel2* mutant neonates showed a significant reduction in oxytocin content, and a single injection of oxytocin just after birth rescued the phenotype of *Magel2* mutant pups, allowing all of them to survive. In addition, the 50% of surviving *Magel2* deficient mice not treated with oxytocin at birth present, in adulthood, several behavioural disturbances, including altered social interaction. Again, acute oxytocin treatment rescues a normal level of social interaction in these mice. Interestingly, similar results have been obtained in PW patients following an intranasal administration of oxytocin. We propose that oxytocin supply might constitute a promising avenue for the treatment of early feeding difficulties and social behaviour troubles in PW patients.



Symposium 2

Environmental enrichment : a useful paradigm to study brain functioning in physiological and pathological conditions

Marcello Solinas (Poitiers, France) and Claire Rampon (Toulouse, France)

This symposium will feature the most recent findings showing how environmental enrichment may be used to study brain functioning in both, physiological and pathological conditions. Internationally recognized researchers will present their work on the anxiolytic effects of environmental enrichment, with a special emphasis on the signaling pathways involved (**A. Chen, Israel**) and its consequences on emotional forms of memory (**G. Segovia, Spain**). The beneficial effects exerted by environmental enrichment on brain pathologies will then be illustrated regarding 1) the vulnerability to drug addiction (**M. Solinas, France**) and 2) its influence on the development of Alzheimer's disease (**C. Rampon, France**).



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The Anxiolytic Effect of Environmental Enrichment

Alon Chen, Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel

Environmental Enrichment (EE) is known to have an anxiolytic effect in several animal models; however, the molecular mechanisms underlying these behavioral changes are not understood. We recently demonstrated that the anxiolytic effect of EE is associated with alterations in the corticotropin-releasing factor receptor type 1 (CRFR1) expression levels in the limbic system. We found that the decrease in anxiety-like behavior following housing in enriched conditions was associated with very low levels of CRFR1 mRNA expression in the basolateral amygdala of C57BL/6 mice. We further demonstrated using a lentiviral-based system of RNA interference, that knockdown of CRFR1 mRNA expression in the basolateral amygdala induces a significant decrease in anxiety levels, similar to those achieved by EE nurture. Our data strongly suggest that reduced expression of CRFR1 mRNA levels in the basolateral amygdala mediates the effect of EE on anxiety-like behavior.



Environmental Enrichment as an Experimental Paradigm to Promote Stress Inoculation-Induced Resilience

Gregorio Segovia, Department of Physiology, Faculty of Medicine, Universidad Complutense, Madrid, Spain

Environmental enrichment (EE) is an experimental setting in which the animals are housed in conditions that potentiate social interactions and sensory and motor stimulation. It is a condition which exposes the animal to constant mild stressors (physical environment changes and enhanced social interactions). Therefore, it could be viewed as an experimental paradigm to promote stress inoculation-induced resilience or “stress immunization”. Indeed, animals housed in an enriched environment show an attenuation of the behavioural and endocrine responses evoked by acute psychogenic stressors. We have reported that the increases in the concentrations of dopamine and acetylcholine, and also corticosterone, in the prefrontal cortex in response to a moderate stressor are reduced by housing the animals in an enriched environment. These results suggest that EE reduces the reactivity to stress of the dopaminergic and cholinergic systems of the prefrontal cortex, an area involved in the regulation of the response to stress. Behaviourally, enriched animals show a faster habituation to a novel environment than control animals. We have also shown that the disruptive effects of acute stress on working memory performance (a cognitive function dependent on the integrity of the prefrontal cortex) tend to be attenuated in animals housed in enriched conditions. Moreover, enriched animals show a reduced memory of aversive events in the passive avoidance paradigm. We have recently proposed that these findings may be interpreted as enriched rats coping better with stressful situations. We have further hypothesized that the activation of the ventral medial prefrontal cortex is involved in this effect of EE. Understanding the effects of EE on the responses to stressors and its putative neurobiological mechanisms would help to develop new tools for the treatment of post-traumatic stress disorder.



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Environmental Enrichment and Drug Addiction Revised

Marcello Solinas

INSERM U-1084, Experimental and Clinical Neurosciences Laboratory; Poitiers-FRANCE.

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In the last years, accumulating evidence has demonstrated that exposure to environmental enrichment (EE) has positive effects on drug addiction. In fact, animals exposed to EE are less vulnerable than animals reared in standard environments (SE) to develop addiction-related behaviors. In addition, exposing already « addicted » animals to EE during periods of withdrawal dramatically reduces the risks of relapse. These findings highlight the interest of EE for the treatment of psychiatric diseases and, from a translational point of view, they suggest that positive environmental conditions may be central to prevent and treat drug addiction. On the other hand, recent studies in our lab found that the effects of EE on drug addiction are complex and may not be always beneficial. In fact, in a first study, we found that exposure to EE during early stages of life if discontinued could produce a depressive-like phenotype and an increase in the vulnerability to cocaine addiction. Furthermore, in a second study, we found that the effects of EE on relapse to cocaine seeking only last as long as EE is provided and rapidly vanish when EE is discontinued. The implications of these findings are discussed in light of the framework that we have recently proposed that considers EE as functional opposite of stress.



How Environmental Enrichment Delays the Progression of Alzheimer's Disease in Transgenic Mice Models

Claire rampon,

Université de Toulouse; UPS; Centre de Recherches sur la Cognition Animale; 118 route de Narbonne, F-31062 Toulouse Cedex 4, France. CNRS; Centre de Recherches sur la Cognition Animale; F-31062 Toulouse, France

Levels of educational and occupational attainment, as components of cognitive reserve, may modify the relationship between the pathological hallmarks and cognition in Alzheimer's disease (AD). We examined whether exposure of Tg2576 transgenic mouse model of AD to environmental enrichment (EE) at a specific period during the amyloidogenic process favored the establishment of a cognitive reserve. We found that exposure to a EE during early adulthood of Tg2576 mice - before amyloidogenesis has started - reduced the severity of AD-related cognitive deficits more efficiently than exposure later in life, when the pathology is already present. Interestingly, early-life exposure to EE, while slightly reducing forebrain surface covered by amyloid plaques, did not significantly impact aberrant inhibitory remodeling in the hippocampus of Tg2576 mice. Thus, transient early-life exposure to EE exerts long-lasting protection against cognitive impairment during AD pathology. In addition, our data define the existence of a specific lifetime frame during which stimulatory activity most efficiently builds a cognitive reserve, limiting AD progression and favoring successful aging.



Symposium 3

Endocannabinoids and the Control of Memory and Emotions

Liano Fattore, Patrizia Campolongo

The endocannabinoid system is a unique neuromodulatory system in mammalian physiology. It consists of cannabinoid receptors, their endogenous lipid ligands (endocannabinoids) and the enzymatic machinery for their synthesis and degradation. In the brain, endocannabinoids regulate ion channel activity and neurotransmitter release and thereby contribute to various aspects of brain function, including memory and emotions.

This symposium will bring together leading basic and clinical experts in the field to provide a deep overview of the physiological and pathological role of the endocannabinoid system in both cognitive and emotional processes, and of its role in the interplay between memory and emotions.



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The Endocannabinoid System And The Regulation Of Memory For Emotionally Arousing Experiences

Patrizia Campolongo

Department of Physiology and Pharmacology, University of Rome “La Sapienza”, Rome, Italy

The activation of neuromodulatory systems affecting the amygdala and its projections to other brain regions, plays a key role in enabling emotionally significant experiences to be well remembered. Although it is vital for a human being to be able to remember emotionally arousing experiences, the efficient encoding of emotional memories can, in certain conditions, become maladaptive. Indeed, severe stress often turns emotional memories into a source of chronic anxiety, which may lead to the development of stress related disorders. In this talk I will present the results of studies that addressed the effects induced by the manipulation of the endocannabinoid system in the modulation of memory for emotional experiences. I will focus on the role of the endocannabinoid system in the modulation of memory consolidation for emotionally arousing experiences, showing how this system interacts with other neuro-modulatory systems in the regulation of such processes.



The Role Of The Endocannabinoid System In Extinction Learning

Beat Lutz

Institute of Physiological Chemistry, University Medical Center of the Johannes Gutenberg University, Mainz, Germany

The endocannabinoid system (ECS) is known to modulate processes such as feeding behaviour, stress responses, seizure susceptibility, anxiety, and extinction of aversive memories. The available pharmacological and genetic approaches have allowed establishing the *necessary* role of the ECS, but have not provided evidence for its *sufficient* role. To be able to investigate the sufficient role of cannabinoid type 1 (CB1) receptor signalling, we applied the Cre/loxP system to generate a mouse line with a silenced CB1 receptor as a default state (Stop-CB1), but with the ability to rescue the CB1 receptor in a region- and cell type-specific manner.

A loxP-flanked stop cassette in the CB1 receptor gene locus represses CB1 receptor presence throughout the entire body, including the brain. By crossing this mouse line with a mouse line ubiquitously expressing Cre recombinase (Ella-Cre), the stop cassette is excised and the CB1 receptor rescued at its endogenous sites and levels. Complete rescue of CB1 receptor protein and functionality was confirmed by histological analysis, electrophysiology, and behavioural paradigms. To address the importance of intact CB1 receptor signalling in distinct neuronal subpopulations, the Stop-CB1 line was crossed with Cre-expressing mouse lines to rescue the CB1 receptor selectively in cortical glutamatergic (Glu-CB1-RS) or forebrain GABAergic (GABA-CB1-RS) neurons.

Depending on the behavioural paradigm chosen, a partial rescue of the Stop-CB1 phenotype was observed in Glu-CB1-RS, GABA-CB1-RS, or both. The presence of CB1 receptor on either glutamatergic or GABAergic neurons appeared to be sufficient for a partial rescue of the anxiogenic phenotype of Stop-CB1 mice, whereas to a large extent a rescue of food intake after starvation and of protection against kainic acid-induced seizures was only found in Glu-CB1-RS mice. Glu-CB1-RS mice did not show a rescue of the impaired extinction after cued fear learning, whereas GABA-CB1-RS animals seemed to differ in the acquisition of fear memories. These first results indicate that there may be another dimension to the ECS that can only be unravelled when not only the necessity of proper ECS signalling in different brain regions and cell populations is investigated, but when also the sufficiency of the different components is taken into account.



Homeostatic Role Of The Endocannabinoid System And Consequences Of Its Dysregulation On Emotional States

Maria-Paz Viveros

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The endocannabinoid system (ECS) plays a crucial role in brain development, emotional homeostasis and motivational status. Our studies are focussed on these aspects during critical developmental periods. We have analyzed short and long-term psychophysiological consequences of adolescent exposure to cannabinoids as well as its interactions with a model of neonatal stress, maternal deprivation, and with other drugs of abuse. We have carried out multidisciplinary analyses from molecular indices of brain plasticity to different aspects of cognitive function as well as stress and anxiety responses in different behavioral tests. The results of these studies, with a special emphasis in the ECS, are particularly relevant within the context of emotional responses and motivations linked to polydrug abuse and the impact of early life stressful events as factors of vulnerability for the development of neuropsychiatric disorders. As for our work on adolescence animal models, we have shown sex-dependent effects of acute and chronic cannabinoid administration on anxiety related behaviour, cognitive function and metabolic parameters as well as sex-dependent functional interactions of cannabinoids with nicotine and MDMA ("ecstasy"), among other drugs. We have revealed that a single prolonged episode of maternal deprivation (24 hours at PND 9) induces short- and long-term sex-dependent psychoneuroendocrine effects, including alterations in the developing brain affecting neurons, glia, major synaptic plasticity players, CB₁ and CB₂ cannabinoid receptors and endocannabinoid levels. On the basis of our results we propose that this model provides a useful tool to further address the neurodevelopmental theory proposed for certain psychiatric disorders, as many of the developmental alterations found in these animals might well be related to their altered behaviour later in life. In addition, this animal model may contribute to clarify the involvement of the ECS in brain development and the consequences of its dysregulation in early developmental periods. Our work highlights the importance of analysing sexual dimorphisms in experimental studies involving not only adult but also immature animals. This strategy may shed light on a possible neurodevelopmental basis for sex differences observed in several psychiatric diseases, as well as on the possibly influence of sex on the modulatory role of the endocannabinoid system throughout neurodevelopment. Finally, our studies about the consequences of cannabinoids administration on anxiety responses have contributed to explain the mechanisms underlying the observed biphasic effects. In particular, to clarify the role of CB1 receptor in this biphasic effect, we used two different conditional CB1 receptor knockout (KO) mouse lines, GABA-CB1-KO (CB1 receptor inactivation in forebrain GABAergic neurons) and Glu-CB1-KO (CB1 receptor inactivation in cortical glutamatergic neurons).



V. Sex-Dependent Differences In The Effects Of Cannabinoids On The Emotional Brain

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Sex dependent differences have been frequently observed in the biological and behavioural effects of substances of abuse, including cannabis. We recently demonstrated that self-administration of the CB1 receptor (CB1R) agonist WIN 55,212-2 is more rapidly acquired, more robustly maintained, and more slowly extinguished in female Lister Hooded rats than in their male counterparts. A follow-up study revealed that also drug- and cue-induced reinstatement of drug-seeking after extinction is stronger in female than in male rats, with ovariectomy typically dampening responding, thus confirming the pivotal role of sex and oestrous cycle in modulating cannabinoid-taking and seeking behaviours. In this study, we investigated the influences of sex in the regulation of CB1R density and function, measured by quantitative autoradiographic binding studies with [³H]CP55940 and CP55940-stimulated [³⁵S]GTPγS binding autoradiography, respectively, in selected brain areas of male and intact female rats. Moreover, since oestrogen has been recently found to affect limbic cannabinoid receptor binding, we also evaluated CB1R density and functionality in brain regions involved in emotional and cognitive functions, i.e. prefrontal cortex (Cg1 and Cg3), caudate-putamen, nucleus accumbens (core and shell), amygdala (Amy) and hippocampus, in ovariectomised female rats (OVX), and in OVX rats pre-treated with estradiol (OVX-E). Our results revealed that in the Amy, cycling females showed a significant decreased CB1R density when compared to males. This group also showed lower CB1R binding site density in Cg1 and Cg3, although the differences did not reach statistical significance. Conversely, OVX group showed higher CB1R density than cycling females in the Cg1, Cg3, and Amy, a difference that appears to be estradiol-dependent since it is no more evident in the OVX-E group. Moreover, within the Amy, in parallel with the decrease in CB1R density, CP55940-stimulated [³⁵S]GTPγS binding was significantly lower in OVX-E female rats relative to both males and cycling females, while no difference was observed either in CB1R densities or function in any of the other brain areas analyzed. Finally, sex and estradiol were found to also affect motor activity, sensorimotor gating and sociability in rats tested in the open field, in the pre-pulse inhibition and social interaction tasks, respectively. In conclusion, by demonstrating that both sex and estradiol affect CB1R density and activity in certain limbic regions, our findings provide a putative biochemical mechanism underlying the reported sex differences in cannabinoid-induced behavioural effects.



Symposium 4

Basal Ganglia Physiology: From Motor to Limbic Function

Izhar Bar-Gad (Israel) & Thomas Boraud (France)

The basal ganglia are a group of interconnected nuclei which integrate information from multiple cortical regions, process it, and convey it back to frontal cortical regions and to brainstem nuclei. Historically, studies of the basal ganglia have focused on the processing of motor information in both the normal state and in different hypo- and hyper-kinetic disorders, most notably Parkinson's disease. However, the basal ganglia receive input from multiple cortical areas conveying not only motor but also associative/executive and limbic information. Thus, current basal ganglia research encompasses also non-motor function in normal behavior and in neurological and psychiatric disorders associated with executive or limbic function. In this symposium we will present recent findings regarding the physiological basis of basal ganglia involvement in normal and pathological behavior. The lectures will encompass a wide range of behaviors and disorders associated with the basal ganglia ranging from the motor to the limbic. The presentations will highlight both the common underlying properties of information processing along the cortico-basal ganglia pathway and the unique neuronal activity underlying different disorders.



The Subthalamic Nucleus and Midbrain Serotonergic Neurons: A Novel Motor-Limbic Interface

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Movement disability in advanced Parkinson's disease (PD) can be treated by high frequency stimulation (HFS) of the subthalamic nucleus (STN) but some patients experience psychiatric side-effects including depression, which is strongly linked to decreases in 5-hydroxytryptamine (5-HT). Our recent experiments show that in rats, HFS of the STN both inhibits the firing of 5-HT (5-hydroxytryptamine; serotonin) neurons in the dorsal raphe nucleus (DRN) and elicits 5-HT-dependent behavioural effects. Here, we investigated the effect of STN HFS on extracellular 5-HT in brain regions of anaesthetized and freely moving rats as measured with microdialysis. Parallel *in vivo* electrophysiological experiments allowed a correlation of changes in extracellular 5-HT with the firing of 5-HT neurons. STN HFS decreased (by up to 25%) extracellular levels of 5-HT in both striatum and medial prefrontal cortex of anaesthetized rats. STN HFS also decreased extracellular 5-HT in the medial prefrontal cortex of freely moving rats. As with changes in extracellular 5-HT, in anaesthetized rats STN HFS evoked a decrease in the *in vivo* firing of midbrain raphe 5-HT neurons that also persisted after cessation of stimulation. To investigate the neural circuitry underpinning these effects, we investigated markers of neuronal activity in the DRN as well as DRN input regions. HFS of the STN increased c-Fos immunoreactivity in the DRN, and decreased cytochrome C oxidase activity in this region. The increase in c-Fos immunoreactivity occurred in DRN neurons immunopositive for the GABA marker parvalbumin. HFS of the STN also increased the number of c-Fos immunoreactive cells in the lateral habenula nucleus, medial prefrontal cortex but not significantly in the substantia nigra. Collectively, these findings support a role for circuitry involving DRN neurons, as well as DRN afferents from the lateral habenula nucleus and medial prefrontal cortex, in the limbic effects of HFS of the STN.



Noradrenergic Control of the Subthalamic Nucleus

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Université Bordeaux Segalen, Neurodegenerative diseases Institute, CNRS UMR5293, Bordeaux, France)

The subthalamic nucleus (STN) plays a key role in the pathophysiology of Parkinson's disease. This was demonstrated by the fact that STN neurons express more bursts in animal models of the disease and by the ability of STN inactivation to alleviate motor deficits. However, the origin of the bursts and the causal link between STN bursts and motor deficits remain unknown. The present study aimed to investigate the role of noradrenergic receptor modulation on the firing activity of STN neurons and the impact of this modulation on locomotor activity in sham and 6-hydroxydopamine-lesioned rats. Using selective agonists and antagonists of α 1- and α 2-adrenergic receptors (AR), we show that local infusion of clonidine, an α 2-AR agonist, induced a switch from tonic to bursty pattern without changing the firing rate. This change in the pattern was prevented by the local infusion of idazoxan, an α 2-AR antagonist. Furthermore, clonidine injection into the STN reduced locomotor activity in sham and 6-hydroxydopamine-lesioned rats. In contrast, local injection of phenylephrine, an α 1-AR agonist, increased the firing rate of STN neurons without changing the firing pattern. In parallel, phenylephrine did not change locomotor activity. This is the first evidence showing the implication of α 1-ARs in the modulation of firing rate and α 2-ARs in the modulation of the firing pattern of STN neurons. Furthermore, our data provide also evidence that activation of the STN α 2-ARs plays a key role in the genesis of subthalamic burst activity, which may be at the origin of motor deficits.



Right Ventral Subthalamic Nucleus Responds to Emotional Voices in Parkinson's Patients

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Emotional and behavioral changes following deep brain stimulation (DBS) were observed in Parkinson's disease (PD) patients and provide an evidence for a possible limbic function of the subthalamic nucleus (STN). To better understand the limbic roles of the STN we have played emotional voices during microelectrode recording (MER) of the STN on PD patients that underwent DBS surgery. The right ventro-medial non-oscillatory region (VMNR) of the STN was associated with larger responses to the emotional stimulations in comparison to left VMNR and both dorso-lateral oscillatory regions (DLOR) of the STN. Therefore, the left DLOR may be favored for treatment of motor symptoms with minimal psychiatric side effects for advanced PD. The right VMNR should be further studied as it may be related to emotional symptoms of PD and other mental-psychiatric disorders. Adjusted stimulation of patients' right VMNR may be used to relieve their emotional symptoms in the future.



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Role of the Striatum in Spatial Learning: A Behavioural and Electrophysiological Approach in the Monkey

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Classical theory about spatial learning infers that the hippocampal system supports allocentric (or place-based) strategies while the basal ganglia are related to cue-based and direction-based strategies. We recently proposed an alternative theory that implies that different territories of the basal ganglia are involved in the different processes of spatial learning. We have developed a task that is adapted from the classical X-maze of Packard & McGaugh (1996) that showed the dissociation of learning between the dorsal basal ganglia and the hippocampus. We have trained two female rhesus macaque monkeys to navigate the maze in a powered wheelchair. We showed that, in this environment, the monkey can use the three competing strategies (allocentric, Cue-based and Direction-based). Using a pharmacological approach, we showed that local inhibition of the shell of the nucleus accumbens induces a strong decrease of the place strategy and the inhibition of the dorsomedial striatum reduces the direction strategy. We are still investigating the striatal territory underlying the cue strategy.



Tic-related Neuronal Activity in the Cortico-Basal Ganglia Loop

Maya Bronfeld, Michal Israelashvili, and **Izhar Bar-Gad**, Gonda brain research, Bar Ilan University, Ramat Gan, Israel

Motor tics are brief, repetitive, involuntary muscle contractions that interfere with ongoing behavior and are a symptom of several neural disorders, most notably Tourette syndrome. While the pathophysiology of tics is still largely unknown, multiple lines of evidence suggest the involvement of the cortico-basal ganglia loop in tic disorders, specifically the striatum. Theoretical models hypothesized an abnormal “action selection” process leading to tic generation in which an aberrant focus of striatal activation causes unwanted inhibition of a group of basal ganglia output neurons, which, in turn, disinhibit a group of cortical neurons and thus leads to the expression of a tic. We transiently induced motor tics in freely behaving monkeys and rats by local microinjections of GABA_A antagonists into the striatum. Multi-electrode recordings following the injection reveal tic related activity throughout the cortico-basal ganglia loop. We characterized the temporal and spatial distribution of tic-related activity in each area and their relation to the spatial and temporal properties of the tic manifestation. Our results indicate that rather than selecting and initiating the abnormal movement the tic-related basal ganglia signal may have a more complex role in the modulation and control of tics.



Symposium 5

The circadian and seasonal network: a combination of clocks, synchronising inputs and outputs

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A network comprised of circadian clocks, synchronizing inputs, various clock outputs and multiple peripheral self-sustained oscillators is responsible for daily and seasonal rhythmicity. In mammals, the focal point is a master clock within the suprachiasmatic nucleus (SCN). Self-sustained circadian oscillators are also present in numerous tissues. To day, all the identified peripheral oscillators or functions depend directly or indirectly on the SCN for their temporal expression. Therefore the SCN clock which has not only the capacity to build a circadian message (which is itself synchronized to 24h by the Light/dark cycle throughout the retina), but can also distribute this signal to other structures. It is thus the complex interactions of neural, hormonal and behavioural outputs from the SCN that drive the circadian expression of events within the body and further the seasonal ones.

In this context, the symposium will present an overview and novel data on key mechanisms involved in this hierarchically well organized circadian and seasonal network



Retinal Circadian Clocks and Non-visual Photoreceptors: Light Input to the Circadian System Ouria

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The mammalian retina contains an endogenous pacemaker that regulates retinal physiology and adjusts daily the temporal phase of the central circadian timing system with environmental time. This entrainment process involves rods, cones and melanopsin-expressing retinal ganglion cells. In contrast with non mammalian retinas, in which the clock has been identified in photoreceptors, the location of the retinal circadian clock in mammals is still controversial. In addition, the impact of specific photoreceptor degeneration on the molecular machinery of the endogenous retinal clock is unknown.

The experimental strategy is based on the isolation of the retina in two separate compartments: inner (inner nuclear and ganglion cell layers) and outer (cones and rods) using laser microdissection and real time RT-PCR. We investigate clock (*mPer1-2-3*, *mClock*, *mBmal1*, *mCry1-2*, *mReverb*) and clock-controlled gene (*mDbp*, *mE4bp4*) expression in these two retinal compartments during the 24 hr cycle at six circadian times in the wild-type mouse. We next evaluated the impact of the absence of melanopsin on the endogenous functioning of the retinal clock by using *Opn4*^{-/-} transgenic mouse model.

We find that 1) all core clock genes are expressed in both inner and outer regions of the wild-type retina. All these genes present a significant circadian rhythm (excepting *Per3*) in the photoreceptor layer whereas in the inner retina, only *Per1-2*, *Clock*, *Ror* are rhythmic. For all genes significantly cycling in both inner and outer compartments, their expressions are not in phase suggesting that the master clock is localized in photoreceptor cells 2) The absence of melanopsin leads to a dysfunction of the clock mechanism mostly in the outer retina, characterized by a loss of circadian clock gene expression. Because circadian organization is widespread in the retina and controls fundamental pathways, disruption of circadian organization in the retina could potentially have a major impact on retinal functions and on SCN functioning.



The sympathetic system as an output of the central clock. It's role in metabolic rhythms.

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Accumulating evidence indicates an association between the development of obesity and type 2 diabetes at the one hand and disturbances in circadian control at the other hand. Disruption of circadian rhythms can be caused by external factors such as shift work and jet lag, but also by pathophysiological factors including aging, depression and sleep disorders. It remains unclear, however, what the precise contribution of the suprachiasmatic nucleus (SCN), i.e., the central circadian pacemaker, is in the regulation of glucose and energy homeostasis.

The SCN uses its projections to neuro-endocrine and pre-autonomic neurons in the hypothalamus to control daily hormone rhythms, e.g. adrenal corticosterone, luteinizing hormone (LH) and pineal melatonin release. The SCN also plays an essential role in maintaining daily blood glucose concentrations. Indeed both glucose production and glucose uptake show a pronounced daily rhythm, with increased glucose uptake as well as glucose production at the time of awakening. Using local intra-hypothalamic administration of GABA and glutamate receptor (ant)agonists we previously demonstrated how changes in autonomic nervous system activity contribute to the daily control of plasma glucose and insulin concentrations. More recent studies evidenced an important role for VIP, but not vasopressin, as an SCN output in the control of hepatic glucose production. In addition, hypothalamic orexin and oxytocin neurons turned out to be important targets for the SCN to transmit its glucoregulatory effects onto the autonomic nervous system.

Finally, using localized bilateral infusions of the sodium channel blocker tetrodotoxin (TTX) in the rat SCN, to silence SCN neuronal activity, combined with euglycemic hyperinsulinemic clamp studies we found that an acute reduction of SCN output resulted in hepatic insulin resistance as well as increased peripheral glucose uptake. Together these results indicate that a withdrawal of SCN neuronal activity at the end of the light period increases activity of the orexin neurons which, in turn, results in an increased hepatic glucose production as well as an increased peripheral glucose tolerance.



The role of the SCN-endocrine outputs in the circadian and seasonal network.

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Disorders of rhythmicity are characteristic of, and may underlie, a variety of troubles. Sleep and circadian rhythms are often disrupted in neurological disorders and increasing evidence indicates that alterations in the sleep/wake cycle accompany (or may be responsible for) many types of neurological disorders. To develop strategies to treat, prevent or delay such disturbances is a new challenge for medicine. The diurnal organisation of living organisms depends on a circadian network comprising circadian clocks, synchronizing inputs, various clock outputs as well as multiple peripheral self-sustained oscillators. In mammals, the focal point of this system is a master circadian clock within the suprachiasmatic nuclei (SCN). Self-sustained circadian oscillators are also present in numerous tissues. Peripheral oscillators (PO) share similar molecular mechanisms to generate rhythms like the central circadian clock, but they are distinct at the functional level. Even though PO in tissue culture or SCN-lesioned rodents can behave independently of SCN outputs, in intact animals all the identified synchronisers of PO (glucocorticoids, feeding behaviour) depend on the SCN for their temporal expression. The circadian clock thus has not only the capacity to build a circadian message, but can also distribute this signal to other structures. It is thus the complex interaction of neural, hormonal and behavioural outputs from the SCN that drive the circadian expression of events. One important question is thus the identification of the outputs pathways used by the circadian clock. To date, it is known that the SCN conveys its “timing” signal by using different tools: neural connections, hormonal cues (e.g. corticosterone, melatonin) and rhythmic behaviour cues. It is in this context of a complex and partially redundant system that we will analyse the role of the hormonal cues.

Melatonin (MEL) as well as corticosterone (CORT), are efferent hormonal outputs of the circadian clock. The clock may use MEL or CORT signals to convey the circadian message to any system that can “read” it, i.e. to any structure/organ possessing MEL or CORT receptors. Potential sites for MEL binding are very numerous since more than 130 structures within the brain and periphery have been identified. Sites for the action of CORT are even more numerous. In the context of the multi-oscillatory nature of the circadian system two modes of action have to be considered: 1) the hormone signal directly drives a rhythm; or 2) the hormone signal entrains PO.



Long-Term Consequences of immobilization stress

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Adult mammals secrete glucocorticoids (GCs) in a circadian fashion and in response to stressful stimuli. Indeed, exposure of animals to stressful conditions induces a wide range of behavioural and physiologic responses, the best characterized being the activation of the hypothalamic-pituitary-adrenal (HPA) (manifested by the release of ACTH and GCs into the blood). The surge observed in ACTH and GCs secretion depends on the stress paradigm used and at lesser degree its duration. It represents the adaptative response to counterattack the negative effects of stress. After the termination of exposure to stressors, the HPA hormones need from 1 to several hours (>8 hr). This represents an evidence for lasting changes in resting activity of the HPA axis after a single exposure to stress. Interestingly and from a physiological point, a strong stress as immobilization, induces anorexia-like effect notably, 24 hr post stress. This suggests greatly that GCs may affect the central regulation of food intake (FI), probably by interacting with factors involved in this regulation. Therefore, we decided to study the long-term effects of a single exposure to immobilization on the expression of anorexigenic and orexigenic factors in different brain structures, principally those related to food intake control. In order to investigate the involvement of the signalling of these factors in the food control, notably in the context of food intake alterations (anorexia caused by stress), we analysed the hypothalamic and dorso vagal complex (DVC) expression of neuropeptide Y (NPY), brain-derived neurotrophic factor (BDNF) and cocaine amphetamin related transcript (CART) mRNAs. For BDNF, we showed that anorexia-inducing immobilization stress (IS) triggers different BDNF recruitment patterns between DVC and hypothalamus. Furthermore, we showed, by using RT-PCR that the mRNAs of the two other peptides display significant increases in stressed rats compared to controls, although with differential peaks. In hypothalamus, NPY and CART transcript up-regulation is observed at the end of IS and persists until 48-72h after IS. In the DVC, expression of the two transcripts peaks significantly at 24h post-stress and decline afterwards; NPY mRNA remains then significantly higher than in controls, whereas CART mRNA is down-regulated after 48h post-stress. The persistence of alteration of the expression of anorexigenic and orexigenic factors during the post-stress period could be highly related to the slow recovery of the hypothalamo-hypophyseal-adrenal (HPA) axis in IS and points to stress-induced plasticity in both nervous centres of food intake regulation.

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The arcuate nucleus and neuropeptide systems in the seasonal adaptation of mammals.

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Many species of temperate regions show seasonal variations in several aspects of physiology and behaviour, including reproduction, hibernation and body weight. They typically inhibit reproduction during winter to conserve scarce energetic resources. This is the case of the jerboa, a rodent adapted to the semi desert-environment of Morocco. The seasonal changes are triggered by the annual changes of photoperiod which in mammals is decoded by a photo-neuroendocrine system composed of the retina, the suprachiasmatic nucleus and the pineal melatonin.

In nature, seasonal adaptations are regulated by both day length and non-photoperiodic cues which vary seasonally such as food availability and/or energy stores. The arcuate nucleus is a potent structure involved in the long-term control of energy stores. It contains peptidergic POMC and NPY neurons which are responsive to a wide array of hormones and nutrients.

In the jerboa (*Jaculus orientalis*), reproductive activity is seasonal; it's activated in spring-early summer and inhibited in autumn. We have previously demonstrated that the GnRH neurosecretory system displays seasonal variations. The seasonal plasticity was also observed in the expression of neuropeptides which regulate gonadotropic activity such as POMC neurons within the arcuate nucleus. In seasonal mammals, the melatonin and sex steroids control reproductive activity by indirectly modulating gonadotropin secretion through an action in the mediobasal hypothalamus. The discovery of the two RF-amide peptides, Kisspeptin and RFRP-3 in seasonal rodents during the last years has helped in uncovering the mechanisms of seasonal reproduction. Kisspeptin neurons were found in the anteroventral periventricular nucleus (AVPV) and in the arcuate nucleus (ARC), whereas RFRP-3 cells were found in the dorso-medial hypothalamus (DMN). Kisspeptin is well known as potent stimulator of GnRH secretion and the principal conduit mediating sex steroids feed-back. Several studies suggest a role of RFRP-3 as inhibitory regulator of the mammalian reproductive axis. Photoperiodic and seasonal variations in the expression level of these peptides have been reported in seasonal species such as hamsters, sheep....with large differences between species. We have recently reported seasonal changes of Kp and RFRP-3 expression within the arcuate nucleus and DMN of the jerboa. A high content of Kp and RFRP was obtained during the sexually active period, suggesting that the two RF-amide neuropeptides act in concert to regulate the gonadotropic activity of this species.

All recent studies point to Kisspeptin and RFRP-3, in the mediation of photic and non photic cues on the reproductive system, and suggest that they play different roles. Seasonal adaptation is a complex process which involves RF-amides peptides, which may communicate with neurochemical systems regulating feeding notably POMC and NPY neurons in the arcuate nucleus and other neuropeptides. Discerning how and why differences in the mechanisms governing seasonal adaptation may help us to understand how some environmental cues drive to divergent patterns of regulatory mechanisms across a wide range of habitats.



Symposium 6

The Neuronal and Glial Functions of Brain Dystrophins

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Two decades of molecular, cellular, and functional studies considerably increased our understanding of dystrophins function and unveiled the complex etiology of the cognitive deficits in Duchenne muscular dystrophy (DMD). An array of dystrophin-gene products have been identified in both brain and sensory organs such as retina, where they are components of distinct multiprotein complexes selectively involved in regulating the structural organization of ion channels and membrane receptors in either neurons or astrocytes. Bringing together concepts from brain and retina studies, we will describe the role of dystrophins in synapse, glial and blood-brain barrier functions and how loss-of-function mutations affect brain and sensory network dysfunctions in DMD.

The symposium will start with a historical overview of the identification and structure-function studies of dystrophin products in the nervous system of invertebrate and mammals, by a pioneer researcher who greatly impacted the scientific community through characterization of the most abundant dystrophin product in CNS, Dp71 and development of a mouse genetic model selectively lacking this protein (D. Yaffe, Israel). Several experts will then describe the multifunctional roles of dystrophins, with a particular focus on Dp71, in the glial and neuronal aspects of retinal physiopathology (M. Roux, France), in the neuronal-vascular-glial interactions involved in the central control of osmoregulatory responses (L. Dorbani-Mamine, Algeria), in blood-brain barrier development and integrity (B. Nico, Italy) and in the function of brain excitatory synapses and cognitive processes (C. Vaillend, France).



DP-71 – The Most Abundant Non-Muscle Product of the Dystrophin Gene

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The huge gene encoding Dystrophin, the protein that is defective or missing in Duchenne and Baker Muscular Dystrophies, was considered in early studies a muscle specific gene. However, we have found that the dystrophin gene is also expressed in other tissues, including brain. The main product in the brain, and most other non-muscle tissues, is a relatively small membrane associated protein of 71 KD that was named Dp71. Dp71 is also expressed in a much regulated pattern during embryogenesis. The production of Dp71 is controlled by an internal promoter located in intron 62 of the huge gene. Dp71 consists of the C-terminal region of dystrophin but lacks the entire spectrin like repeats and the N-terminal actin binding domains. Later studies discovered additional three small products of the gene—Dp116, Dp140 and Dp260, consisting of the C-terminal and the cysteine rich domains of dystrophin and various extensions into the spectrin like repeats region.

The complex structure of the dystrophin gene is highly conserved during the evolution; multiple products are encoded by the dystrophin like genes in distantly related organisms and by the closely related gene encoding utrobin. This indicated the importance of the truncated dystrophin gene products and their unique functions. Indeed, studies in a number of labs indicated cell type specificity of the small products. Lack of Dp71 seems to be involved in mental retardation in human and in impaired learning capacity in Dp71 null mice.

Dp71 is not expressed in the muscle; ectopic expression of Dp71 in skeletal muscles results in a muscular dystrophy like phenotype, suggesting a competitive inhibition of membrane binding of dystrophin.



DP-71 in the Hypothalamo-Neurohypophysial System Of Mice

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Dystrophin of 427 kDa was the first Duchenne muscular dystrophy (DMD) gene product identified in muscle. It mediates interactions between actin filaments and extracellular matrix involving a membranous and cytoplasmic dystrophin-Associated proteins complex (DAPC). Otherwise the DMD gene has internal promoters driving the production of smaller proteins in other tissues. One of them, that of 71 kDa (Dp71) is the major form of dystrophin expressed in brain and retina. Its ability to associate with the DAPC and channels suggests that Dp71 is involved in brain development, synaptogenesis, cerebral plasticity and essential for ionic homeostasis.

Our aim is to elucidate dystrophin's involvement in the control osmotic homeostasis. Using several techniques, we examine the effect of the lack of Dp71 on the hypothalamo-neurohypophysial system (HNHS) structural and functional plasticity. The HNHS composed of magnocellular neurons is responsible of Arginin-Vasopressin (AVP) secretion into the bloodstream. It has a significant and reversible plasticity based on the dynamics of glial cells.

The study is realized on Dp71-null mice and their wild-type (Balb/c) submitted to 8 days salt loading.

Our results showed that Dp71 and Dp140 are the principal dystrophins expressed in the SON. When Dp71 is present in astrocyte end-feet surrounding vessels of Balb/c, the Dp140 appeared in AVP neurons of Dp71-null mice. The two DAPC components, dystroglycan and 1-syntrophin were also analyzed in Dp71-null mice where their expression decreased.

Following salt loading, the AVP levels are increased in the SON of wild-type mice but not in Dp71-null mice. In parallel, in control and stimulation conditions, the plasma osmolality of Dp71-null mice is lower than of the wild-type in control. These results suggest that the absence of Dp71 leads to a change in the set point of osmoregulation. Its presence in astrocyte end-feet emphasizes the importance of neuronal-glial-vascular interactions for the central detection of osmolality.



DP-71 and Glial Dystrophin–Associated Proteins in the Blood Brain Barrier of the Dystrophic Mdx Mouse

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In this study, we have investigated the role of the Dp-71 and dystrophin–associated proteins (DAPs) and their relationships in the blood-brain barrier (BBB) and perivascular basement membrane organization, in the brain of the dystrophic mdx mouse. To this purpose, we have analyzed: 1) The expression of the glial Dp71 and DAPs α - β dystroglycan and syntrophin, aquaporin-4 water channel (AQP4), and Kir 4.1, by immunocytochemistry, laser confocal microscopy, immunogold electron microscopy, immunoblotting, and RT-PCR; 2) The ultrastructure of the basement membrane and the expression of laminin and agrin; 3) The co-localization of AQP4/ α - β dystroglycan, and of Kir-4.1/agrin, by dual immunofluorescence. Results have shown that in mdx brain as compared to control ones, these differences are recognizable: 1) A significant reduction in protein contents and mRNA expression of the Dp 71 and DAPs; 2) A thickened and discontinuous basement membrane, showing a significant reduction in laminin and agrin expression; 3) A molecular rearrangement of the α - β dystroglycan, coupled with a parallel loss of agrin and Kir 4.1 on basement membrane and glial endfeet. Overall, these data indicate that in mdx brain the deficiency in dystrophin and Dp71 is coupled with a reduction of the DAPs components associated with a altered anchoring to the basement membrane.



Lessons from Retinal Dystrophins

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Problem Statement: Dystrophins are expressed not only in muscles, but also in many parts of the central nervous system, including the cerebellum, hippocampus and retina. This leads in many Duchenne patients to cognitive deficits, as well as an abnormal electroretinogram, close to the one found in night-blind patients. This latter element is puzzling, as patients do not seem to suffer from visual deficits. This has attracted attention to retinal dystrophins, which are expressed in Müller glial cells (Dp71), notably in the processes surrounding blood vessels, and in photoreceptors and possibly in bipolar and/or amacrine cells (Dp427, Dp260 and Dp140). We have examined how the absence of these proteins lead to an abnormal electroretinogram, and if Dp71 absence impacted the blood-retinal-barrier integrity.

Approach: Comparison of the mdx^{3Cv} (which lacks all dystrophins) and/or Dp71-null mice to WT was performed by immunohistochemistry and confocal microscopy, as well as by electron microscopy.

Results: Absence of Dp71 alters the blood-retinal barrier integrity and leads to an abnormal development of retinal vessels. When longer dystrophins are missing (mdx^{3Cv} mouse), the morphology of the synapse between photoreceptors and bipolar cells is profoundly altered. In addition, the distribution of proteins involved in calcium signaling in bipolar cells is modified in mdx^{3Cv} but not Dp71-null retinas.

Conclusion: Together, these results stress the fragility of Duchenne retina in absence of Dp71, and open new perspectives to understand not only the abnormal electroretinography in Duchenne patients, but also possibly their cognitive deficits.



The Molecular, Neurophysiological and Behavioral Profiles of Mice Lacking Brain Dystrophin Products

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The association of the Duchenne muscular dystrophy (DMD) syndrome with cognitive and behavioral alterations is well recognized. The nature and severity of the impairment is however highly variable among patients, which may depend on individual mutation profiles with distinct impact on the functions of various dystrophin-gene products generated from several promoters in the brain. While genotype-phenotype relationships remain unclear, studies in specific DMD mouse models such as in the Dp427-deficient *mdx* and Dp71-null mice revealed unexpected roles for the Dp427 and Dp71 in critical brain mechanisms. Brain Dp427 likely modulates synapse plasticity and morphology through a role in the clustering mechanisms of central GABAA receptors. We showed that the loss of this protein in mice results in selective cognitive and behavioral deficits. Our recent results suggest that functional rescue of a truncated Dp427 using an exon-skipping strategy may alleviate some of the neurophysiological deficits in the adult brain, while overexpression of utrophin, a promising paralog candidate for compensation and treatment of myopathy, does not overcome behavioral deficits in *mdx* mice. Dp71 expression appears ubiquitous in brain and this short form of dystrophin may endorse ambivalent roles in both glial and neuronal cells. Our multidisciplinary study of the Dp71-null mouse unveiled major alterations of glutamatergic synapse organization, signaling and maturation, abnormally enhanced neurotransmission and deficient synapse plasticity and structure, behavioral disturbances and selective deficits in learning and memory performance. In all, the current data suggest that brain dystrophins take part in specialized molecular scaffolds of proteins that cluster neurotransmitter receptors and/or ion channels at the synapse and/or glial-vascular interface. The genesis of mental retardation in DMD is multifactorial and likely encompasses alterations of the GABAergic and glutamatergic system as well as blood-brain barrier integrity.



MNS 2012

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September 30 – October 3, 2012

Plenary Lecture 3

An update on Alzheimer's disease

Murat Emre (Turkey)



Plenary Lecture 4

Neuroendocrine Aging: GH/IGF-1 Axis, Energy Balance Regulation and Cognition

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The Growth-Hormone (GH)/IGF-1 axis plays a key role in the aging and longevity process in many animal models from *C. elegans* to mammals. Since early adulthood, its activity decreases by 10% every decade and morbidity is increased in adult GH-deficient human subjects. Aging is associated with imbalance in the secretion of GHRH and somatostatin. Quantification of rat pituitary and hypothalamic gene expression as assessed by cDNA membrane array, indicates that GH itself represents 85% of total gene expression in the gland of young Sprague-Dawley rats, while MCH, the most expressed transcript, accounts for only 0.8% of total hypothalamic transcripts. The proportion of genes modified with ageing in the hypothalamus and pituitary is modest (1.5% and 5.2%, respectively). Among pituitary specific RNAs, GH expression is markedly decreased with age. At the hypothalamic level, somatostatin and GHRH expression is minimally affected, while neuropeptide transcripts involved in feeding behaviour (orexin, MCH, POMC, CART) are significantly altered. The Lou C rat strain is considered as a model of resistance to diet-induced obesity and, consequently, of « successful aging ». As compared to its parent strain, the Wistar rat, aging in Lou C/Jall rats is associated with a delayed decrease in pulsatile GH secretion in the presence of a lower IGF-1 tone and an increase in the expression of hypothalamic orexigenic neuropeptides. Aged Lou C rats also display preserved memory capacities. Increased longevity and decreased GHRH in the hypothalamus are also observed in brain-invalidated IGF-1 receptor heterozygous mice. Caloric restriction or drug affecting mTOR (rapamycin) and AMPK (resveratrol) pathways affect GH/IGF-1 levels and may delay the aging process and its consequences in primates. Finally, circulating IGF-1 and brain somatostatin have been associated with Alzheimer's Disease. Altogether, it is tempting to speculate that a delayed decrease in GH pulsatility with lower IGF-1 levels is a marker of healthy aging, not only in terms of preserved metabolism but also for cognition and synaptic plasticity.

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Symposium 7

Neuroglia: The Forgotten but Emerging Player in Neurodegeneration

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Neurodegenerative diseases including Alzheimer's disease have been mainly associated with neuronal dysfunction and alterations ignoring, somehow, the involvement of neuroglia in their apparition, evolution and treatment. Recent advances in gliology emphasized the role of glia in the progression and handling of the insults to the nervous system. In this sense, multiple research directives, including ourselves are centred in understanding the role of neuroglial elements in these processes and study their role in the neuronal network alteration and failures that appear, as well as determining the common and/or differential plastic capabilities of neurones and neuroglia.

The human brain is formed by neuronal networks embedded into astroglial syncytia. The astrocytes perform numerous functions providing for overall brain homeostasis, importantly assisting in brain plasticity, determining the micro-architecture of the grey matter and defending the brain through evolutionary conserved astroglial programmes. Therefore, The brain pathology, is, to a very great extent, a pathology of glia, which, when falling to function properly, determines the degree of neuronal death, the outcome and the scale of neurological deficit. The neuroglia appears as a brain warden, and as such it is intrinsically endowed with two opposite features: it protects the nervous tissue as long as it can, but it also can rapidly assume the guise of a natural killer, trying to eliminate and seal the damaged area, to save the whole at the expense of the part.

Thus, Neuroglial cells are importantly involved in all neurological diseases determining the progression and outcome of different neuropathological processes. Therefore, astroglia, microglia, oligodendroglia and NG2 glial cells are specifically involved in neurodegenerative diseases including Alzheimer's disease (AD) and various forms of dementia as well as in spinal cord injury and degeneration; affecting neuronal function and therefore suggesting that neurodegenerative processes are not only exclusive of neurons but they are also a determinant and major glial component. The proposed symposium is dedicated to the state-of-the-art overview of the pathological potential of glial cells in various forms of neurological and neurodegenerative conditions.



Neuroglia: From Brain Homeostasis to Pathophysiology

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The neuronal doctrine, which shaped the development of neuroscience was born from a long-lasting struggle between reticularists (led by Camillo Golgi), who assumed internal continuity of neural networks and neuronists (championed by Santiago Ramon y Cajal), who defined the brain as a network of physically separated cellular entities, defined as neurones. Today, however, we know that integration and information processing in the brain occurs through close interactions of two cellular circuits represented by neuronal networks embedded into internally connected astroglial syncytium. Our understanding of glial function changed dramatically over last two decades. This change concerns the whole concept of how the brain is organized, and how the development, life and death of neural circuits are controlled. There is compelling evidence demonstrating that these are the astrocytes that are creating the compartmentalisation in the CNS, and these are the astrocytes that are able to integrate neurones, synapses, and brain capillaries into individual and relatively independent units. Astroglial syncytium allows intercellular communication route, which permits translocation of ions, metabolic factors and second messengers. The resulting potential for parallel processing and integration is significant and might easily be larger, but also fuzzier, than the binary coded electrical communication within the neuronal networks. The neuronal-glia circuitry endowed with distinct signalling cascades, form a “diffuse nervous net” suggested by Golgi, where millions of synapses belonging to very different neurones are integrated first into neuronal-glia-vascular units and then into more complex structures connected through glial syncytium. These many levels of integration, both morphological and functional, presented by neuronal-glia circuitry ensure the spatial and temporal multiplication of brain cognitive power.

Neuroglial cells are intimately involved in all forms of neurological diseases and these are neuroglia, which, to a very large extent, determine the progression and outcome of neuropathological process. Astrocytes are specifically involved in various neurodegenerative diseases including Alzheimer’s disease, Amyotrophic lateral sclerosis, Parkinson’s disease and various forms of dementia. Recent evidence suggest that early stages of neurodegenerative processes are associated with atrophy of astroglia, which causes disruptions in synaptic connectivity, disbalance in neurotransmitter homeostasis and neuronal death through increased excitotoxicity. At the later stages astrocytes became activated and contribute to neuro-inflammatory component of neurodegeneration.



Astrocyte Degeneration in Amyotrophic Lateral Sclerosis: Mechanism and Rescue

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A major constraint to the comprehension of the pathogenesis of Amyotrophic Lateral Sclerosis (ALS) has been long represented by the conviction that this disorder selectively affects motor neurons in a cell-autonomous manner. However, the failure to identify the events underlying the neurodegenerative process and the increased knowledge of the complex cellular interactions necessary for the correct functioning of the CNS has recently focused the attention on the contribution to neurodegeneration of glial cells, including astrocytes. Astrocytes can hurt motor neurons by secreting neurotoxic factors, but they can also play a deleterious role by losing functions that are supportive for neurons. Recently, we reported that a subpopulation of spinal cord astrocytes degenerates in the microenvironment of motor neurons in the hSOD1^{G93A} mouse model of ALS. Mechanistic studies *in vitro* identified a role for the transmitter glutamate in the gliodegenerative process via the activation of its inositol 1,4,5 triphosphate (IP₃)-generating metabotropic receptor 5 (mGluR5).

Since non-physiological formation of IP₃ can prompt IP₃ receptor (IP₃R)-mediated Ca²⁺ release from the intracellular stores and trigger various forms of cell death, here we investigated the intracellular Ca²⁺ signalling that occurs downstream of mGluR5 in hSOD1^{G93A}-expressing astrocytes. Contrary to wild-type cells, stimulation of mGluR5 causes aberrant and persistent elevations of intracellular Ca²⁺ concentrations in the absence of spontaneous oscillations. The interaction of IP₃Rs with the anti-apoptotic protein Bcl-X_L was previously described to prevent cell death by modulating intracellular Ca²⁺ signals. In mutant SOD1-expressing astrocytes, we found that the sole BH4 domain of Bcl-X_L, fused to the protein transduction domain of the HIV-1 TAT protein (TAT-BH4), is sufficient to restore sustained Ca²⁺ oscillations and cell death resistance. Furthermore, chronic treatment of hSOD1^{G93A} mice with the TAT-BH4 peptide reduces focal degeneration of astrocytes, slightly delays disease onset, and improves both motor performance and survival.



Neuroglial Alterations in Alzheimer's Disease are Concomitant with Neurogenic Impairments

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Neurodegenerative diseases including Alzheimer's disease (AD) have been mainly associated with neuronal dysfunction and alterations ignoring, somehow, the involvement of neuroglia in their apparition, evolution and treatment. Neuroglial cells, fundamental for brain homeostasis represent the intrinsic brain defence system. In fact, the human brain is formed by neuronal networks embedded into astroglial syncytia. Astroglial cells are engaged in neurological diseases determining the progression and outcome of neuropathological processes including AD. The recently acquired knowledge also allows us to regard neurodegenerative diseases as gliodegenerative processes, in which glial cells determine the progression and outcome of neuropathological processes such as AD. We have recently probed this active pathological role, by showing: (i) an astroglial generalised atrophy with a concomitant astrogliosis just restricted to Ab plaques presence ii) alterations in glutamate glial metabolism and (iii) an early ramified resting microglial recruitment in the affected areas, even before the presence of activated/macrophagic microglial cells. These neuroglial alterations appear in parallel with a marked reduction of cell proliferation and neurogenesis in both hippocampus and subventricular zone, appearing even earlier than the AD associated pathological hallmarks, plaques and tangles. Thus, the concomitant glial and neurogenic alterations are fundamental for the disruption of neural networks connectivity together with the neurotransmitters imbalance, underlying the mnemonic deficits associated with AD; and new therapeutic approaches targeting simultaneously these changes might be of major relevance in the treatment of the disease.



NG2-glia: A Relevant Novel Glia with Multiple Functions in Normal Brain and Neurodegenerative Processes

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NG2-glia are a distinct class of CNS glial cells that have the antigenic phenotype of oligodendrocyte progenitor cells (OPCs). During development, OPCs generate myelinating oligodendrocytes and adult NG2-glia, which persist as a major population of stellate cells throughout white and grey matter. NG2-glia have a number of defining characteristics: (1) they are specifically identified by their expression of the NG2 chondroitin sulphate proteoglycan (CSPG) and alpha receptors for platelet derived growth factor (PDGF R); (2) they have an oligodendrocyte lineage; (3) they are capable of generating oligodendrocytes throughout life; (4) they form direct synapses with neurons during development; (5) they express neurotransmitter receptors and respond to neuronal synaptic activity; (6) under normal circumstances, they are quiescent, slowly dividing cells; and (7) they respond rapidly to CNS insults by increased proliferation and regeneration of oligodendrocytes, in addition to participating in glial scar formation. The only known function of NG2-glia is to generate oligodendrocytes, although it is not known whether this is their sole function. There is no direct evidence of a function for NG2-glia at synapses, but it is presumed that synaptic signalling plays a role in sustaining the adult population or regulating their differentiation into oligodendrocytes. The effects of oligodendrocyte loss and myelin degeneration are devastating, as illustrated by the demyelinating disease Multiple Sclerosis. Hence, there is a strong evolutionary drive for maintaining a substantial population of NG2-glia, that otherwise appear to be functionally redundant. In human brains, myelination extends to age 50 in cortical regions, and MRI studies suggest myelin breakdown accelerates as aging progresses and underlies age-related cognitive decline. This is partly offset by increased oligodendrocyte generation from NG2-glia, but their diminished capacity for regeneration in the ageing brain is likely to be critical in the cognitive decline.



Role of Glial Cells in Oxidative Stress Resistance in Neurodegenerative Diseases.

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It has been reported that molecular hydrogen selectively reduces hydroxyl radicals, the most cytotoxic of reactive oxygen species (ROS), and can thereby effectively protect cells. ROS-induced damage is one of the reasons to cause Parkinson's disease (PD). We have previously reported that hydrogen in drinking water reduced dopaminergic neuronal loss by buffering ROS both in substantia nigra and in striatum in MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-treated mice. In the present study, drinking water with saturated hydrogen (hydrogen water) prior to MPTP administration, but not after MPTP administration, showed significantly less decrease of dopaminergic neurons in substantia nigra and fibers projected to striatum. Hydrogen also attenuated activation of microglia and astrocyte in substantia nigra 7 days after MPTP administration. The neuroprotective effects of hydrogen could be achieved by continuous drinking of hydrogen water for 7 days, and lasted for several days after the stop of hydrogen consumption. As a molecular mechanism, hydrogen increased chaperone molecule, heat shock protein 72 (Hsp72) in substantia nigra compact part. It has been reported that Hsp72 has the ability to reduce apoptotic cell death by interaction to several critical factors for apoptosis. Therefore, it has been implicated that hydrogen can potentiate the expression of Hsp72 in nigrostriatal pathway, inducing neuroprotection in PD model mice. Precise mechanism how hydrogen induces Hsp72 expression and the role of glial cells will be discussed.



Symposium 8

Adaptive neuroendocrine regulations in stress and food intake control: from molecular to integrated approaches

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Neuroendocrine regulations are essential for several vital functions including the stress response and food intake control. Several pathways originating at the hypothalamus and the sympatho-adrenal system, and involving a variety of neurotransmitters and neuropeptides are continually described and are still intensely investigated to indentify the molecular cues behind our behaviors. In this symposium, we will present our recent data obtained using several interesting models including animals from the wild that highlight important effects of neuroendocrine regulators. Dr Lee Eiden will present recent data on the role of neuropeptides at the splanchnic-adrenal synapse, which ensure neurotransmission during stressful situations to an endocrine gland. Drs Rabia Magoul and Mohammed Errami will present their latest findings on the characterization of peptidergic and non-peptidergic sytems in the hypothalamus that exert major regulatory functions during stress and food intake control. Finally, Drs Maria Malagon and Youssef Anouar will show their data obtained on new intracellular effectors that control cell metabolism and secretory activity during neuroendocrine regulations. The overall aim of the symposium is to present different studies in neuroendocrinology which take into account regulations at the molecular, cellular and organismic levels.



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PACAP Neurotransmission and the Transduction of Stress Signaling

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The neuropeptide PACAP (pituitary adenylate cyclase-activating polypeptide) has recently been shown to be the neurotransmitter mediating signaling to the adrenal medulla during stress. PACAP release at the splanchnic-adrenal synapse stimulates both epinephrine secretion, and the induction of catecholamine biosynthetic enzymes allowing replenishment of released catecholamines within the gland. In addition to induction of catecholamine biosynthetic enzymes such as tyrosine hydroxylase and phenylethanolamine N-methyltransferase, PACAP is responsible for the induction of a number of other genes, including those mediating protection from cellular toxicity due to excessive calcium influx. We have been studying the signaling pathway(s) that mediate this cellular plasticity, and find that a unique cAMP-dependent activation of the extracellular response kinase (ERK) is responsible for gene induction, while a calcium-dependent signaling pathway subserves, in parallel, release of catecholamines and other informational molecules from the adrenal gland. We have additional evidence that these pathways also function in neurons of the central nervous system. The study of PACAP neurotransmission is paradigmatic for the dissection of signaling pathways for multiple targets within neuroendocrine cells, for which pharmacological agents of much greater specificity than at the first messenger (receptor) level can be obtained.



Parvocellular Accessory Neuropeptides and Environmental Stressors

Rabia Magoul

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The hypothalamic response to a stressful environmental situation implicates the neuroendocrine corticotropin releasing hormone (CRH) system of the hypothalamic parvocellular paraventricular nucleus (pPVN) as well as other accessory neuropeptides such as neurotensin, vasopressin, oxytocin and cholecystokinin coexpressed within CRH neurons and controlling the corticotrope axis activity as well. These accessory neuropeptides accompany the CRH in its action on the anterior pituitary to potentiate its effects on pituitary ACTH secretion in situations of high demand on the HPA axis. In situ hybridization studies assessing the expression of some accessory neuropeptides within pPVN neurons suggest a phenotypic plasticity of the pPVN neurons following immune stress in rat. The aim of our work was to further explore this phenotypic plasticity concept of the pPVN neurons involving classic and novel accessory neuropeptides. Accessory neuropeptides occurrence within the CRH neurons as well as their expression within the pPVN in response to various stressors were studied in rat and jerboa by immunohistochemistry. Our results among others show that the CRH neurons are able to express various accessory neuropeptides. Some of these neuropeptides fluctuate following acute stressors, suggesting their participation to the phenotypic plasticity of pPVN neurons. Others such as vasopressin, oxytocin and EM66 are insensitive to the same tested stressors. Since the duration of the stressful stimulus is critical to control the pPVN neuronal phenotypic plasticity involving accessory neuropeptides, this provides additional evidence for the complexity of such phenotypic plasticity. In conclusion, the CRH neurons are able to express a wide variety of accessory neuropeptides whose levels may depend on experimental conditions (stressor type, its duration, species ...). Thus, the chemical phenotype of such neurosecretory neurons is not immutable (phenotypic plasticity) and may change according to stress circumstances. Consequently, the contribution of each putative secretagogue of ACTH release depends on environmental stressors characteristics and/or species.



Endocannabinoid System and the Regulation of Food Intake

Mohammed Errami

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The use of cannabis derivatives as recreational and therapeutic drugs can be traced back to the earliest civilization and today, extracts of cannabis are among the most commonly used drugs for psychotropic effects. Cannabinoid receptors (mainly CB1) are expressed at high levels in many brain regions and the anatomical distribution is consistent with behavioural effects of cannabinoids, including: euphoria, decreased motor activity, impairment of memory, antinociception and modulation of food intake. In the brain, the regulatory effect of cannabinoids on feeding behaviour is believed to be mediated at low levels. First, it tonically reinforces the motivation to find and consume foods, through significant interactions with mesolimbic pathways involved in reward mechanism. Second, it transiently regulates the levels and/or action of hypothalamic orexigenic and anorectic neuropeptides. At peripheral level, the modulation effect of cannabinoids on feeding behaviour is believed to be mediated through CB1 receptors located in the gut, hepatocyte and adipocyte cells. To date, there are few studies investigating the mechanisms that underlie the effects of cannabinoids on feeding behaviour, and more specifically the involvement of hypothalamic neuronal systems, particularly, 5-HT, NPY and PMOC neurones in the cannabinoids effect. Our results suggest that one of the possible mechanisms allowing the stimulation of food intake by CB1 receptor agonists is through an inhibition (or delaying) of the ventromedial hypothalamic serotonin neurotransmission implicated in the regulation of the satiety processes and the stimulation of hypothalamic neuropeptide systems implicated in the increase of feeding behaviour.

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Molecular Regulation of Peptide and Neurotransmitter Secretion in Neuroendocrine Cells

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Rab proteins control vesicle trafficking by regulating components of the transport machinery. Particularly, we have shown that Rab18 inhibits secretory granule movement, but the molecular mechanisms involved and the identity of Rab18 effectors remain unknown. We will discuss our recent data on the analysis of the motility of Rab18-associated granules in response to the activation of the secretory pathway, the relationship between Rab18 granules and the microtubule network, as well as on the identification of Rab18 effectors. Specifically, video-microscopy studies in PC12 cells cotransfected with expression vectors coding for the granule marker NPY and for Rab18, revealed that secretory granules, either containing or not Rab18, exhibited similar saltatory movements, including anterograde and retrograde net movements, under basal conditions. However, upon K⁺ stimulation the percentage of NPY granules moving anterogradely increased, whereas the number of anterograde Rab18 granules decreased. We also found a close spatial relationship between Rab18-bearing granules and microtubules, which was impaired after microtubule depolymerization by nocodazole. Inasmuch as Rab18 modified granule transport dynamics, we investigated the relationship between this GTPase and components of the microtubule-based transport machinery. Thus, FRET experiments showed that Rab18 interacts with kinesin-1 light chain in its active form (after K⁺ treatment or using a constitutive active Rab18 mutant) and with huntingtin in its inactive conformation, supporting the view that Rab18 impairs the transport of secretory granules by regulating the activity of these microtubule-associated proteins. Finally, by using the yeast two-hybrid system, we have identified additional, novel Rab18 interacting proteins that likely contribute to the effect of this GTPase on granule traffic dynamics. In all, our data has enabled to unveil the underlying molecular mechanisms by which Rab18 controls vesicle traffic in neuroendocrine cells.

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Role of the Novel Antioxidant Enzyme Selenoprotein T in the Nervous and Neuroendocrine Systems

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PACAP is a neurotrophic peptide that exerts numerous effects in the nervous and endocrine systems through various signaling pathways. We have previously identified a new thioredoxin-like protein named selenoprotein T (SelT), whose expression is stimulated by PACAP during neuronal cell differentiation but whose function is unknown. In rat, SelT is abundantly expressed in tissues with a high metabolic activity such as in embryonic and endocrine organs. SelT gene knockout resulted in early embryonic lethality, implying that SelT plays an important role in these tissues. To determine the function of SelT in nervous and neuro-endocrine organs, its gene was ablated through conditional knockout in the brain and pancreas. Mice with SelT gene deletion in the CNS were viable but their brains displayed a reduced size (-15%) relatively to the unchanged weight of the animals. Unbiased measurement revealed 15-25% reduction in the volume of different brain areas including the cortex, hippocampus or cerebellum. Such a decrease may result from a cell loss of neuronal and/or glial origin. Indeed, neuroblasts from E15 brain-specific SelT^{-/-} mice exhibited a survival deficit associated to increased intracellular ROS levels compared to wild type animals. Conversely, SelT overexpression protected neuronal cells against oxidative stress via a redox mechanism. In the pancreas, SelT is exclusively expressed in insulin-producing β cells and its gene knockout resulted in a hyperglycemic response and a higher glucose to insulin ratio compared to WT littermates. In vitro experiments confirmed a deficit of pancreatic cells in insulin secretion after SelT gene knockdown. The mechanism involved is currently investigated. Taken together, these data indicate that the PACAP-regulated gene SelT plays an important role in the nervous and neuro-endocrine systems, probably by protecting cells against oxidative stress during development and homeostatic responses. This work was supported by INSERM, University of Rouen and the Conseil Régional de Haute-Normandie.



Symposium 9

GDRINeuro Symposium: “The Rhythms of Life: from Bench to Bedside”

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The French-Morocco International Network in Neuroscience (GDRINeuro) defined biological rhythms and adaptive processes to the environment as one of topics of priority. In this framework, north-south themes of research have been developed in a real partnership pointing out the importance of desert mammal as models. Despite the wealth of knowledge accumulated in the last decades on suprachiasmatic nucleus organization and functioning, the impact of the circadian clock on human health is still largely unknown, and the translation of experimental data to human problems in health and disease requires special attention and reconsideration. The symposium will focus on these issues, dealing with the impact of endogenous rhythm regulation in health and disease. In this context, the symposium will present a novel data on neural and hormonal key mechanisms of regulation of the brain clock and their impact on the SCN-driven functions such as reproduction. It will particularly focus on other environmental factors that may be strong enough to synchronize the biological clock of a desert Mammal, the Dromedary, as well as on other pineal hormone that seasonally controls clock protein activity in the SCN and reproductive function in a desert rodent, the jerboa. In addition, the symposium will present novel data on the regulatory role of melatonin upon reproductive function at the level of the pars tuberalis of the pituitary of the Syrian hamster including two recently discovered hypothalamic peptides. An overview and future perspectives will then be provided on the infectious diseases and sleep with attention to the inter-relationships of infection and circadian functions, which is a key issue for human health particularly in Africa. Finally, the symposium will also devote attention to the potential relationships between neurodegeneration and chronobiology, focusing on primate model of dopamine degeneration, which hallmarks Parkinson' disease.



The Daily Ambient Temperature Cycle is a True Synchronizer of the Camel Circadian Clock Outputs: Body Temperature and Melatonin Rhythms

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To survive, most mammals have to adapt to their biotope. In arid and desert areas, the dromedary (*Camelus dromedarius*) is exposed to extreme changes in environment: temperature, scarcity of food supply, dryness associated with a lack of watering points, etc.. In such habitat, besides photoperiod which marks each season, we assumed that other environmental factors may be strong enough to synchronize the biological clock and to allow animals to anticipate seasonal changes in their physiological functions. We thus studied the effect of a well known environmental parameter, the ambient temperature cycle. This cue is a rhythmic and seasonal signal and under dehydration, in this species, it affects thermoregulation. For this study, as a marker of activity of the clock, we chosen the diurnal rhythm of body temperature We first demonstrated that this rhythm of body temperature is under control of the circadian clock and also depending of the photoperiod. Then after, we established that the rhythm of body temperature (hence as an output of the clock) can be also, in some experimental conditions, entrained by the ambient temperature cycle. To be sure of that interpretation we also studied this “entraining” capacity of the 24h ambient temperature cycle on another known output of the clock, the melatonin rhythm. The data obtained demonstrate that after a shift in the ambient temperature cycle, not only the body temperature cycle but also the melatonin rhythm was shifted. It appears thus, in the Dromedary, that the daily cycle of ambient temperature is, like the light-dark cycle, a true synchronizing cue. We conclude that for studies aiming to control seasonal rhythms like reproduction in the dromedary, not only photoperiod but also the ambient temperature cycle have to be considered.



Pineal 5-Methoxytryptophol Seasonally Controls Reproductive Function in a Desert Rodent, the Jerboa *Jaculus Orientalis*.

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The jerboa is a seasonal breeder living in high continental shelves of Middle Atlas Mountains in Morocco. In this specie, the maximal expression of the daily rhythm of pineal 5-Methoxytryptophol (5-ML) occurs in late summer-early autumn period, when animals are in sexual quiescence. In the jerboa, 5ML modulates the reproductive function since it induces gonad quiescence when daily injected in early spring under constant long photoperiod, the period of sexual activity. In addition, 5-ML control upon sexual function depends of seasons. At now, the site of action of 5-ML in the brain of the jerboa remains unknown since 5ML receptors have not yet been determined. To determine the target structure of 5ML and verify if its action depends of seasons we used the expression of c-Fos protein. We also tried to determine the mechanisms by which this pineal hormone may control the reproductive function by measuring gene clock proteins expression - Sixty four adult female jerboas were captured in the field in early spring and transported to the animal facility where they were maintained in natural photoperiod conditions. Animals were fed a diet of grain wheat, sunflower seeds ad libitum and lettuce leaves every 3 days.

At each season, 16 jerboas were divided in 3 groups and subcutaneously injected 2h after sunrise by 5ML (n= 6), MEL (n=6) and controls (n=4). 1h30 min later, brains were fixed and cut in 25µm coronal sections for c-Fos, BMAL1, PER1 and PER2 immunocytochemistry. The results show that 5ML induces c-Fos in the SCN in autumn, when 5ML rhythm is at its maximal expression. In the paraventricular thalamic nucleus (PVT), c-Fos is induced in spring- summer period during which the amplitude of 5ML rhythm is low. In addition, 5ML modulates BMAL1 content in the SCN and PVT during summer and that of PER2 in autumn. In the jerboa, 5ML acts specifically upon the SCN and PVT dependently of seasons. In this specie, the reproductive function may be modulated seasonally via 5ML control on BMAL1/PER2 clock gene proteins in addition to melatonin action.

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Hypothalamic RF-amide Neurons are Critical for the Melatonin Control of Seasonal Reproduction:

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Hypothalamic RF-amide neurons are critical for the melatonin control of seasonal reproduction. Adaptation of reproductive function to the seasonal variations of environmental factors is critical for species perpetuity. Most mammals use the annual variation in day length as a seasonal zeitgeber. Indeed, the photoperiodic message is translated via melatonin, a pineal hormone whose nocturnal secretion increases with night length. It is well established that the annual rhythm in melatonin secretion synchronizes reproduction with seasons but the neuroendocrine pathway involved is still unidentified. Recent data in the literature identified two members of a family of RFamide peptides as being involved in the control of GnRH neuron activity. Kisspeptin (Kp), expressed in neurons of the arcuate nucleus, is a very potent activator of GnRH release and therefore LH/FSH secretion and gonadal activity. RFamide-related peptide 3 (RFRP3), expressed in neurons of the dorsomedian hypothalamus, regulates GnRH neuron activity but has been described as a stimulator or inhibitor according to the species. Recently, using the male Syrian hamster as a model of seasonal rodent, we observed that expression of both Kp and RFRP3 is strongly down-regulated in short day conditions, when animals are sexually quiescent. We demonstrated that this down-regulation is mediated by the large production of melatonin in short days. Finally, we reported that a chronic central infusion of either Kp or RFRP3 in short day sexually inactive hamsters reactivates testicular activity despite photoinhibitory conditions. Notably, the reactivation of the reproductive function by chronic RFRP3 infusion was associated with an increase in Kp expression, suggesting that the Kp neurons might be one relay for the effect of RFRP3 on GnRH neuron activity. In conclusion, our data have set the hypothalamic peptides Kp and RFRP3 as critical components of the neuroendocrine pathway mediating the synchronizing effect of melatonin on reproductive activity. Experiments are in progress to delineate the cellular mechanisms by which melatonin down-regulates these two RFamide peptides.



Alteration of Circadian Rhythms in a NonHuman Primate Model of Parkinson's Disease

Cooper Howard

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The clinical diagnosis of Parkinson disease (PD) rests mainly on the identification of the hallmark motor symptoms related to dopamine deficiency that are a consequence of degeneration of the Substantia nigra pars compacta. Although the major emphasis in research has focused on motor-related problems, there is increasing evidence that non-motor and perhaps non-dopaminergic related symptoms are sometimes present before diagnosis and inevitably emerge and worsen with disease progression. We investigated the alterations of daily and circadian rhythmicity in relation to the appearance and progression of motor deficits and the decrease in brain dopamine levels in a non-human primate MPTP model of PD. A Parkinsonian state was induced in monkeys by treatment with MPTP. Clinical status was evaluated using a Parkinsonian Monkey Rating scale (PMRS), circadian rest-wake activity rhythms were monitored by recording locomotor activity and hormonal rhythms (cortisol, melatonin) assessed from urinary samples. DA function was evaluated using PET scans (C-PE2I, DAT) and post mortem control of TH neurons in the brain and retina. Prior to MPTP treatment, the animals showed robust daily rest-activity rhythms under a light dark (LD) cycle, with precise onsets and offsets of locomotor activity. In a continuous light cycle (LL), monkeys expressed robust circadian rest-activity rhythms with periods close to 24hrs. Following MPTP treatment, daily rest-activity rhythms were similar to pre-treatment, although the level of motor activity generally decreased with less precise onsets and offsets of activity. In contrast, monkeys showed a significant alteration of the circadian rhythmicity in constant conditions (LL) characterized by a varying from a distinct decrease in the amplitude of the rhythm to complete lack of rhythm. Use of a masking paradigm showed that responses to light remained intact and cortisol and melatonin rhythms appeared to persist in MPTP treated monkeys. PET scan and TH immunohistochemistry showed a 70-80% reduction of the dopaminergic system in the striatum but no reduction in the retina. The results of this study show that severe alterations of circadian functions occur after following MPTP treatment and stress the importance of non-motor symptoms in PD.

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Sleep and Infections

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It is common experience to feel “sleepy” during an infection, given that somnolence (increased sleep) characterizes sickness behavior, and some infections lead to sleep disturbances as primary symptom. However, although much knowledge on the multifaceted effects of inflammatory mediators, and especially cytokines, has accumulated, including their effects on sleep, the reciprocal interactions between sleep and infections, as well as the pathogenesis of sleep disturbances during infections still need to be clarified and will be here discussed. Sleep disorders during infections range from insomnia during HIV/AIDS to characteristic alterations of sleep structure and sleep/wake alternation in human African trypanosomiasis (“the fatal sleep” of sleeping sickness). Past and current epidemiological issues recall attention on potential relationships between viral infections, such as influenza, and narcolepsy. Neural dysfunction during infection can be due to inflammatory signalling which involve cytokines, including chemokines, prostaglandins and other molecules, as well as to intercellular dialogue in the brain (neuron-glia, glia-glia, glia-recruited leukocytes). Sequels of infections which implicate sleep disorder could engage autoimmune mechanisms. The potentially selective vulnerability/susceptibility to all such signals of neural cell groups involved in sleep-wake regulation still needs to be unravelled. This would greatly contribute to our understanding not only of pathogenetic mechanisms of specific infections but also of brain functioning in health and disease. On the other hand, sleep has important regulatory effects on the innate and adaptive arms of the immune system, which engage “day workers” and “night workers” cells. The interactions between sleep and infections therefore require attention and interdisciplinary efforts in terms of both basic and translational research.



Symposium 10

Chronic Pain Mechanisms: from Peripheral Determinants to Spinal Cord Integration

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About 6% of the population suffer from poorly treated pain at any one time and mechanically evoked pain sensations are particularly problematic. The unmet clinical needs make chronic pain a major challenge to clinical practice and basic science. In particular, the underlying cellular and molecular mechanisms that cause pain sensitization in pathological conditions are little understood. The present symposium will consider the role of peripheral transduction pathways, and of spinal integration mechanisms, in the onset and maintenance of chronic pain in animal models. Nociceptive neurons encompass an extremely heterogeneous population with respect to their morphological, anatomical, electrophysiological and molecular properties. Over the past three years considerable progress has been made in defining the sensory neuron subsets that respond to different tissue damaging stimuli. However, in spite of the efforts, the functional significance of this remarkable diversity has remained elusive. **John Wood** will first present recent data on the involvement of TRP channels and Piezos in mechanosensation, as well as new findings on the role of voltage gated sodium channels in distinct types of pain sensations. **Felix Viana** will consider other sensory modalities by defining the cellular and molecular determinants of excitability in cold thermoreceptors and nociceptors in different neuropathic pain models. **Aziz Moqrich** will first describe the contribution of his team to the expansion of the repertoire of molecules defining discrete subsets of primary nociceptive neurons. He will then provide hints into how a precise neuronal subtype is generated, how it matures and what kind of particular sensory modalities it perceives.

Nociceptive information is then conveyed to the dorsal horn of the spinal cord. **Sherine Abdel Salam** will show that miR134/LIMK1 modulate the spinal integration of nociceptive inputs through changes of actin turn-over and downstream alterations of AMPA receptors trafficking. Finally, **Marc Landry** will decipher molecular mechanisms that regulate intrinsic properties of spinal neuron excitability, thus controlling the output from the spinal cord to the brain. All studies used a comprehensive set of complementary experimental approaches including electrophysiology, biochemistry, characterization of mutant mouse strains, transcriptomics, and behavioural techniques.



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Peripheral Pain Pathways; Mechanosensory Mechanisms and Molecules

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About 6% of the population suffer from poorly treated pain at any one time and mechanically evoked pain sensations are particularly problematic – for example half the population over 60 have osteoarthritis than can result in mechanically evoked pain. Despite this, the underlying transduction mechanisms that cause mechanically-evoked pain are little understood. Over the past three years considerable progress has been made in defining the sensory neuron subsets that respond to different tissue damaging stimuli. Recent data on the involvement of TRP channels and Piezos in mechanosensation will be presented, as well as new findings on the role of voltage gated sodium channels in distinct types of pain sensations.

Abrahamsen, B., et al The cell and molecular basis of mechanical, cold and inflammatory pain. *Science* (2008)321(5889):702-5 2008

Coste B, et al. Piezo1 and Piezo2 are essential components of distinct mechanically activated cation channels. *Science*. 2010 Oct 1;330(6000):55-60 2010



Functional Characterization of Mammalian Cold Thermoreceptors and Nociceptors

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Application of cold temperatures to the skin can evoke pleasant or painful sensations depending on the temperature reached. Following nerve injury, the thermal threshold for cold pain is shifted to warmer temperatures, a condition known as cold allodynia. The cellular and molecular determinants of peripheral cold sensitivity are still poorly understood, especially under pathological conditions, a situation that merits further investigations.

In trigeminal and dorsal root ganglion neurons in culture we identified a subpopulation of TRPM8-expressing neurons activated by cold temperature and cooling compounds (e.g. menthol). A large fraction of these neurons was also activated by capsaicin, suggesting a possible role in cold nociception. Cold sensitivity was augmented by menthol and reduced by specific blockers of TRPM8 channels. The temperature threshold of different neurons varied over a broad range. Electrophysiological studies established a correlation between the density of TRPM8 channels and cold sensitivity. In addition, a fraction of cold-sensitive neurons expressed a slowly inactivating potassium current operating in the subthreshold voltage range. This current (I_{K_D}) was blocked by α -dendrotoxin and submicromolar doses of 4-AP, characteristic for Kv1 channels. Moreover, pharmacological block of I_{K_D} shifted the threshold of cold-sensitive neurons to higher temperatures and augmented cold-evoked nocifensive responses in mice. Similar behavioural effects of I_{K_D} blockade were observed in TRPA1 KO mice.

Disrupting membrane lipid rafts with methyl- β -cyclodextrin, a cholesterol scavenger, potentiated the activation of TRPM8 channels by cold or menthol. In contrast, preventing glycosylation of TRPM8 channels with tunicamycin had the opposite effect, a strong dampening of cold sensitivity with an average shift of $\sim 6^\circ\text{C}$ in cold threshold. At the biophysical level, the opposite effects on temperature threshold correlated with bidirectional shifts in the voltage-dependent gating of TRPM8 channels.

In summary, cold sensitivity of sensory neurons is determined by multiple mechanisms including: the action of extrinsic modulatory agents, the density of expressed TRPM8 channels, the co-expression of voltage-gated K^+ channels that act as an excitability brakes, the localization of TRPM8 within specific membrane domains and posttranslational modifications. The concerted action of several mechanisms imparts great flexibility to the thermal sensitivity of cold receptors.

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Functional Significance of Nociceptive Primary Sensory Neurons Diversity

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Unravelling the precise *in vivo* function of a particular neuronal subpopulation is one of the most challenging issues in neurobiology. Nociceptive primary sensory neurons represent a powerful model system to address this fundamental question. These neurons convey a large cohort of perceptual sensory modalities including thermal, mechanical and chemical stimuli. Nociceptive neurons encompass an extremely heterogeneous population with respect to their morphological, anatomical, electrophysiological and molecular properties. In spite of the efforts, the functional significance of this remarkable diversity has remained elusive. We have designed a strategy aimed at expanding the molecular characterization of the nociceptive system by identifying new factors expressed in specific subsets of DRG neurons. During my presentation, I will first highlight our contribution to the expansion of the repertoire of molecules defining discrete subsets of primary nociceptive neurons and then I will describe our original and multidisciplinary approach that combines genetic engineering, physiology and behaviour to explore the functional specialization of discrete subsets of nociceptive neurons. Results emanating from this work will provide hints on how a precise neuronal subtype is generated, how it matures and what kind of particular sensory modalities it perceives. In this respect, our work is pioneering in the field. If we know how a precise neuronal subtype is generated, we can subsequently analyse not only basic aspects of its physiology, but also more medically oriented aspects like its functional role under pathological conditions, its chronic changes in response to inflammation and analgesic treatments.



Calcium-Dependent Hyperexcitability of Spinal Neurons

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The maintenance of chronic pain states requires the regulation of gene expression, which relies on an influx of calcium. Calcium influx through neuronal L-type calcium channels (LTCs) play a pivotal role in excitation-transcription coupling, but the involvement of LTCs in chronic pain remains unclear. We used a peptide nucleic acid-based antisense strategy to investigate the role of the LTC subtypes Cav1.2 and Cav1.3 in long-term pain sensitization in a rat model of neuropathy (Spinal Nerve Ligation). Our results demonstrate that specific knockdown of Cav1.2 in the spinal dorsal horn, reversed the neuropathy-associated mechanical hypersensitivity, and the hyperexcitability and increased responsiveness of dorsal horn neurons. We also demonstrated an up-regulation of Cav1.2 mRNA and protein in neuropathic animals concomitant to specific Cav1.2-dependent phosphorylation of the CREB transcription factor. Moreover, SNL animals showed enhanced transcription of the CREB/CRE-dependent gene COX-2, which also depends strictly on Cav1.2 activation.

Next, we addressed a mechanism of regulation of Cav1.2. Translational regulation by microRNAs is a key factor in the expression and function of eukaryotic genomes. We show here, that a single microRNA, miR-103, simultaneously regulates the expression of the three subunits forming Cav1.2-LTC in a novel integrative regulation. This regulation is bidirectional since knocking-down or over-expressing miR-103 respectively up- or down-regulate the level of Cav1.2-LTC translation. In addition, we show that miR-103 knockdown in naïve rats results in hypersensitivity to pain. Moreover, we demonstrate that miR-103 is down-regulated in neuropathic animals and that miR-103 intrathecal applications successfully relieve pain.

Taken together, our data demonstrated that the maintenance of chronic neuropathic pain depends on L-type calcium channels comprising specifically Cav1.2, and that miRNAs can be considered as novel possible therapeutic targets in neuropathic chronic pain.



MiR-134/LIM Kinase1: How Far Can This Duo Modulate Neuropathic Pain?

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Spinal cord lesions may induce severe neuropathic pain. While more than 8% of the world's population suffer from neuropathic pain, the mechanisms underlying this pain remain unclear. The neuronal actin cytoskeleton is critically involved in morphological plasticity and synaptic reorganization acting as a key player in neuropathic pain mechanisms.

LIM Kinase1 (LIMK1) is a protein kinase responsible for actin polymerization by inhibiting Cofilin/ADF (Actin Depolymerisation Factor) activity. LIMK1 expression is controlled by the microRNA, MiR-134 that represses LIMK1-mRNA translation. MiR-134 is considered as a negative regulator of dendritic spine volume and LIMK1 has been reported to promote actin polymerization in dendrites. Moreover, LIMK1/cofilin regulate the insertion and trafficking of the AMPA excitatory glutamate receptors (AMPA) at the synapse. Therefore, it is likely that miR-134/LIMK1 modulates the transmission of nociceptive information in the spinal dorsal horn.

Our objective was to investigate the effects of miR-134/LIMK1 on the reorganization of pain circuits in spinal dorsal horn and on pain sensitization.

Firstly, we investigated miR-134 distribution in the spinal dorsal horn of both sham and neuropathic animals. Then we co-detected miR-134 with different synaptic markers. We showed by qRT-PCR analysis a decrease of miR-134 expression in neuropathic animals when compared to shams which was concomitant with an increase of LIMK1. Animals have also been subjected to intrathecal injection of miR-134 knockdown (miR-134 KD) probes and functional consequences on pain behavior were studied. Interestingly, in these conditions, a significant increase in pain withdrawal threshold (less pain) was observed when tested for evoked (Von Frey test) or spontaneous (dynamic weight bearing test) pain behavior. We also demonstrated the effect of miR-134 KD transfection on the trafficking of AMPAR. Evenly, our preliminary electrophysiological recording showed a significant decrease in minis AMPA' amplitude in the spinal cord superficial laminae after miR-134 KD intrathecal application.

Taken together, our results suggest that miR-134 down regulation in neuropathic conditions exerts an anti-nociceptive role.



Symposium 11

Mapping Brain Activation by Functional MRI and Optical Neuroimaging: Cellular and Vascular Basis and Insights into Brain Function

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Watching the Brain: A Brief Introduction to Issues in Functional Neuroimaging

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Coding in the brain circuits is characterized by distributed spatiotemporal dynamics of activity. A major challenge in the neuroscience field is to image the spatial distribution and follow the temporal dynamics of the activation of large cellular populations in vivo. In this short introduction I will present the different contrast sources that made possible a multifaceted investigation of network activity in vivo and the critical issues to improve these functional recordings.



High-Resolution fMRI of Face- and Object Processing in Awake Behaving Monkeys

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To understand cortical function it is imperative to gain a better understanding of the processes that take place within the cortical ribbon. We investigate how fMRI can be used to study such processes at the scale of cortical layers and columns in the visual cortex of anesthetized and awake macaques. However, achieving this goal also depends on understanding the neural processes that drive the fMRI responses.

To this end we compared BOLD, functional CBV and CBF responses for positive and negative BOLD signals in V1. We found that CBV was increased for both types of responses. Furthermore, the laminar signatures of CBV and CBF for negative BOLD responses were distinctly different, e.g. CBV increased in deep layers and CBF decreased superficially. These differences may allow us to better distinguish cortical processes mediated by the different cortical layers. Also, we showed that functional CBV cannot unambiguously distinguish between stimuli that yield positive and negative BOLD signals. Since CBV fMRI is often used for non-human primates, this can improve the interpretation of CBV-based studies, but also, comparing BOLD and CBV responses might provide a means of separating different cortical processes. The latter is a topic of future study, i.e. what type of processes exactly does the negative BOLD response reflect.

In the temporal cortex, we mapped face- and object selective columns in awake and anesthetized monkeys. High-field fMRI allowed us to map the face-selective network in the entire temporal lobe (including MTL), where we discovered several new face-selective patches, and revealed that the network is to a large extent the same in awake and anesthetized monkeys (opioid anesthesia). We hypothesize that the BOLD signal reflects the ascending input. Further studies, particularly the application of laminar-resolution fMRI to the temporal lobe may reveal the role of the different cortical processes in visual perception and memory.



Functional Connectivity of Prefrontal Cortex in Health and Disease: Insights from functional Near-Infrared Spectroscopy

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Functional near infrared spectroscopy (fNIRS) has gained quite an interest over the last 10 years in cognitive neuroscience studies due to its non-invasive, rapid and unobtrusive nature. Recently several groups including ours have focused their attention to deciphering the prefrontal cortex functional connectivity maps during health and disease. We hypothesized that these connectivity maps can be formed via the use of traffic network engineering with a basis on an information theoretic approach.

Specifically, we were interested in how much information is relayed from a node (a channel of the fNIRS measurements) to the remaining nodes (channels), how much information is carried to a node from the remaining nodes. These two informations (outgoing traffic vs. incoming traffic) can be employed to generate two different connectivity maps and then metrics computed from these maps are used to classify the overall efficiency of information sharing among brain regions.

I will lay out the theoretical background of this method that we call “brain connectivity via traffic engineering” and present convincing data on how it can be exploited to classify healthy from diseased brain (i.e. controls vs. schizophrenics).



Functional Imaging of the Vestibular Cortex using Near-Infrared Spectroscopy

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Functional near-infrared spectroscopy (fNIRS) is a non-invasive brain imaging method that uses light to record regional changes in cerebral blood flow in the cortex during activation. fNIRS uses portable and wearable sensors to allow measurements of brain activation during tasking. In this study, fNIRS was used to investigate how the brain processes information from multiple sensory modalities during dynamic posturography.

Ten healthy volunteers (6M/4F; ages 26 +/- 9 yrs) participated in the posturography study while undergoing fNIRS testing. All posturography was performed using a NeuroCom (Clackamas OR, USA) Equitest™ posturography platform while fNIRS data was recorded. FNIRS signals were recorded during testing of four postural conditions corresponding to SOT I (fixed floor – eyes open in light), SOT II (fixed floor – eyes open in dark), SOT IV (sway-referenced floor – eyes open in light), and SOT V (sway-referenced floor – eyes open in dark). Comparisons among these four conditions allow examination of subject balance and brain responses to the loss of accurate visual and proprioceptive feedback. FNIRS data was recorded using a 32-channel continuous wave fNIRS instrument (CW6 real-time system; TechEn Inc; Milford, MA). The fNIRS bilateral head cap contained 16 detectors and 8 sources two different wavelengths of light at 690 nm and 830nm.

We found there was bilateral activation in the temporal-parietal areas (superior temporal gyrus, STG, and supramarginal gyrus, SMG) when both vision and proprioceptive information was degraded; forcing reliance on primarily vestibular information in the control of balance. This is consistent with previous reports of the role of these regions in vestibular control and demonstrates the potential utility of fNIRS in the study of cortical control of vestibular function during standing balance tasks. We believe that this is the first study to measure vascular brain activity in these areas during computerized dynamic posturography.



Optical Signature Of Olfactory Activation

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Sensory activation of the olfactory bulb in rodents is a relevant model to study mechanisms of brain activation and their link with functional neuroimaging signals. The olfactory bulb includes well-defined functional modules, the olfactory glomeruli, containing high densities of synapses, capillaries and astrocytes. Wide field optical imaging of odor-evoked glomerular activity using optical contrasts make possible the recording of spatiotemporal maps with a spatial resolution of 20 μ m and a temporal resolution of 100ms. The study of complementary physiological signals such as local changes in tissue oxygenation, blood volume, blood flow or mitochondrial flavoproteins fluorescence provides new insights both into brain energetics and functional neuroimaging signals.

In order to record activation maps either sequentially or simultaneously during a single activation, we have developed a multimodal wide field macroscope that encompass a high speed spectral source (450-700nm) based on digital micro-mirrors, a modulated laser diode (680nm), CCD or CMOS cameras with high sensitivity and high frame rate, a custom built olfactometer, and a microcontroller module for hardware synchronization. In this context, the chronic cranial window, photon path-lengths calculation in turbid media, and wavelengths optimization for multispectral imaging are among the methodological issues that have been solved.

We have successfully recorded the first flavoprotein fluorescence maps following activation of the olfactory bulb in the anesthetized rodent. Dynamic maps of the relative changes in oxy-hemoglobin, deoxy-hemoglobin, blood volume and blood flow have also been recorded for the first time in the olfactory bulb and in response to increasing odor stimulus intensity. These odor-evoked hemodynamic patterns were found to be concentration-dependent and differ significantly from those observed in the somatosensory cortex. Future work will focus on understanding such dissimilarities which could arise either from physical causes related to light absorption and diffusion in tissues, or from physiological differences between the functional architecture of the olfactory bulb and the somatosensory cortex.



Symposium 12

Serotonin Implication in Neuropsychiatric Disorders: A Translational Approach

Giuseppe Di Giovanni, Philippe De Deurwaerdère

Serotonin (5-hydroxytryptamine; 5-HT) participates in a multitude of brain functions probably due to its wide-spread distribution in the CNS of mammals. It is not surprising therefore that abnormal 5-HT transmission is involved in various neuropsychiatric diseases and the aim of this symposium is to present a thorough examination of the 5-HT mechanisms underlying some of these pathologies. Recent studies have underlined the influence of 5-HT neurons in Parkinson's disease. Notably, impairment of 5-HT neurons in a rat model of the disease may promote non motor symptoms including anxiety and depression together with alterations of discharge frequencies of neurons in the basal ganglia (Dr C **Delaville**, France/USA). Obsessive compulsive disorders are cognitive alteration involving aberrant 5-HT transmission. 5-HT drugs are considered as potential treatments of the disease in clinics (Pr J **Zohar**; Israel). Indeed, behavioural studies in rodents have stressed the role of cortical 5-HT in cognitive flexibility and response inhibition via a distinct role of 5-HT_{2A} and 5-HT_{2C} receptors (Dr V **Boulougouris**, Greece). This is consistent with the general view that 5-HT and 5-HT_{2C} receptors control neuronal network excitability. This has been evidenced in epilepsy by data showing that 5-HT_{2C} receptors suppress neuronal network hyperexcitability and seizure activity (Pr G **Di Giovanni**, Malta). Molecular and cellular data also support a role for 5-HT and 5-HT_{2C} receptors in modulating K⁺-channels (Dr M **Pessia**, Italy).

Combined, these preclinical and clinical data show a collective effort and distinct research strategies to further understand the implication of 5-HT in neuropsychiatric disorders.



Serotonin and Noradrenalin Depletions Can Promote Anxiety and Depression in a Rat Model of Parkinson's Disease: An Electrophysiological and Behavioural Study

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The loss of dopamine (DA) neurons has been the pathophysiological focus of the devastating motor conditions of Parkinson's disease (PD). Beyond DA, PD is a multi-system disorder characterized also by the loss of serotonin (5-HT) neurons from the dorsal raphe nucleus and noradrenalin (NA) neurons from the locus coeruleus. 5-HT and NA are widely recognized in the development of depression and anxiety and both symptoms are reported with a high prevalence in PD patients. However, a specific role for each neurotransmitter in the pathophysiology of PD is not clearly determined.

Here, we investigated, in rats, the respective influence of DA, 5-HT and NA depletions on motor and non-motor behaviors as well as on the neuronal activity measured in vivo by single cell extracellular recordings in subthalamic (STN), globus pallidus (GP) and substantia nigra *pars reticulata* (SNr). DA, 5-HT and NA depletions were achieved by using classic protocols with 6-hydroxydopamine/desipramine, parachlorophenylalanine and DSP-4, respectively. We showed that NA or DA, but not 5-HT depletion significantly decreased locomotor activity and enhanced the proportion of bursty and irregular STN neurons. Anxiety-like states required DA depletion plus the depletion of 5-HT or NA. Anhedonia and "depressive-like" behavior emerged only from the combined depletion of all three monoamines, an effect paralleled by an increase in the firing rate and the proportion of bursty and irregular STN neurons. As for the STN, DA depletion increased the proportion of bursty neurons in GP and SNr. 5-HT, but not NA depletion modified GP and SNr neuronal activity.

Thus, our data show that 5-HT and NA modulate specifically the basal ganglia activity and provides evidence for the exacerbation of behavioral deficits when 5-HT and/or NA depletions are combined with DA depletion. These data bring up new insight into the influence of 5-HT system in non-motor symptoms of PD.



Serotonergic Modulation of Cognitive Flexibility in Rodents

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Cognitive flexibility is dependent upon the orbitofrontal cortex (OFC). Serotonin (5-HT) is strongly implicated as well. However, there is little information on the role of different 5-HT receptors in reversal learning. This presentation will show a series of experiments in rodents implicating specific 5-HT receptors in the same ability. Specifically: Experiments 1-2 investigated the effects of systemic administration of the 5-HT_{2A} receptor antagonist M100907 and the 5-HT_{2C} receptor antagonist SB242084 on an instrumental two-lever spatial discrimination and serial spatial reversal learning task. Experiments 3-8: The effects of SB242084 and M100907 infusions within the OFC, medial prefrontal cortex (mPFC) and nucleus accumbens (nAc) were examined in the same task.

Experiments 1-2: Neither M100907 nor SB242084 altered performance during spatial discrimination and retention of the previously reinforced contingencies. M100907 significantly impaired reversal learning by increasing both trials to criterion (only at the highest dose) and incorrect responses in Reversal 1, a pattern of behaviour manifested as increased perseverative responding on the previously reinforced lever. In contrast, SB242084 improved reversal learning by decreasing trials and incorrect responses to criterion in Reversal 1, with significantly fewer perseverative errors. Experiment 3-5: Infusions of SB242084 within the OFC, but not mPFC or nAc, dose-dependently facilitated reversal learning in the same way as in Experiment 2. Experiments 6-8: No effects were noted with infusions of M100907 within the same three brain regions.

These data support the view that 5-HT_{2A} and 5-HT_{2C} receptors have distinct roles in cognitive flexibility and response inhibition, contrasting with published data on impulsive responding. The improved performance in reversal learning observed following 5-HT_{2C} receptor antagonism suggests these receptors may offer the potential for therapeutic advances in neuropsychiatric disorders where cognitive deficits are a feature, including OCD, and that this effect may be mediated by 5-HT_{2C} receptors within the OFC.



Role of Serotonin in Epilepsy: Focus on 5-HT₂ receptors

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Studies in experimental models have showed a potential role for serotonergic transmission in epilepsy, suggesting serotonin receptors (5-HTRs) as promising candidates as a target for new antiepileptic drugs. Indeed, 5-HT is known to regulate a wide variety of focal and generalized seizures, including absence epilepsy both in human and in animal models. In particular, agents that elevate extracellular 5-HT levels, such as 5-hydroxytryptophan and 5-HT reuptake blockers, inhibit both focal (limbic) and generalized seizures. Conversely, depletion of brain 5-HT lowers the threshold to audiogenically, chemically and electrically evoked convulsions. More recently, increased threshold to kainic acid-induced seizures was observed in mice with genetically increased 5-HT levels. The serotonergic system is very complex and several receptor subtypes may be relevant to epilepsy. At least 14 distinct G protein-coupled 5-HTR and one ligand-gated ion channel receptor (5-HT₃) are divided into seven distinct classes (5-HT₁ to 5-HT₇). 5-HT_{2A/2C}Rs are the major focus of this talk. Early findings showing that mice lacking the 5-HT_{2C}R are extremely susceptible to audiogenic seizures and are prone to spontaneous death from seizures will be presented together with new experimental evidence in different animal models of epilepsy. Thus, serotonergic neurotransmission mediated by 5-HT_{2C}R subtype suppresses neuronal network hyperexcitability and seizure activity.



Role of Potassium Channels in Serotonin Receptor Signalling: Implications for Psychiatric Disorders

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Serotonin (5-HT) has been implicated in the aetiology of many psychiatric illnesses and in psychotomimetic effects of hallucinogens. 5-HT binds to a plethora of receptors (Rs) that belong to the superfamily of G protein-coupled receptors (GPCRs), except the 5-HT₃ subtype which is a ligand-gated cation channel. 5-HTRs represent today the most common cellular targets for therapeutic drugs in neuropsychiatry. The classical view of functional monomeric GPCRs has recently been changed by compelling evidence suggesting that GPCRs function in vivo as homodimers and/or heterodimers and that this also applies for 5-HTR. 5-HT produces complex electrophysiological effects modulating membrane conductance, especially acting at potassium channels. Indeed, K⁺ selective ion channels regulate numerous and heterogeneous neuronal functions including action potential duration, neurotransmitters' release and cell excitability. In particular, K⁺ currents play a key role in the flexible properties of intracortical axons and contribute significantly to intracortical processing. Blockade of K⁺ channels is part of the mechanism underlying 5-HT-induced glutamate release from thalamocortical terminals. Furthermore, 5-HT receptors control the excitability of dopaminergic neurons from the ventral tegmental area and substantia nigra by modulating K⁺ conductance. In heterologous expression systems, the serotonergic regulation of human K⁺ channel activity involves the dual coordination of both RPTP and specific tyrosine kinases coupled to the 5-HT_{2C} receptor. The major focus of this talk is to report recent evidence on the molecular identity of distinct 5-HT receptors, the regulation of CNS circuitries by means of K⁺ conductance modulation and to provide an overview of new therapeutic targets for psychiatric disorders.



Plenary Lecture 5

Understanding Actions, Intentions and Emotions of Others

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An exciting discovery in neurosciences over the last years has been that of a mechanism that unifies action perception and action execution. The essence of this mechanism –the mirror mechanism- is the following. Each time individuals observe an action done by others, a set of neurons that code that action are activated in the motor system. Since the observers are aware of the outcome of their motor acts, they also understand what the others are doing without the necessity of an intermediate cognitive mediation. In my talk, I will present first some new discoveries on the mirror mechanism in the monkey. I will present then evidence that humans possess the mirror mechanism and that the anatomical location of parieto-frontal mirror networks of the monkeys and of humans closely coincide. Subsequently I will discuss the limits of the mirror mechanism in understanding others. I will stress that the parieto-frontal mirror mechanism is, however, the only mechanism that allows a person to understand others' actions from the inside giving the observing individual a “first-person” grasp of other individuals' motor goals and intentions.



Plenary Lecture 6

Reward, Risk and Neuroeconomic Decision Making

Wolfram Schultz

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Rewards produce learning (positive reinforcement), approach behaviour and positive emotions (pleasure, desire). We investigate basic neuronal reward processes using neurophysiological and neuroimaging methods. Dopamine neurons are activated by rewards and reward prediction stimuli. The signal reflects reward prediction error which represents a crucial signal for learning. As electrical and optogenetic activation of dopamine neurons elicits learning and approach behaviour, the data suggest a role for dopamine neurons in reward processing. Rewards can be viewed as probability distributions of reward values. The key parameters defining probability distributions are expected value and standard deviation, which in economics is also referred to as 'risk'. This definition leads to the common notion of risk as probability of losing by considering nonlinear subjective value functions and their notable asymmetry (loss avoidance). Value and risk are fundamental variables for economic decision making. Neurons in specific reward centres of the brain process reward value and risk in distinct forms. These responses increase monotonically with higher standard deviations of binary equiprobable distributions of reward magnitudes. The terms 'risk aversion' and 'risk seeking' indicate that risk influences the subjective valuation of outcomes; this concept constitutes a basic tenet of economic utility theory. As neuronal correlate, risk enhances neuronal value responses in lateral frontal cortex of risk seekers.



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Symposium 13

Towards New Therapies in Stroke Rehabilitation

M. Sahiner (Turkey) & G. Hoogland (The Netherlands)

Chaired by: **G. Hoogland**, Department of Neurosurgery, Maastricht University Medical Center, Maastricht, the Netherlands and **M. Sahiner**, Department of Physiology, Acibadem University, Istanbul, Turkey



Nutraceuticals for stroke protection: A focus on α -linolenic Omega-3 Fatty Acid

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Stroke is the third leading cause of death, due to its high incidence and the severity of the insult. Restoration of cerebral blood flow is achieved only in ~5% of patients by recombinant tissue plasminogen activator treatment. Numerous therapeutics identified in preclinical studies aimed at blocking the ischemic cascade failed in clinical trials. This failure in translation from preclinical stroke models to clinical trials has led to a re-evaluation of properties required for therapeutics against stroke to achieve “best-in class” status. Since neuroprotection alone appears ineffective, an emerging direction is to seek drugs which are mechanistically combinatorial in nature, which could protect the whole neurovascular unit and target time-dependent neurotoxic mechanisms. This capability exists with preconditioning, with research efforts directed to interrogate how the brain protects itself and to discover new molecules that render the brain resistant to subsequent ischemia. Preconditioning elicits complex endogenous neuroprotective responses that act by pleiotropic mechanisms to block death pathways, promote survival pathways and increase resistance. In addition to chemical preconditioners, natural/endogenous compounds - such as the omega-3 polyunsaturated fatty acid, alpha-linolenic acid (ALA) - has been demonstrated to be excellent preconditioners. Nutraceuticals are a major new concept in preconditioning to combat stroke, in which brain preconditioning is achieved through supplementation of an essential item in the diet. A nutraceutical is the combination of “nutrition” and “pharmaceutical”, as defined in 1989 by Stephen DeFelice to promote the concept of foodstuffs as therapeutics, which demonstrate reasonable clinical evidence of medical benefit, but cannot be claimed as such to the public under present regulatory policy. It is therefore required to narrow the concept of nutraceuticals to a single compound purified from foods that provides protection against disease; such compounds may be sold in medicinal forms not usually associated with food to evaluate nutraceutical efficiency as a drug at the preclinical level, with eventual translation to the clinic or daily life. Consequently, evaluating ALA as an interesting preconditioner against stroke represents a novel view in the context of nutraceutical and functional foods.

The surprising pleiotropic properties of ALA to trigger responses that are multi-cellular, mechanistically diverse and with a wide temporal range mirror those responses typically elicited by preconditioning, resulting in neuronal protection, and brain artery vasodilation and neuroplasticity stimulation. In addition, ALA supplementation by modification of the daily diet prevented MCAO-induced mortality and cerebral damage in animal cerebral ischemia models, essentially evading the problem of delivery to the brain, which has normally to be addressed for chemical drugs. Inclusion of omega-3 prophylactically in the diet may induce a preconditioning effect, circumventing what is probably the major barrier in the field, which is timely delivery of a therapeutic (“time is brain”). Ultimately, the future of preconditioning may largely depend not only upon its successful translation to the clinical arena, but also to daily life. This novel concept of nutraceutical preconditioning may not be restricted to omega-3 PUFAs such as ALA, but may in fact extend to other existing or novel nutraceuticals.

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In vivo brain repair? Electrical Fields Attract Newborn Brain Cells

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Neurogenesis is known to occur at the subventricular zone (SVZ), where the highest number of stem/progenitor cells in adult brain are hosted. Following proliferation in the SVZ, newborn cells mainly migrate rostrally towards the olfactory bulb. Although specific factors influencing the neurogenesis have been identified, tools controlling the direction of migration of newborn cells are not available. We applied electrical fields (EFs) to the rat motor cortex. Results showed a striking increase cell proliferation in the SVZ following cortical EFs. We also found a remarkable increase in the number of BrdU-positive cells in the area below the electrodes. Furthermore, double labeling of cortical BrdU-positive cells with NeuN showed that newborn SVZ cells not only migrate to the cortex, but also differentiate into mature neurons. Finally, based on the fact that subependymal 5-hydroxytryptamine (5-HT, or serotonin) plexus overlaps with the SVZ neurogenic area and the existing knowledge of the effects on 5-HT on neurogenesis,



we proposed that enhanced 5-HT in the SVZ could be responsible for the proliferation boost following cortical EFs. Intriguingly, we found clearly enhanced density of the serotonergic fibers in the SVZ and a concurrent increase in neuronal activity in the dorsal raphe nucleus (DRN), the brain's main serotonergic nucleus. Our findings reveal a novel approach to influencing the proliferation and migration of the adult brain's progenitor cells. We showed that the application of specific electrical fields can direct migration of newborn brain cells from the SVZ to the area of interest. In addition, our results suggest that this process to be coordinated by altered serotonergic input to the SVZ. We propose the possibility of cortical brain repair after epidurally applied electrical fields based on the existence of electrotaxis of newborn brain cells.

Stroke awareness in the Saudi community: Prompt Public Health Measures Must be Implemented

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Background Stroke is very prevalent in the Kingdom of Saudi Arabia, approaching 43.8 per 100,000 population. Stroke outcome is known to be affected by the level of stroke awareness in the community. We conducted this study to assess the level of stroke awareness in the Saudi population.

Methods A survey of 21 questions, pertaining to stroke awareness (stroke symptoms, and signs and stroke risk factors), was distributed to Saudi population (aged 15-70) in malls, super markets, health clubs, mosques, universities and schools.

Results 2862 (82% response rate) completed the questionnaire. 1844 (64%) were able to define stroke correctly. 1428 (49.9%) named mass media as the source of their knowledge. 1301 (45.9%) believe stroke and brain death share the same pathological mechanism and outcome, particularly those under the age of 40 ($p < 0.05$). Only a small proportion was able to identify stroke risk factors (hypertension 957 (33.4%), diabetes mellitus 482 (16.8%), tobacco smoking 1065 (37.2%), dyslipidemia 889 (31.1%), old age 971 (33.9%), heart disease 1161 (40.6%), ethnicity 109 (3.8%), obesity 718 (25.1%) Additionally, a smaller proportion was able to recognize stroke symptoms and signs (speech difficulty 1321 (46.2%), blurred vision 1114 (38.9%), dizziness 759 (26.5%), numbness 534 (18.7%), focal weakness 1303 (45.5%).

Conclusion There is an alarming deficit in the level of stroke awareness in the Saudi population. Urgent public health measures to correct this deficiency, that will match the rate of similar countries, is promptly needed.



Symposium 14

Molecular and Behavioral Aspects of Lead Neurotoxicity

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The aim of the proposed symposium is to address the issue of lead (Pb) toxicity, and particularly its effects on central nervous system (CNS). Being a xenobiotic metal with no known essential function, Pb is very toxic, and there are several reports showing that death occurs in workers who are exposed to high or moderate levels of Pb particularly in mining and in Pb manufacturing. Moreover Pb alters brain function, and there is increasing body of evidence that Pb affects neurotransmitter systems. During this symposium (i) **Prof. Azeddine Sedki** will talk about the dietary/nutritional risk factors in children and young women for chronic lead poisoning in an urban setting in Morocco (ii) **Prof. Ahmed Ahami** will talk about the behavioral consequence of Pb neurotoxicity on mnemonic ability in the human and animal. (iii) To understand the mechanisms by which Pb affect neurotransmission, **Prof Dietrich Büsselberg** will talk about Pb interaction within the synapse and how Pb impair synaptic plasticity by targeting molecules such as calcium/calmodulin, protein kinase C, and nitric oxide synthase as well as the transcription machinery involved in the maintenance of synaptic plasticity. (iv) Finally, Pb effects on neurotransmission seem to be triggered through other mechanisms that **Dr. Samir Ahboucha** will address as well as potential therapeutic strategies.



Lead Exposure in the Environment and Human Population in Morocco

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Coexisting chronic lead poisoning and iron deficiency anemia are common in urban areas in developing regions, particularly in young children and pregnant women. Globally, it is estimated 40% of children worldwide have elevated blood lead levels $>5 \mu\text{g}/\text{dL}$. The adverse outcomes attributable to lead poisoning are 12.9 million DALYs, representing 0.9% of the global burden of disease, due to impaired cognitive development and reduced school performance; thus, these disorders have substantial health, social and economic costs. Elevated body lead levels are common in Moroccan infants and young children, and there are a large number of potential sources for dietary and environmental lead exposure. The relative contribution of different routes or sources to human lead poisoning can be identified on the basis of the individual's blood lead isotope ratio. Nutritional status plays a role in altering susceptibility to lead absorption and toxicity, and absorption of lead is increased in children with iron deficiency. Thus, iron fortification may be an effective and sustainable strategy to accompany environmental lead abatement. Morocco is currently introducing a national food fortification program that includes iron fortification of wheat flour. The optimal iron fortificant for wheat flour fortification is currently debated, and although elemental iron compounds are commonly used (and have been proposed for the Moroccan program), they may be only poorly absorbed in the face of inhibitory compounds found in whole wheat. Sodium iron ethylene diamine tetraacetic acid (NaFeEDTA) is a promising iron fortificant and metal chelator, and it has been recently recommended for wheat flour fortification. It may be superior to other iron fortificants in its ability to reduce body lead burden, due to: 1) its iron is highly bioavailable in the face of dietary inhibitors; and 2) potentially, its ability to chelate lead in the gut and bloodstream. The aim of this work is to investigate dietary/nutritional risk factors in children and young women for chronic lead poisoning in an urban setting, and in particular, the role of iron and zinc deficiency.



Impact of Lead Sub-Chronic Toxicity on Recognition Memory and Motor Activity

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The aim of this research was to investigate the impact of lead nitrate administered in drinking water during 90 days (sub-chronic toxicity), on body weight gain, motor activity, brain lead accumulation and especially on recognition memory of Wistar rats. Two groups of young female Wistar rats were used. Treated rats received 20 mg L⁻¹ of lead nitrate diluted in drinking water, while control rats received drinking water only, for 3 months. An evolution of body weight, motor activity, object recognition memory and measure of brain lead levels has been evaluated. The body weight was taken weekly, whereas the memory abilities and the motor activity are measured once every fortnight alternatively, by submitting rats to the Open Field (OF) test and to the Novel Object Recognizing (NOR) memory test. The results have shown a non significant effect in gain of body weight. However, a high significance was shown for horizontal activity ($p < 0.01$), long memory term ($p < 0.01$), at the end of testing period and for brain lead levels ($p < 0.05$) between studied groups.



Synaptic Mechanisms of Lead Neurotoxicity

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Numerous health risks are associated with chronic exposure to metallic compounds. Particularly lead (Pb²⁺) has been demonstrated as a potent neurotoxin which severely impairs in vivo cognitive functions at concentrations lower as 2.5 micrograms/dL. Synaptic transmission is not only crucial for transmitting action potentials, but also for learning and memory processes through the induction of long term potentiation (LTP). With the presence of lead, LTP is impaired, and there is an enormous body of evidence published in several reviews. Here, the cellular mechanisms will be highlighted and the major pre- and post-synaptic target sites will be identified. Lead (Pb²⁺) directly affects neurotransmission by binding to specific (calcium-) target sites at the pre-synaptic and post-synaptic terminals. These target sites include: (i) voltage-gated calcium channels (VGCCs); (ii) calcium-dependent proteins (e.g. transporters) and the associated pathways and (iii) receptor gated channels like the N-methyl-D-aspartate (NMDA) receptor/channel complex. Presynaptically voltage gated calcium channel currents are impaired by Pb²⁺ and thus lowers the elevation of the intracellular Ca²⁺ concentration. Despite the ability of Pb²⁺ to reduce calcium currents through VGCCs, however, Pb²⁺ might be able to enter the neuron through this gate. Lead modifies the subsequent neurotransmitter release via inhibition of signaling pathways and finally the fusion of synaptic vesicles with the pre-synaptic membrane is impaired. Postsynaptically Pb²⁺ binds to receptor gated channels, especially the NMDA receptor channel complex and, therefore, reducing the Ca²⁺-entry. Overall, a postsynaptic depolarization is less likely to reach the threshold to generate action potentials. Consequently processes depending on calcium entry (like the long term potentiation) are impaired. Taken together, lead impairs synaptic function which is at least one reason why lead causes learning and memory impairment.



Pb Neurotoxicity and Neurotransmission: Behavioral and Therapeutic Aspects

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Heavy metals such as lead (Pb) are environmental toxins the effects of which can affect brain function. These neurotoxins can accumulate in particular brain regions and induce brain changes during development and in adults. Indeed, some of them have been associated with neuronal and glial dysfunctions, and neuronal changes have been suggested to affect several neurotransmitter systems including the serotonergic (5-HT), and the dopaminergic (DA) systems. Effect of lead on neuronal function may affect long term potentiation with consequences on locomotor and mnemonic performances. Recent studies performed by our group evaluate the glial and neuronal system changes following Pb intoxication during development and in adult male Wistar rats. These studies have demonstrated that Pb intoxication induce glial changes (gliosis) assessed immunohistochemically by the glial fibrillary acidic protein marker and neuronal change of several neuronal systems including the DA and 5-HT. There is also evidence that the effects of Pb intoxication on glial and neuronal changes were more severe in the animals treated since intrauterine age, supporting thus the view of vulnerability to these neurotoxins at early developmental stages. Potential therapeutic strategies against lead neurotoxicity may involve the use of natural compounds such as olive leaf extract that reduces apoptosis and inflammation or drugs that restores chronic lead exposure-impaired long-term potentiation.



Symposium 15

Alzheimer's disease: shift in focus

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The aim of this Symposium is to illustrate the growing consensus on the need to focus towards discovery of the biomarkers for the diagnosis of Alzheimer's disease during its long preclinical phase. The underlying idea is not to teach the patients bad news earlier, since the cure for this neurodegenerative disease is not available, but rather to propose the reinforced prevention to the subjects at risk. Indeed, animal studies have indicated that the strategies such as regular physical/cognitive activities and limited caloric restriction appear efficient in delaying the onset and progression of Alzheimer-like pathology.

The symposium will start with the presentation by Dr Carole Rovère who will illustrate the physiological role of cytokines and chemokines (e.g. TNF-alpha and MCP-1) and how this physiological role shift in pathology towards the neuroinflammation.

Next, Dr Aline Stéphan will comment on the early functional impairments associated with amyloid-beta, the causative factor of Alzheimer's Disease. These impairments involve altered rhythmic activity of hippocampal GABAergic neurons, responsible for the propagation of the theta oscillations, and their relation to the subtle cognitive impairments.

Prof Sylvain Williams will report on the very first electrophysiological impairments (theta/gamma oscillation uncoupling) that may turn out to be useful biomarkers for preclinical stage of Alzheimer's Disease and how they may be related to the biochemical alterations such as extremely early increase in hippocampal TNF-alpha.

The Symposium will close by the presentation from Prof Denis Guilloteau who will expose the new developments in molecular imaging as biomarker including amyloid plaques and neuroinflammation.



Role of Cytokines and Chemokines in Neuroinflammatory Diseases: Possible Therapeutic Targets?

Carole Rovère

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Inflammation is a key component of host defense responses to infectious agents and injury, but it is also recognized as a major contributor to diverse acute and chronic central nervous system disorders. Inflammatory molecules trigger the recruitment of immune cells to the lesions sites. Accordingly, in acute brain trauma, such as stroke, as well as during chronic affections like multiple sclerosis or Alzheimer's disease, inflammation occurs in order to clean up the lesion and to limit its area. Nevertheless, prolonged or overwhelming inflammation displays cytotoxic effects, aggravating the severity of the disease. Among molecules produced during inflammation associated to neuronal death, the pro-inflammatory cytokines, interleukin-1 beta, interleukin-6 and Tumor Necrosis Factor alpha and chemokines such Monocyte Chemoattractant Protein-1 seem to be particularly important.

Several studies have demonstrated that these inflammatory factors are not only expressed in neuroinflammatory conditions but are also constitutively present in the brain in both glial cells and neurons in physiological conditions. After stroke injury, peripheral blood cells produce pro-inflammatory cytokines, which induce adhesion molecules expression, recruitment of immune cells into the parenchyma and immune and glial cells activation. Therefore, recent studies attribute the detrimental role of cytokines in stroke to their massive increase in plasma, although the potential contribution of neuroinflammation to stroke has not yet been clearly investigated. With respect to chronic neuroinflammation, a critical role of cytokines and chemokines has been established in animal models of multiple sclerosis. Besides, Alzheimer's disease is characterized by senile plaques surrounded by many activated immune cells producing a large number of inflammatory-related molecules such as cytokines and chemokines.

Although considerable data suggest that inflammation contributes to many brain pathologies, and therefore represents a plausible therapeutic target for intervention, the dual potential in promoting beneficial but also detrimental effects complicates the development of therapies.



Amyloid Beta–induced Alteration of the Hippocampo-septal Pathway: Consequences for Hippocampal Network Activity and Memory

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Hippocampal network dysfunction largely contributes to the early memory deficits associated with Alzheimer's disease (AD). Because distinct classes of GABAergic neurons modulate differently the glutamatergic pyramidal cell activities in this structure, identifying the vulnerability of specific hippocampal interneurons in early phase of AD would improve our understanding of the progression of AD-related cognitive disturbances. Using the injection of a combination of amyloid beta peptides into the hippocampi of healthy adult rats to mimic the seeding amyloid aggregates, we have established that injected rats present a specific reduction of Calbindin- and Calbindin/Somastostatin -positive neurons in CA1, that are main component of the hippocampo-septal projection. This indicates the loss of an inhibitory input to the septohippocampal network concomitantly with intrahippocampal Amyloid beta (A β). We furthermore observed that intrahippocampal A β depositions weaken and detune theta oscillatory activity in the dorsal hippocampus of rats during recognition memory recall. This effect seems to be due to their impact on the physiology of medial septal neurons. Indeed, the activity of the rhythmic-bursting GABAergic neurons at the septal level is largely reduced and these neurons are the ones phase-locked to the hippocampal theta rhythm. This demonstrates that intrahippocampal A β induce aberrant septohippocampal network oscillatory activity and strongly points the back hippocampo-septal projection neurons as a vector for alterations of hippocampal theta oscillations during exploration and recall. Finally our findings that the highly interconnected hippocampo-septal neurons are damaged after hippocampal amyloid pathology corroborates the observation in human studies that interconnected neural networks with the higher densities of connectivity, are also more vulnerable to dysfunction in AD.



Very Early Changes in Hippocampal Network Rhythms Before A β Appearance in an Alzheimer Mouse Model

Sylvain Williams

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One of the most important symptoms of Alzheimer's disease is a dramatic reduction in episodic memory, a task dependent on the hippocampus. These symptoms occur usually later in life but the underlying neuronal changes probably developed over decades. There is now more emphasis in the Alzheimer's disease field to find very early biomarkers of the disease so that an effective pharmacological approach may be used to prevent the occurrence of disease or slow down the disease process. There has been suggestion that early alterations of hippocampal networks might lead to perturbations of hippocampal oscillatory activity which are essential for episodic memory. Brain oscillations in the theta (3-12Hz) and gamma frequency bands (30-250Hz) are crucial for supporting normal cognitive and executive functioning. Moreover, it was recently found that the magnitude of the coupling between these two oscillations (or coupling strength) was positively associated with memory in humans and in rats. Therefore, hippocampal oscillations might be altered in the early stage of AD. In this presentation, I will show evidence in a mouse model of AD (CRND8 mice), that high-gamma frequency band (200Hz) becomes uncoupled to theta frequency oscillations in the subiculum, the main output region of the hippocampus. I will show some of the physiological consequences of this uncoupling and suggest how alterations of GABAergic interneurons may be responsible in this process. The results provide indications that theta-gamma uncoupling may be an early biomarker in AD.



Molecular Imaging for Amyloid Plaques and Neuroinflammation

Denis Guilloteau

CHRU Tours, France

The strength of imaging techniques for early diagnosis is based on the fact that significant modifications (increase or decrease) of molecular targets occur before the appearance of clinical signs. It would constitute a major progress if diagnosis of neurodegenerative diseases could be made prior to the appearance of clinical symptoms. Molecular imaging also enables the optimization of drug therapy by imaging the drug effects at molecular and cellular level as well as by the assessment of disease progression with and without therapy. The first step of the molecular imaging is to choose the relevant molecular target to explore the disease.

New diagnostic criteria for AD that have been recently proposed, suggest that both diagnostic of “prodromal AD” (also called “Mild Cognitive Impairment (MCI)”) should rely on the use of in vivo biomarkers of amyloid pathology such as PET imaging using ligands of amyloid plaques. We will report our promising results using ¹⁸F-AV45 (Florbetapir) in order to distinguish AD but also MCI patients from healthy controls. However the usefulness of these radiotracers may be limited as amyloid plaques do not appear in the early stages of the disease and as in advanced stages the load of amyloid seems to be in “plateau” and not correlated with the severity of the disease.

Other targets appear to be very exciting and may be more relevant, such as neuroinflammation. Preliminary results using a new radiopharmaceutical (DPA-714) to visualize the translocator protein 18 kDa (TSPO), targets which are up-regulated in pathological conditions coincidentally with microglial activation, will be discussed.



Symposium 16

Synaptic Plasticity in Learning and Memory: Experimental and Computational Approaches

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One of the most fundamental challenges facing neuroscience research is to understand the mechanisms of brain plasticity. Synaptic plasticity is a key concept brain research. This concept sheds light on synapses' formation, maintenance and modification. This requires using multidisciplinary approaches ranging from neuroanatomical and neuronal recording studies to computational studies. Such approaches allow us to examine a wide variety of phenomena associated with learning and memory at all levels of complexity, ranging from molecules, synapses, cells, neuronal ensembles, and neural systems, to the behavior of the whole animal. In our symposium, we will point out several studies that had been done concerning the neural basis of plasticity, learning and memory using multidisciplinary approaches. The main questions still remain; what are the effectors of synaptic plasticity? And how can we go further beyond what is already known, nowadays?



Evaluation of Lithium Chloride Treatment on Brain and Synaptic Plasticity

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The brain is often exposed to oxidative stress. Certain brain and nervous system diseases involve free radical processes and oxidative damage. Lithium chloride (LiCl) treatment for neural diseases, such as manic depressive disorder, causes impairment of anti-oxidative defense and alters energy and amino acid metabolism of the brain. By evaluating the effect of several doses of LiCl on some neurotransmitters and oxidative enzymes in rat brain, we found that LiCl significantly reduced NO levels as compared with controls and that Vitamin C succeeded to reduce its noxious effects on experimental animals, except in the case of high doses of treatment. However, by treating with Lithium Carbonate, we suggest that it has a major impact on the prophylaxis and treatment of mania and bipolar disorder. We present here the first evidence that lithium treatment disrupts behavioural and electrophysiological indicators of hippocampal functions *in vivo*. In lower concentrations, which may be accepted in the therapeutic range, lithium treatment increased swimming speed, producing better performance to learn the place of the hidden platform in Morris water maze. Spatial memory disruption was also observed in therapeutic dose of lithium. Although basal synaptic activity in the DG is strengthened in rats treated with lower doses of lithium, they showed LTP depression, which did not reach significant difference from control rats. In toxic concentrations, LTP depression was obvious although the strengthened basal synaptic activity and the regular Morris water maze performance. Molecular studies are needed to explain lithium effect on hippocampal synaptic plasticity.



Spatial Distribution of FGFR2 in Normal and Lesioned CNS of the Urodele Amphibian *Pleurodeles waltlii*

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Fibroblast Growth Factors (FGFs) have been implicated in numerous cellular processes including proliferation, migration, differentiation and neuronal survival. One of these growth factors, Fibroblast Growth Factor-2 (FGF-2), is apparently implicated in the ability of the adult salamander (*Pleurodeles waltlii*) to recover locomotion following complete transection of the spinal cord. In a previous study, we reported up-regulation of FGF-2 during regeneration of damaged axons and recovery of hind limb locomotion. Here we investigated the spatial distribution of FGFR2 – one of the receptors that mediate the effects of FGF-2. We find that in intact animals FGFR2 is mainly expressed in the most posterior part of body spinal cord. However, lesioning of the spinal cord in the mid-trunk region produces increased expression in brainstem and decreased expression in sub-lesional spinal cord. This suggests that FGFR2 might play at least an indirect role in the spontaneous regeneration observed in this species.



Decision making as a competition mechanism in the cortex-basal ganglia loop circuit: experimental approach

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In order to understand decision making mechanisms, neuroscientists have to borrow formalism from other field and analyze their own data through these predefined filters. One of the favored one is the Actor-Critic model proposed originally in robotics. In this talk, I will discuss the theoretical model we proposed which posits that the CBG loop performs action selection in multiple choice conditions through competition mechanisms along feedback loops. Consequently, in the framework of the action-critic model, the CBG loop could be assimilate to the actor part. The role of the critic is supposed to be played by the reward related dopaminergic system which interfaces with the actor at the striatum level. I will present experimental data supporting this hypothesis.



A Connectionist Approach to Decision Making in the Basal Ganglia

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The basal ganglia (BG) are crucial structures for decision-making processes, i.e. the cognitive processes resulting in the selection of a set of actions among several alternative scenarios. Modelling of BG circuitry has played an important role in our understanding of these mental processes, over the last 20 years. Until now, many developmental changes have occurred regarding these models due to continued progress in anatomy, physiology and biochemistry research. In turn, these advances have provided us with novel views regarding the dynamic associations between BG regions. These interactions reflect their connectivity across motor, cognitive and associative loops, which are involved in the decision making process. Furthermore, even though numerous experimental studies have been led by cognitive dysfunctions related to BG, the connectionist neuronal network approach has rarely been employed to describe the decision-making process mechanisms. There are two reasons to support the importance of this class of descriptive model: (i) through this approach, we can precisely follow the information flow underlying decision-making as an emerging property of BG circuits and (ii) since educated decision-making involves preliminary learning relying on synaptic plasticity and thus on synaptic weights modification, we can provide a more plausible description of the whole phenomenon at the cell scale level.

In this work, we show how the connectionist approach can shed additional light on the function of the input and output structures of the BG, on their transfer functions and we thus clarify this process in a mechanistic way.



Symposium 17

Neurobiology of Stress : New Vistas

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Stress responses are elicited by a variety of stimuli and are aimed at counteracting direct or perceived threats to the well being of an organism. In the mammalian central and peripheral nervous systems, specific cell groups provide signaling circuits that indicate the presence of a stressor and elaborate an adequate response, ultimately restoring homeostasis. Many signaling systems, such as CRH or CART, could modulate the responses of the hypothalamo-pituitary-adrenal (HPA) axis and the sympatho-adrenal system, suggesting that they may have a role in the regulation of the neuroendocrine and autonomic responses during stress. Subsequently, stress interferes with normal and pathological processes including addiction. In some cases, the organism fails to counteract stress; this can lead to the disturbance of several processes like neurogenesis, or to a pathological state like depression. This in general depends on the stress paradigm and its severity. The role of each stress paradigm (mild vs strong) in the generation of these negative effects and the neuronal circuitry involved will be discussed in view of novel data and literature.



Differential Effect of Stress on Neurogenesis in Rat Adult Central Nervous System

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The production of new neurons has until recently been considered to occur only during the embryonic and early postnatal periods with no significant role in the adult brain. It is now well accepted that neurogenesis occurs in several parts of the adult brain of mammals. Two regions have been defined as neurogenic niches, namely, the olfactory bulb (OB) and hippocampus. Stress is known to modulate negatively neurogenesis, notably in the hippocampus. Furthermore, using a homotypic and unpredictable stress paradigm (immobilization used repetitively during 3 weeks), we noticed that stress reduces significantly the rates of cell proliferation and differentiation in the dorsal vagal complex in the brainstem as we have shown recently. How this kind of stress modulates neurogenesis in OB, was the question we addressed in this study. Chronic immobilization stress induced a significant increase in the level of proliferation and differentiation in the OB. The total neurosphere number per rat in subventricular zone (SVZ) primary cultures, indicating that intrinsic neural stem cell frequency was also increased by chronic stress. The newly produced neurons could participate in the olfactory discrimination as stressed rats have shown that they can discriminate efficiently novel odors compared to controls.



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Osmoregulation, Vasopressin Expression and Free Radicals.

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Fluid restriction constitutes a stressful situation that animals have to face. The hypothalamic-neurohypophysial system is responsible for the expression and release of vasopressin which induces renal reabsorption of water, thus ensuring the balance of plasma osmolality.

Our team focused on cellular and molecular mechanisms that regulate vasopressin expression and, particularly on the role of noradrenergic afferents connecting the neuroendocrine hypothalamus. The participation of several actors was exhibited in these complex cellular interactions: nitric oxide, astrocytes, extracellular matrix ... Recently, we demonstrated that free radicals are essential for the increased expression of vasopressin during osmotic stimulation, highlighting a new role of free radicals as physiological mediators.



Stress and Addiction

Sakire Pogun

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There are important interactions between addiction and stress; brain regions involved and neurobiological regulation are similar in both cases. Stress can trigger compulsive drug-taking behavior. Stress hormones, and specifically corticotropin releasing factor (CRF) change the value of reward and increase desire without actually increasing enjoyment. Stress is also very closely associated with relapse. Stress may influence responses to nicotine by altering general metabolism and also by effecting nicotine-responsive neurotransmitter systems. Acute intake of nicotine causes stress-like responses and elevates cortisol levels; chronic use may dysregulate the HPA axis, subsequently the vulnerability for dependence and relapse may be related to stress and deficient cortisol reactivity. Alternatively, corticosteroids dampen some of nicotine's effects. Genetic predisposition to anxiety and stress has been shown to influence nicotine self-administration. The effect of nicotine in animal studies and smoking in humans suggest a close link between the nicotinic cholinergic system and affective state. Tobacco addiction rates among persons with major depression are much higher compared to the general population and the success rate in smoking cessation is very low in depressed smokers. In fact, some patients may be smoking tobacco for self-medicating depressive symptoms. On the other hand, there is data to suggest increased cholinergic activity and/or sensitivity, including the over-activation of nicotinic acetylcholine receptors (nAChRs) in depression. Literature on the antidepressant effects of nicotine in rodents is controversial. Although the antidepressant effects of nicotine has been demonstrated in animal models of depression, there are also reports showing that nicotine increases the plasma concentration of corticosterone and induces anxiogenic behavior. Additionally both nicotinic agonists and antagonists are reported to have antidepressant properties, suggesting differential regulation of the cholinergic tone on nAChRs. Another important factor is the possible confounding effect of sex differences. The talk will briefly review literature findings on the interactions between stress and addiction and provide examples from our work on rodents, with emphasis on nicotine addiction.



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Co-interaction between Central Oxytocin and Corticotropin Releasing Hormone Systems

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The hypothalamic neuropeptide oxytocin (OT) controls parturition and lactation in mammals and centrally orchestrates various types of social behaviors. In addition, OT exerts pronounced anxiolytic effects, which lead attenuation of stress and fear responses in mammalian species, including human. We recently gained genetic access to hypothalamic OT neurons in live rats by viral vectors to dissect the connectivity of OT neurons with various intra- and extrahypothalamic regions and exemplarily showed that optogenetic stimulation of local OT axons in the central nucleus of amygdala (CeA) – key brain regions controlling fear response – attenuates freezing behavior in fear-conditioned rats. Presently we are exploring an interaction of OT with the corticotropin-releasing hormone (CRH)- producing neurons, employing both viral-mediated cell-type specific targeting of CRH neurons and transgenic animal models, expressing genes of interest under the control of CRH promoter. As one of important finding obtained by now, we observed close oppositions of OT dendrites (but not OT axons) with CRH cell bodies in the hypothalamic paraventricular nucleus (PVN), which represents central limb of the hypothalamic-pituitary-adrenal (HPA) axis. The functional role of optogenetically-evoked dendritic OT release locally in the PVN followed by the analysis of the HPA axis activity is under our current investigation. In conclusion, the dissecting of mechanisms of co-interaction between two functionally opposing brain systems, such as OT and CRH systems, opens possibility to probe the dual neuropeptide control of stress response. Furthermore, advanced genetic approaches now allow studying the effects of neuropeptide release either from axons or dendrites in experimental models of anxiety, stress and fear.



Symposium 18

New Insights in Neuron-glia Interactions

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Research on glia cells, in particular astrocytes in the brain, has in recent years led to a thorough reappraisal of their role for brain function, extending greatly beyond the classic view as mere providers of structural and nutritional support to neurons. The concept of the “tripartite synapse”, composed of neuronal and astrocytic elements, recognizes the important role that astrocytes are thought to play for regulating information transfer at synapses in the central nervous system in a highly dynamic and multifaceted way.

The aim of this proposal is to present the latest results regarding the contribution of astrocyte to synaptic transmission and plasticity, in physiological and pathological context. Robert Zorec will talk about vesicle trafficking in the context of antigen-presenting reactive astrocytes. Aude Panatier will present her latest work on the contribution of glia-derived purines to setting efficacy at individual synapses through presynaptic A2A receptors. Alfonso Araque will talk about the role of glia in mediating cholinergic-induced plasticity in vivo. Finally, Giorgio Carmignotto will talk about the key role played by astrocytes in epilepsy.

All the speakers are internationally recognized leaders in the field of neuron-glia interactions.



The Fabrics of Astrocyte Vesicle Traffic in Health and Disease IFN- γ -induced Increase in the Mobility of MHC Class II Compartments in Astrocytes Depends on Intermediate Filaments

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In immune-mediated diseases of the central nervous system, astrocytes exposed to interferon- γ (IFN- γ) can express major histocompatibility complex (MHC) class II molecules and antigens on their surface. MHC class II molecules are thought to be delivered to the cell surface by membrane-bound vesicles. However, the characteristics and dynamics of this vesicular traffic are unclear, particularly in reactive astrocytes, which overexpress intermediate filament (IF) proteins that may affect trafficking. The aim of this study was to determine the mobility of vesicles in wild type (WT) and in cells devoid of IF. The identity of MHC class II compartments in (WT) and IF-deficient astrocytes 48 h after IFN- γ activation was determined immunocytochemically by using confocal microscopy. Time-lapse confocal imaging and Alexa Fluor546-dextran labeling of late endosomes/lysosomes in IFN- γ treated cells was used to characterize the motion of MHC class II vesicles. The mobility of vesicles was analysed using ParticleTR software. Confocal imaging of primary cultures of WT and IF-deficient astrocytes revealed IFN- γ induced MHC class II expression in late endosomes/lysosomes, which were specifically labeled with Alexa Fluor546-conjugated dextran. Live imaging revealed faster movement of dextran-positive vesicles in IFN- γ -treated than in untreated astrocytes. Vesicle mobility was lower in IFN- γ -treated IF-deficient astrocytes than in WT astrocytes. Thus, the IFN- γ -induced increase in the mobility of MHC class II compartments is IF-dependent. Since reactivation of astrocytes is a hallmark of many CNS pathologies, it is likely that the upregulation of IFs under such conditions allows a faster and therefore a more efficient delivery of MHC class II molecules to the cell surface. In vivo, such regulatory mechanisms may enable antigen-presenting reactive astrocytes to respond rapidly and in a controlled manner to CNS inflammation.



Astrocyte is an Endogenous Partner of Neurons during Basal Synaptic Transmission

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Basal synaptic transmission is fundamental for information processing in the brain. It occurs at individual synapses and involves the release of neurotransmitters evoked by single action potentials. Since last two decades, evidence indicates that astrocytes are active partners of neurons during synaptic transmission. Classically, it was considered that these glial cells detect and in turn modulate synaptic transmission during intense and sustained neuronal network activity. However, the ability of astrocytes to detect and regulate basal synaptic transmission remained unclear and controversial. Here we show that astrocytes in CA1 region of hippocampus detect synaptic activity induced by single synaptic stimulation at functional compartments along the astrocytic process. This detection is mediated by metabotropic glutamate receptors subtype 5. Moreover, we uncovered that following their activation by basal synaptic transmission, astrocytes release purines to increase the efficacy of transmission in CA1 pyramidal cells through activation of presynaptic adenosine A_{2A} receptors. This work provides a new perspective of fundamental brain function since astrocytes are now intimately involved with neurons in the regulation of elementary synaptic communication in the brain.



Astrocytes Mediate in vivo Cholinergic-induced Synaptic Plasticity

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Long-term potentiation (LTP) of synaptic transmission represents the cellular basis of learning and memory. Astrocytes have been shown to regulate synaptic transmission and plasticity. However, their involvement in specific physiological processes that induce LTP in vivo remains unknown. We have investigated the participation of astrocytes in the cholinergic-induced hippocampal LTP. We have found that in vivo cholinergic activity evoked by sensory stimulation or electrical stimulation of the septal nucleus increases calcium in hippocampal astrocytes and induces LTP of CA3-CA1 synapses, which requires cholinergic muscarinic (mAChR) and metabotropic glutamate receptor (mGluR) activation. Stimulation of cholinergic pathways in hippocampal slices evokes astrocyte calcium elevations, postsynaptic depolarizations of CA1 pyramidal neurons, and LTP of transmitter release at single CA3-CA1 synapses. Like in vivo, these effects are mediated by mAChRs, and this cholinergic-induced LTP (c-LTP) also involves mGluR activation. Astrocyte calcium elevations and LTP are absent in IP3R2 knock-out mice. Downregulation of the astrocyte calcium signal by loading astrocytes with BAPTA or GDPbS also prevents LTP, which is restored by simultaneous astrocyte calcium uncaging and postsynaptic depolarization. Therefore, cholinergic-induced LTP requires astrocyte calcium elevations, which stimulate astrocyte glutamate release that activates mGluRs. The cholinergic-induced LTP results from the temporal coincidence of the postsynaptic activity and the astrocyte calcium signal simultaneously evoked by cholinergic activity. We conclude that the astrocyte calcium signal is necessary for cholinergic-induced synaptic plasticity, indicating that astrocytes are directly involved in the storage of information in the brain.



The Contribution of Astrocytes to Focal Seizure Generation

Carmignoto G

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Focal epilepsies are characterized by recurrent unprovoked seizure discharges arising from specific and localized brain regions that may spread to large brain portions or the whole brain. The cellular and molecular events responsible for the generation and propagation of these focal discharges is still not sufficiently understood. We recently developed a new experimental model of focal onset seizure-like ictal discharges (ID) that allow us to trigger reproducible propagating IDs from a specific restricted site (Gomez-Gonzalo et al 2010; Losi et al 2010). Local NMDA application in slices containing entorhinal cortex (EC) and temporal cortex (TeC) in the presence of 4-aminopyridine evoked IDs that propagate from the focal area of generation to adjacent regions with a speed similar to that reported in vivo. By using this novel approach and confocal microscope calcium imaging with simultaneous dual patch-clamp recordings, we found that a calcium elevation in astrocytes correlates with both the initial development and the maintenance of a focal ID. Selective inhibition or stimulation of astrocyte calcium signalling blocked or enhanced, respectively, IDs. Our data reveal that neurons engage astrocytes in a recurrent excitatory loop (possibly involving gliotransmission) that promotes seizure ignition and sustains the ictal discharge. We also studied astrocyte and GABAergic interneuron interactions during the propagation of focal IDs. Given the recognized role of feedforward inhibition in the control of ID propagation, we hypothesized that such a role may rely also on a distinct GABAergic interneuron-to-astrocyte signalling. In G42 mice, we found that the feedforward inhibition that effectively opposes focal seizure propagation originates from an intense firing in local parvalbumin, fast-spiking interneurons. The observation that astrocytes from the EC exhibit a massive GABAB-mediated calcium elevation hint at a possible role of these cells in the control of seizure propagation. Our understanding of neuron-astrocyte interactions in the epileptic brain network may help to develop new therapeutic strategies to control seizures.



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POSTER PRESENTATIONS



P001

A REVIEW OF BIOCHEMICAL MARKERS FOR EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE

Meha Fatima AFTAB, Surgical technology - Dow Institute of medical technology.

BACKGROUND: Alzheimer's disease a major cause of cognitive decline has worsened the life of elderly. Many people are still either not diagnosed or diagnosed with an un specific but predictive mini-mental state examination. In developing countries, the new costly techniques cannot be implemented. However, some cost effective and specific techniques have been worked on, discussed in this review article.

PURPOSE: To review efficacy of biochemical markers for early diagnosis of Alzheimer's disease.

METHODS: Methods used were pilot study, cohort studies, longitudinal studies and comparative studies. Studies utilizing these methods for diagnosing other neuropathologies were excluded for review writing.

RESULT: Amyloid beta and CSF-Tau have been proved to most relevant markers for early diagnosis of Alzheimer's disease with sensitivity of 58% and specificity of 86% for amyloid beta and 100% sensitivity and specificity for CSF-tau. Ratio of phosphorylated tau protein to AB42 provided sensitivity, 86% and specificity, 97%. Amyloid beta-derived diffusible ligands are shown to cause build up of amyloid beta protein plaques. F2-isoprostane a CSF monoamine metabolite when present show oxidative stress caused by abnormal metabolism of amyloid precursor protein. some blood test, plasma, urinary, inflammatory, neuronal and serum markers are the newly devised minimally invasive techniques that may be more convenient for the patients. Genetic markers are also good predictors of Alzheimer's disease with 20-25% hereditary cases and may prove to be beneficial in early diagnosis.

CONCLUSION: It is inferred that Amyloid beta and CSF-Tau are the most sensitive and specific markers of early pathology of Alzheimer's disease. Ratio of CSF tau to AB 42 is also an efficient technique. Applying these techniques on samples obtained from suspected patients can give a definitive diagnosis for Alzheimer's disease hence delaying onset.



P002

IMMUNOCYTOCHEMICAL STUDIES OF THE NEURODEGENERATIVE DISEASES THE UBIQUITIN PROTEASOME SYSTEM

Zouambia MOHAMED, Biology - Neuroscience.

Many neurodegenerative diseases share the same hallmark, the accumulation of the aberrant proteins as intracellular inclusions. It was shown that the ubiquitin proteasome system (UPS) (Lowe and Al, 1988; Ciechanover and Brundin., 2003) plays an essential role in elimination of these abnormal proteins. The first indication of the implication of the UPS was demonstrated within patients suffering from the Alzheimer's disease. These patients present helical filaments per pairs (Mori and Ihara., 2003; Perry and Al, 1987). These markers were used as pathological signs of many diseases in humans (Alves-Rodrigues and Al, 1998). Several reports were published thereafter on the implication of the UPS in the neurodegenerative diseases (Fergusson and Al, 1996). The aberrant proteins are ubiquitinated and transferred to the 26S Proteasome complex

The present study is related to the immunoreactivities of the sub-units of 26S proteasome for the principal forms of tauo- and synucleinopathies. Several cerebral diseases were studied. Many studies showed that the weakening of the function of the proteasome is associated with the cellular senescence. However, the data available are reduced in fragments and are contradictory (Bulteau, Petropoulos and coll, 2000; Reinheckel, Ulrich and coll, 2000; Keller and coll, 2000).



P003

NEUROTRANSMITTERS RESPECIFICATION IN HUNTINGTON'S DISEASE

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Rinske VLAMINGS, School for Mental Health and NeuroScience - Neuroscience,
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Harry STEINBUSCH, School for Mental Health and NeuroScience - Neuroscience,
Yasin TEMEL, School for Mental Health and NeuroScience - Neuroscience,

Huntington's disease (HD) is a neurodegenerative disorder characterized by progressive cognitive impairments and chorea. The latter has been linked to an increased dopaminergic neurotransmission in the striatum. Treatment with dopamine (DA) antagonist or DA depleting drugs can reduce chorea. However, the origin of this hyperdopaminergic status remains unknown. Tracing studies have shown that dopaminergic input to the striatum comes from the substantia nigra pars compacta (SNc), ventral tegmental area (VTA), and a specific cell population of the dorsal raphe nucleus (DRN).

Using Immunohistochemistry, we tested the hypothesis that elevated striatal DA level is related to alterations in these regions in a transgenic rat model of HD (tgHD) and in the DRN of human HD specimens.

We found that the origin of increased levels of DA in the striatum might be linked to an increase in the number of dopaminergic cells in the VTA, SNc and the DRN of tgHD rats. In addition, we observed increased number of dopaminergic and reduced number of serotonergic cells in the DRN of tgHD rats and HD patients. We suggest that the underlying mechanism for this hyperdopaminergic status in HD can be due to a change in phenotype of the non-dopaminergic cells, like serotonergic cells into dopaminergic cells.



P004

IN VIVO EFFICACY OF (CUG)_n OLIGONUCLEOTIDES TO TREAT HD

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Susan MULDER, Prosensa - Prosensa,
Jeroen VAN DE GIESSEN, Prosensa - Prosensa,
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Huntington's disease (HD) is caused by an expanded (CAG)_n tract in the Huntingtin gene (HTT) that is translated into an expanded polyglutamine (polyQ) stretch in the protein. The polyQ stretch causes a toxic gain of function and plays a central role in the disease. Currently no therapy is available to overcome HD. We hypothesize that direct silencing of prolonged (CAG)_n transcripts offers the most straightforward solution for improvement of HD features in patients. Previously we have shown that PS57, a fully modified (CUG)₇ 2'-O-methyl phosphorothioate antisense oligonucleotide (AON), can effectively reduce huntingtin transcripts and protein levels when transfected in patient derived HD fibroblasts.

We report here on the use of a chemically modified version of PS57 to test in vivo efficacy. Symptomatic transgenic HD rats (carrying a truncated huntingtin cDNA fragment with 51 CAG repeats under the control of the native rat huntingtin promoter) received 15 times an injection in the right lateral ventricle with a modified PS57 version during 18 weeks. Behavioral assessments including motor and cognitive performance in combination with mood and anxiety tests were performed on a monthly base.

Various brain tissues were isolated and Q-RT-PCR analysis revealed silencing of expanded Htt transcript levels after AON treatment compared to control treated rats. Effects on Htt protein level and histological evaluation of brain sections both from AON treated as control rats are currently being analyzed. In summary, we conclude that use of (CUG)_n triplet repeat AONs in HD has therapeutic potential, and that results so far offer interesting openings for future studies.



P005

LESION OF DOPAMINERGIC TERMINALS IN THE AMYGDALA PRODUCES ENHANCED LOCOMOTOR RESPONSE TO D-AMPHETAMINE, FACILITATION OF AMPHETAMINE SELF-ADMINISTRATION AND OPPOSITE CHANGES IN DOPAMINERGIC ACTIVITY IN PREFRONTAL CORTEX AND NUCLEUS ACCUMBENS.

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The effects of 6-OHDA lesions of dopamine terminals within the amygdala were investigated on i) (+) amphetamine-induced locomotor hyperactivity and ii) the acquisition of intravenous self-administration of (+) amphetamine.

The lesioned rats exhibited increased locomotor activity in response to (+) amphetamine (0.75 and 1.5 mg/kg), but not at the higher dose (3 mg/kg). Self-administration of (+) amphetamine was also significantly greater than in controls. By post-mortem biochemical measurements, we showed that bilateral 6-OHDA lesions of DA innervation of the amygdala leads to an increase in DA activity in the nucleus accumbens (DOPAC/DA ratio +24%) and a reduction (DOPAC/DA ratio -40%) in the prefrontal cortex.

We hypothesize that i) there is an interaction between dopaminergic activity in the amygdala and the nucleus accumbens/prefrontal cortex ii) that the behavioural effects were mediated by amygdala-accumbens interactions. Increased understanding of the interregulations between dopaminergic activity in forebrain structures may help explain forebrain functions and/or dysfunctions.



P006

CONTROL OF THE PALLIDO-SUBTHALAMIC AND PALLIDO-NIGRAL PATHWAYS BY DOPAMINE D2 RECEPTORS IN THE RAT

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The globus pallidus (GP) is a basal ganglia nucleus playing a key role in the indirect pathway. In addition to GABA innervations from the striatum and glutamate innervations from the striatum and subthalamic nucleus (STN) respectively, GP neurons receive dopamine inputs from the substantia nigra pars compacta (SNc). However, the functional role of this SNc-GP pathway is not clearly determined. Therefore the present study aimed to investigate the role of dopamine in the modulation of pallido-subthalamic and pallido-nigral pathways.

To this end, extracellular single unit recordings were carried out in adult male Sprague Dawley rats under urethane anesthesia in GP, STN and substantia nigra pars reticulata (SNr) following the intrapallidal injections of quinpirole, a D2 dopamine receptor agonist.

Our results show that local injection of quinpirole principally increased the firing rate of GP neurons (65%), decreased the firing rate of 14% neurons and was without any effect for 21% of GP cells. In parallel, this injection principally decreased the firing rate of STN neurons (62,5%), with an increase in only 29,5% and without any effect for 8% of STN recorded cells. Accordingly, in SNr quinpirole decreased the firing rate of the majority of neurons (82%), increased this rate in only 9% and was without any effect for 9% of SNr recorded cells. In contrast to the firing rate, quinpirole injection into the GP did not change the firing pattern of GP, STN and SNr neurons.

Our results show that D2 dopamine receptors located into the GP play a key role in the modulation of the GABAergic pallido-subthalamic and pallido-nigral pathways. Furthermore, our data challenge assumptions about the important role of extrastriatal dopamine in the modulation of basal ganglia function.



P007

THE EFFECTS OF HIGH FREQUENCY STIMULATION OF THE SUBTHALAMIC NUCLEUS ON MOOD: A ROLE FOR THE LATERAL HABENULA?

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Objective High frequency stimulation (HFS) of the subthalamic nucleus (STN) improves motor disability in Parkinson's disease. Despite sustained motor improvement, a number of patients potentially develop post-operative behavioral complications, including depression. Our previous studies demonstrated STN HFS to inhibit serotonin (5-HT) neurotransmission, which might be responsible for the behavioral side effects. Interestingly, a direct projection from the STN to the 5-HT system does not exist. In this study we investigated the role of the lateral habenula (LH) in STN HFS induced changes in 5-HT neurotransmission and mood. **Methods** Rats were implanted with bilateral STN stimulation electrodes (STN HFS or sham HFS) and treated with bilateral LH injections (quinolinic acid or vehicle injections). The rats were divided into 4 equal groups: 1) Sham HFS + LH vehicle injected controls; 2) STN HFS + LH vehicle injections; 3) Sham HFS + LH quinolinic acid lesions; 4) STN HFS + LH quinolinic acid lesions. Stimulation was performed at clinically relevant parameters. Motor, anxiety and mood related behavior was assessed. **Results** STN HFS and LH lesions did not alter spontaneous locomotor activity in the open field test. Times spent in the open/closed arms of the elevated zero maze was not altered by STN HFS or LH lesions, reflecting unchanged anxiety-like behavior. STN HFS did result in decreased sucrose consumption in the sucrose intake test and decreased food consumption in the food intake test reflecting anhedonic-like behavior. Interestingly, LH lesions prevented STN HFS induced decrease of sucrose intake but not food intake. **Conclusion** Our experiments demonstrate STN HFS to induce changes in mood related behavior, but not in motor and anxiety behavior. This might be mediated through STN HFS induced inhibition of 5-HT neurotransmission. The LH may be a key structure between the STN and dorsal raphe 5-HT system important in the regulation of mood.



P008

EFFECT OF ANTI-PARKINSONIAN TREATMENTS ON MOTOR AND NON-MOTOR DEFICITS INDUCED BY MONOAMINERGIC DEPLETIONS IN A BILATERAL RAT MODEL OF PARKINSONISM

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Problem statement: Parkinson's disease (PD) is a neurodegenerative disorder characterized by the loss of dopamine (DA) neurons in the substantia nigra. PD is also characterized by a loss of noradrenaline (NA) cells in the locus coeruleus and serotonin (5-HT) cells in the dorsal raphe. Besides motor symptoms, non-motor symptoms (depression and anxiety), are also seen in PD patients. Motor symptoms are generally treated by levodopa or in advanced stages with high frequency stimulation (HFS) of the subthalamic nucleus (STN) alone or combined with levodopa. However, the origin of the loss of levodopa efficacy in severe PD patients is not clearly determined. The present study aimed to characterize the consequences of dopamine, noradrenaline and serotonin alone or combined on the efficacy of antiparkinsonian treatments (levodopa and/or STN HFS) on the motor and non-motor deficits.

Approach: This study was carried out on rodents: a sham group and four groups with different monoamine depletions. DA depletion was performed by stereotaxic bilateral injection of 6-hydroxydopamine (6-OHDA) into the medial forebrain bundle. An intra-peritoneal (i.p.) injection of N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine (DSP-4) was given to induce a noradrenergic deficiency and parachlorophenylalanine (PCPA) for the depletion of serotonin. Two stimulating electrodes were implanted bilaterally into the STN. Motor behaviour was assessed in an open-field, anxiety in the elevated plus-maze and "depressive-like" behaviour was studied using the forced swim test.

Results: Our results show that DA and/or NA depletion induced motor deficits. STN HFS can only reverse the motor deficit induced selectively by DA depletion. Anxiety behaviour, which is DA dependent, was improved by levodopa. Depressive like behaviour was potentiated with the depletion of the three monoamines and can be reversed by the two antiparkinsonian treatments.

Conclusion: The present study provides evidence on the key role played by the three monoamines depletions in the pathophysiology and therapy of Parkinson's disease.



P009

NEUROPROTECTIVE AND NEUROTHERAPEUTIC EFFECTS OF BEE VENOM ON NEURODEGENERATIVE DISEASES

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Acute and chronic neurodegenerative diseases are illnesses associated with high morbidity and mortality, and few or no effective options are available for their treatment. A characteristic of many neurodegenerative diseases — which include stroke, brain trauma, spinal cord injury, amyotrophic lateral sclerosis, Huntington's disease, Alzheimer's disease, and Parkinson's disease — is neuronal cell death. Given that central nervous system tissue has very limited, if any, regenerative capacity, it is of utmost importance to limit the damage caused by neuronal death. Bee venom, which is also known as apitoxin, consists of several biologically active peptides, including melittin, adolapin, mast cell degranulating peptide and phospholipase A2. Moreover, bee venom contains a variety of bioamines, such as apamin, histamine, procamine, serotonin, and norepinephrine, which facilitate nerve transmission and healing in a variety of nerve disorders. This gives bee venom the ability to travel along the neural pathways from the spine to various trigger points and injured areas to help repair nerve damage and restore mobility.

This review overviews; (1) causes and mechanisms of neurodegenerative diseases which pertains to neuronal cell death, (2) evidence linking composition comprising bee venom to its substantial potential for preventing and treating of neurodegenerative diseases associated with neuronal cell death (3) how improving our knowledge of the mechanisms mediating neuroprotective and neurotherapeutic activities of bee venom against neuronal cell death may led to novel therapeutic strategies for the treatment of neurodegenerative diseases. Future challenges remaining will be to elucidate signaling responses activated by bee venom in neurons. In other words, bee venom inhibits neuronal cell death and activation of proapoptotic signaling in neurons.

These findings emphasize the clinical importance of bee venom for treatment of neurodegenerative diseases. Further investigation is necessary to elaborate the mechanisms involved and to permit full exploitation of neuroprotective and neurotherapeutic potentials of bee venom.



P010

EFFECT OF VERBAL AUDITORY CUES ON CORTICAL MOTOR EXCITABILITY IN PARKINSON'S DISEASE. EVIDENCE FROM MOTOR EVOKED POTENTIAL

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Background: Parkinson's disease (PD) patients rely on external sensory inputs to guide movements. Aim: study the effect of verbal auditory cues on cortical motor excitability of PD patients. Participants and Methods: The study included 17 PD patients and 15 healthy controls. Motor evoked potential (MEP) was recorded from abductor pollicis brevis muscle at baseline, following repetitive rhythmic thumb abduction-adduction at preferred speed and with verbal cues. Number Repetitive movement cycles (RMC), resting motor threshold (RMT), central motor conduction time (CMCT), MEP amplitude ratio and cortical silent period (CSP) mean duration were measured. Results: At baseline, PD patients had significantly higher MEP amplitude ratio and shorter CSP mean duration than controls ($p=0.9$, 0.01 respectively). At their preferred speed, PD patients had significantly lower RMC compared to controls ($p=0.005$) and compared to baseline, they had significantly lower RMT, prolonged CMCT and increased CSP mean duration ($p=0.04$, 0.05 and 0.01 respectively). With verbal cues, both PD patients and controls could increase significantly RMC (0.000 , 0.028 respectively) but still lower in patients ($P=0.002$). Following verbal cues, none of MEP parameters has changed significantly among patients compared to controls and compared to performance without cues. Controls had significant shortening in CMCT and prolongation of CSP mean duration ($p=0.046$, 0.001 respectively). Conclusion: Parkinson's disease patients have significant cortical hyperexcitability than healthy subjects. Performing a repetitive motor task with or without verbal auditory cues may normalize cortical excitability level in PD patients.



P011

NEURONAL CELL LOSS IN THE SUBTHALAMIC NUCLEUS OF EXPERIMENTAL PARKINSON'S DISEASE RATS

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Problem Statement - Parkinson's disease (PD) is a neurodegenerative disorder caused by a progressive loss of dopaminergic neurons in the substantia nigra pars compacta (SNc). This leads to a substantial increase of the metabolic activity of the subthalamic nucleus (STN) and electrophysiologically to burst activity. Enhancement of STN metabolic and neuronal activity increases the demand for energy and has the potential to increase the formation of reactive oxygen species. This might result in oxidative stress induced damage to STN neurons. In line with this, we tested here the hypothesis that dopamine depletion will result in neuronal cell loss in the STN.

Approach - Rats were rendered parkinsonian by bilateral intrastriatal injections of 6-hydroxydopamine (6-OHDA), producing a partial dopamine (DA) depletion of SNc. The study contained sham operated (n=6), mild (n=6) and moderate (n=12) DA depleted rats. Brains were removed and the STN was sectioned (30 μ m) and stained for Nissl substance. Design based-stereological analysis of the STN was performed, including the volume, number of cells and volumes of cells.

Results - Mild and moderate DA depletion resulted in a 21% and 12% reduction in number of cells in the STN respectively. No differences in STN volume and cell volumes were found.

Conclusions - Our results suggest that neuronal cell loss takes place in the STN of 6-OHDA treated rats. The mechanisms underlying loss of STN cells needs further investigation using markers of cell damage and death.



P012

THE DOPAMINERGIC AGONIST QUINPIROLE TRIGGERS 5-HT_{2C} RECEPTOR-DEPENDENT CONTROLS ON BOTH PURPOSELESS ORAL MOVEMENTS AND THE ACTIVITY OF THE HYPERDIRECT PATHWAY IN BASAL GANGLIA.

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Excessive dopamine transmission in associative/limbic areas of basal ganglia is thought to underline a variety of behavioral disorders including dyskinesia. The excessive DA tone induces alterations on other neurochemical pathways and numerous authors have suggested that serotonergic controls, notably via the 5-HT_{2C} receptor, are triggered in case of DA changes.

Here, we studied in rats the contribution of 5-HT_{2C} receptors using the 5-HT_{2C} antagonist SB243213 in the effects elicited by the dopaminergic agonist quinpirole on purposeless oral movements, c-Fos expression in basal ganglia nuclei and the electrophysiological activity of substantia nigra pars reticulata (SNr) neurons, the main output of basal ganglia, responding to the electrical stimulation of the cingular cortex.

The results showed that SB243213 (1mg/kg i.p.), without effect by itself, blocked the purposeless oral movements induced by 0.5 mg/kg i.p. quinpirole. The levels of the protein c-Fos, barely affected by quinpirole or SB-243213, were significantly increased in the subthalamic nucleus (STN) when the treatments were combined. Similarly, in urethane-anesthetized rats, SB-243213 unmasked a facilitatory effect of quinpirole on the spontaneous discharge of SNr neurons. Interestingly, the effect elicited by the electrical stimulation of the cingular cortex, leading to an excitatory-inhibitory-excitatory response, was subtly changed by the drugs. Quinpirole enhanced the amplitude of the early excitatory response, involving the hyperdirect pathway, and this effect was abolished by SB-243213.

In conclusion, these results extend previous evidence that excessive DA tone triggers 5-HT_{2C} receptor-dependent controls in basal ganglia. The interaction occurs likely on the hyperdirect pathway in line with the role of the STN in mediating the purposeless oral movements induced by DA and 5-HT_{2C} agonists.



P013

EFFECTS OF TETRABENAZINE ON CHOREIFORM MOVEMENTS IN THE TRANSGENIC RAT MODEL OF HUNTINGTON'S DISEASE

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Problem statement: Open-label studies indicate that tetrabenazine (TBZ), a reversible inhibitor of the vesicular monoamine transporter type 2, is effective in reducing the chorea in patients with Huntington's disease (HD). Animal models of HD are used to understand the pathophysiology of the disease and to find new therapies. In this respect, few years ago the first transgenic rat model of HD (tgHD) has been introduced. These animals show hyperkinetic movements, which have not been well characterized. Here we assessed these movements in detail and investigated the effect of TBZ therapy. Approach: We evaluated the hyperkinetic movements of a group (n= 11) of 17 months old homozygous male tgHD rats. The animals were videotaped in their home cage environment before and after receiving a subcutaneous injection with TBZ (2.5 mg/kg) or vehicle. Each animal received both conditions. The evaluation was done every 15 minutes, before and after the animal received an injection, during a 5-minute assessment period. The observer was blinded with respect to the condition of the rats. Results: The tgHD rats showed abrupt, rapid, brief and un-sustained irregular movement of the neck. None of these movements were observed in other parts of the body. We found that administration of TBZ reduced the number of these hyperkinetic movements on average with 55% ($p < 0.01$). Conclusion: The hyperkinetic movement disorder observed in the tgHD rats can be considered as a choreiform movement, based on the characteristic of the movement and the positive response to TBZ administration.



P014

REGION-DEPENDENT MODULATION OF L-DOPA-INDUCED DOPAMINE RELEASE BY NORADRENERGIC TERMINALS IN THE HEMIPARKINSONIAN BRAIN

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The therapeutic benefit of L-DOPA is commonly attributed to the restoration of dopamine (DA) extracellular levels in the striatum of Parkinsonian patients. The increase in DA release induced by L-DOPA is mediated by serotonergic neurons and therefore occurs in extrastriatal brain regions. Because noradrenalin (NA) transporters display a high affinity for DA, NA terminals may also be involved in the heterologous regulation of L-DOPA-induced DA release in the Parkinsonian brain.

In 6-hydroxydopamine-lesioned rats, we used multi-site intracerebral microdialysis coupled to high performance liquid chromatography to monitor DA extracellular levels simultaneously in the striatum, substantia nigra pars reticulata (SNr), hippocampus and prefrontal cortex (PFC). We tested the sensitivity of DA release induced by an acute intraperitoneal (ip) administration of L-DOPA (12 mg/kg 20 minutes after 15 mg/kg benserazide ip) to the NA reuptake inhibitors desipramine (10 mg/kg, ip) and reboxetine (3 mg/kg, ip) or to a lesion of NA terminals using the NA neurotoxin DSP-4 (50 mg/kg ip).

L-DOPA induced a stronger increase in DA release in the striatum compared to the SNr, PFC and hippocampus. Both the administration of desipramine and reboxetine (20 minutes before L-DOPA) potentiated L-DOPA-induced DA release in the SNr (+107% and +139% respectively), PFC (+150% and +170%), hippocampus (+139% and 565%) but not in the striatum. The lesion of NA terminals using DSP-4, that dramatically and specifically reduced the NA tissue content, potentiated the effect of L-DOPA mainly in SNr and hippocampus.

These data show that the heterologous reuptake of DA by NA fibers participate in the heterogeneity of L-DOPA-induced DA release in the Parkinsonian brain. This might be a therapeutic strategy aimed at potentiating extrastriatal DA release to improve the motor benefit of L-DOPA while dampening the emergence of side effects attributed to excessive DA tone in the striatum.



P015

CIRCADIAN ALTERATIONS IN MOUSE AND NON-HUMAN PRIMATE MPTP TREATED MODELS OF PARKINSON DISEASE

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Although the clinical diagnosis of PD is based on motor symptoms related to depletion of nigral dopamine (DA), there is increasing evidence that non-motor symptoms are an important feature of the pathology. Our study aimed to assess long-term alterations of circadian rest-wake activity and cognitive performance in mouse and monkey MPTP models of PD. Circadian rest-activity rhythms were continuously monitored under different light regimes in both species over several months. In monkeys, clinical state was evaluated using a PD Rating scale and hormonal rhythms (melatonin, cortisol) using RIA. DA function was assessed using PET scans and/or post mortem quantification of TH neurons. MPTP treatment induced DA neuronal degeneration of 70% in mice and 70-80% in primates. In mice no alterations in general motor activity, circadian rhythmicity or cognitive performance were observed even nearly one year post treatment. Both control and treated animals showed equivalent decreases of locomotor activity and of several circadian parameters with age. Monkeys before treatment showed robust daily rest-activity rhythms under a light dark cycle whereas following MPTP treatment total locomotor activity decreased but daily rhythms were largely conserved, although the amplitude of the rhythm was damped and activity onsets and offsets were imprecise. In constant light conditions, circadian activity rhythms were severely degraded with a loss of rhythmicity in the most extreme cases. Hormonal rhythms, however, were unaffected. Our study shows that severe disturbances of circadian functions occur after MPTP treatment in the non-human primate but not in the mouse model of PD, emphasizing the limitations of the mouse for the study of non-motor symptoms. In contrast, results in the non-human primate model stress the importance of dopaminergic degeneration in non-motor symptoms of PD.



P016

MOLECULAR GUIDANCE OF TRANSPLANTED EMBRYONIC CELLS IN THE LESIONED SUBSTANTIA NIGRA IN AN ANIMAL MODEL OF PARKINSON DISEASE.

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Cell replacement therapy has been proposed as a possible mean to replace lost dopaminergic (DA) neurons in Parkinson's disease (PD). We have previously shown that ventral mesencephalon (VM) cells obtained from mouse fetuses grafted into the lesioned SN of adult mice, can survive, differentiate into dopamine neurons, and most importantly develop significant contingents of projections through the medial forebrain bundle to the lesioned striatum. In this work we aim to determine if the lesion of the substantia nigra and/or the transplantation of embryonic cells in this model, modulates the expression of guidance molecules known to be involved in the establishment of the nigrostriatal pathway during embryogenesis. We showed that the lesion of the substantia nigra has no effect on the localization of expression of guidance molecules along the nigrostriatal pathway, 1 and 6 days after the lesion. However, we observed that intranigral transplanted cells express guidance molecule receptors such as neuropilin-2, 6 days after transplantation. This suggests that embryonic transplanted cells may be able to respond to molecular cues expressed in the adult microenvironment. As molecule expression in the environment may influence the expression of receptors on transplanted cells and vice versa, transplanted cells may induce a modulation of guidance molecule expression in the vicinity of the nigrostriatal pathway, we will further determine the expression of guidance molecules and their receptors not only in the transplanted cells but also in their neighbor regions using real time quantitative PCR. Identifying the guidance molecules involved in the navigation of grafted cells may help to improve the efficiency of neuron reconnection in Parkinson's disease cell therapy.



P017

STUDY OF BRAIN STRUCTURES ON MRI OF PARKINSON'S

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Problem Statement: The aim of our work is to track the different kind of deformations, that has suffered the parkinsonian brain, at the level of brain tissues (WM, GM, CSF). At first, after a step of pretreatments, we segment the three matters of healthy and parkinsonian brains using the FCM algorithm, and then we will compare the results. Then we segment the ventricles by approach regions and we refine the result using deformable models. **Approach:** Pretreatment: Before segmentation, we must apply a pretreatment phase, including: • **Noise filtering:** is to filter the image to reduce noise in areas where it operates, but at the same time to avoid the smoothing of edges. The main goal pursued by the anisotropic diffusion Perona and Malik the result using deformable models. • **Skull stretching:** The brain is extracted by a robust method, using morphological operations. This eliminates the radiometric classes that do not interest us (the skin, air, bone, fat). **Hough.** Segmentation: After pretreatment, we segment the brain structures by using FCM algorithm, and we calculate surface of the segmented structures. A registration between healthy and Parkinsonian segmented brains allows comparing the surfaces of cerebral tissues. **Results:** The surfaces of the MB and MG a Parkinsonian brain are lower than those of a healthy brain. These results are satisfactory and confirm the interpretation of the physician, namely atrophy in the white matter and gray matter, which involves the deformation of the cerebrospinal fluid and internal structures. **Conclusions/Recommendations:** We have segmented the structures of a healthy brain, and those of a Parkinsonian brain, and we have compared them. Segmentation of brain tissue shows degeneration of white and gray matter. Our results are satisfactory and confirm the interpretation of the doctor. However, this must be confirmed by the study of MRIs of the same subject Parkinson, taken at different times.



P018

SUICIDE AND SELF-INJURY OF OFFENDERS IN CUSTODY: ASSESSMENT, INTERVENTIONS AND MANAGEMENT

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Problem Statement: Suicide and self-injury in offenders are a public health concern which requires concerted effort to explore the prediction of, and vulnerability to, such behaviors in different offending populations. Prisoners are a socially excluded population, experiencing various health and social inequalities, with complex needs. Studies have demonstrated that the rate of suicide in offending populations is far higher than in the general population. Approach: It is a review article of relevant studies that have identified characteristics, risk factors which are over represented in prison suicide and methods of its prevention. Results: Suicide and self-injury are common in offenders being charged with or convicted of a violent or sexual offense, those being in the early stages of custody or having a history of drug and/or alcohol misuse and psychiatric morbidity. The majority of prison suicides occur in local or 'dispersal' prison establishment types and the most common method of death is by hanging. There are particular subgroups within prison suicides of particular risk factors. For example, early suicides, or those who die within the first stage of custody, are more likely to be on remand and be drug dependent Those who die within the later stages of custody are sentenced, and more likely to be convicted of a violent crime and serving a life sentence. Recommendations: to prevent suicide in custody officers directly questioning offenders regarding known risk factors for suicide; items of clothing being removed if it is believed that they may be used for self-harm; installing closed circuit television in custody suites; training in dealing with mental health problems; effective communication between disciplines; and handovers to include the provision of all relevant facts and information surrounding detainees. Developments and improvements need to occur at all stages of the custodial process, including pre-prison; reception screening; induction or prison establishment.



P019

THE EFFECT OF REMINISCENCE ON LIFE SATISFACTION AMONG ELDERLY PEOPLE

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Elderly individuals most often stop doing daily routines assuming that they are deprived of power. Because elderly individuals feel worthless and powerless, aging is considered as a significant obstacle in gaining satisfaction from life. Older people who are not able to manage daily life by themselves may have a different view of life satisfaction than those with preserved self-care capacity. It may well be that the transition from being healthy and independent of help with activities of daily living to having to live with reduced self-care capacity alters the view of aspects contributing to life satisfaction. Therefore, this study was conducted to evaluate the effect of reminiscence on life satisfaction among elderly people. A pre-post quasi-experimental design was utilized in this study. A sample of convenience of 30 institutionalized older adults was recruited from Dar El-Hana Geriatric home. Socio-demographic/medical data sheet, Mini-Mental State Exam (MMSE) scale and Life Satisfaction Scale were used to achieve the purpose of this study. A reminiscence program session was held for 90 minutes for a total of 10 weeks (20 sessions), the program focus on particular stages of life using a semi-structured interview. Findings of this study indicated that, reminiscence intervention significantly improved life satisfaction among elderly individuals (the difference between pre and post test in relation to life satisfaction where $t= 3.469$ at $p=.042$). To conclude reminiscence intervention is an effective alternative intervention which can help living-alone elderly adapt to the aging process. Further studies about reminiscence on a larger number of elderly from different geographical areas are recommended.



P020

THE IMPACT OF AN EDUCATIONAL PROGRAM ABOUT ADDICTIVE BEHAVIOR ON THE PERFORMANCE OF NURSES IN MENTAL HOSPITALS

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Increased attention to preparing addictions counselors and related professionals to use evidence-based practices has brought new attention to the preparation programs for addictions counselors. Research and theory about adult learning emphasizes the importance of students as active participants in problem and experience based learning. This study presents some key principles about teaching and learning for nurses' staff working with substance dependents. Therefore, this study was conducted to examine the impact of an educational program of addictive behaviors on the nurses' performance working with clients with substance dependence problems as regard their therapeutic attitudes, knowledge, and practice.

A pre-post quasi-experimental design was utilized in this study. A sample of 40 nurses was recruited from El Abbasia Mental Health Hospital. Socio-demographic data sheet, Substance Abuse Attitude Survey (SAAS), Substance Dependence Knowledge Questionnaire (SDKQ), and Motivational Interview Skills Checklist (MISC) was utilized to achieve study aim. An educational program session was held for 45 minutes for a total of 7 weeks (14 sessions), the program focus on particular skills of motivational interviewing. Finding of the study indicated that: statistically significant differences were found between levels of knowledge and practicing of motivational interview skills before and after the program, while attitude levels of nurses didn't reach a statistical significant difference except regarding the treatment intervention attitude before and after the program.

To conclude, an educational program is an effective alternative intervention which can help nurses to intervene efficiently with substance dependences patients. Further studies about re-education of nurses on a larger number from different geographical areas are recommended



P021

CORRELATES FOR SELF-INJURIOUS BEHAVIORS AMONG CHILDREN WITH AUTISTIC DISORDERS

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One of the most perplexing and challenging forms of behavior problem in autism is self-injury. Autistic disorder is a life long disability, and most child affected with this condition remain unable to live independently and require family or community support or institutionalization, so, the goal of treatment for these children are to reduce disruptive behaviors and to promote learning, particularly. Therefore, the aim of this study was to assess the correlates for self-injurious behaviours among children with autistic disorders. A descriptive correlational design was utilized in this study. A sample of purposeful of fifty autistic children were recruited from Out-patient Clinic in Institute for Postgraduate Childhood Studies-Center for Children with Special Needs (Autism Unit) in Ain-Shams University and Center for Social and Preventive Medicine (child psychiatry out-patient clinic) at Abu-EL-Rish University Hospital. Four tools were used to measure the current study variables, sociodemographic and medical data sheet, childhood autism rating scale, diagnostic self-injury behaviors scale and Vineland adaptive behavior scale. Findings revealed that there is an association between severity of self-injury and higher degree of autism, higher communication delay, lowers age and intelligent quotient. To conclude, SIBs represent a very common problem in children with autism. Further researches are needed to outline the course of self-injurious behaviors in autism throughout the life span, in order to develop appropriate treatments that are directed at correcting or even preventing the primary causes of this behavior are recommended.



P022

ANXIOLYTIC EFFECTS OF ACUTE ADMINISTRATION OF ORMENIS MULTICOLIS IN THE MALE SPRAGUE-DAWLEY RAT

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In history, chamomile has been (and still is) used in a variety of ways: healing baths, teas, poultices, air fresheners, hair rinse, cosmetics, insect repellents, wine flavoring, dyes, companion planting, potpourris, and landscaping. Chamomile is medically specific to be useful with all of the following: soothing, calming, sedative, relaxation, anti-inflammatory, tenseness, aching muscles, indigestion, acidity, hay fever, asthma, morning sickness, eczema, sore nipples, and exhaustion. Chamomile is known for its calming effect on smooth muscle tissue, and is still a popular remedy for nervous stomach, menstrual cramps, and other common problems related to stress. Ormenis multicolis is among several medicinal herbs that are popular in Hispanic folk medicine. Recent studies (Amsterdam JD. et al, 2009) have revealed diverse therapeutically interesting pharmacological properties especially the chamomile effects in anxiety and depressive disorders.

The purpose of this study is to evaluate the anxiolytic and anti antidepressive effects of Ormenis multicolis aqueous extract, in order to determine its potential interaction with central nervous system in male Sprague-Dawley rats. Male Sprague Dawley rats were administered centrally and intraperitoneally by variable doses of aqueous extract of Ormenis multicolis. Anti stress and anti depressives effects are evaluated using respectively the dark/light box and porsolt tests 40 min after the treatment.

In the light/dark transition test, the extract of chamomile increased the time spent in the light area and the number of transitions between the two compartments by treated rats compared to controls rats. In the porsolt test, the extract of chamomile administered intraperitoneal (i.p.) significantly reduced the immobility time of the test in treated rats compared to control rats.

Obtained results show that the aqueous extract of Ormenis multicolis have an important action on stress and depression.



P023

A GENDER-SPECIFIC ASSOCIATION OF INTERLEUKIN-1 RECEPTOR ANTOGONIST POLYMORPHISM WITH SCHIZOPHRENIA SUSCEPTIBILITY

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Objective: Recent genetic studies have revealed that the IL1 gene complex is associated with schizophrenia in the Caucasian population; however, data from north-african population are underrepresented. In order to further assess the role of IL1Ra in schizophrenia, we examined a functional multiallelic polymorphism localized in the intron 2 of this receptor gene associated with altered level of IL1Ra.

Methods: In the present case/controlled study, we have analyzed the (86pb)n polymorphism of the IL1-RN gene by PCR genotyping in 247 patients with schizophrenia and 150 healthy controls from the Tunisian population.

Results: We showed that the frequencies of IL1RN*2/2 genotype and allele 2 were higher in the patient group vs. the control one, and the difference was statistically significant (13.8% vs. 3.3%, $p=10^{-3}$, OR=5.8 and 35.2% vs. 20.3%, $p=10^{-4}$, OR=2.1 respectively). When we have evaluated the association between this genetic polymorphism and the clinical variables of schizophrenia, we found that the frequency of the 2/2 genotype and the allele 2 were significantly higher in the male patients group ($p=5.10^{-4}$ and $p=10^{-4}$ respectively) compared to the male control group, indicating a substantially increased risk for sex-onset schizophrenia with inheritance of the IL1RN2 allele.

Conclusion: the intron 2 polymorphism in IL1RN or a genetic polymorphism at proximity seems to be associated specifically with schizophrenia in the Tunisian male population. This work is the first describing the IL1RN polymorphism associated with schizophrenia in a large North African population. Also, the gender difference in IL1Ra secretion has been showed in other pathologies but not in IL1RN polymorphism associated with schizophrenia.

Limitations: Although the subjects were from the same Tunisian region, we cannot rule out the possibility of a population structure effect in our findings. Further studies employing family-based samples are needed in order to confirm these results.



P024

INCREASED LOCOMOTOR ACTIVITY AND DOPAMINE RELEASE IN THE NUCLEUS ACCUMBENS OF ADULTS RATS FOLLOWING KETAMINE ADMINISTRATION WERE OBSERVED AFTER NEONATAL TRANSITORY INACTIVATION OF THE ANTEROMEDIAN PREFRONTAL CORTEX

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Schizophrenia would result from a defective connectivity, between several integrative regions, stemming from developmental anomalies. Various abnormalities reminiscent of early brain development disturbances have been observed in the patients' left prefrontal cortex (PFC). The existence of a striatal dopaminergic (DA) dysregulation in schizophrenia is commonly acknowledged. Psychomimetic drugs such as the non-competitive NMDA/glutamate antagonist ketamine, can induce psychotic symptoms in healthy humans and exacerbate these symptoms in patients with schizophrenia. The striatal DAergic dysregulation in schizophrenia may be dependent of prefronto-striatal dysconnexion involving glutamatergic NMDA receptors.

This study was designed to investigate the effects of ketamine in adult rats on DA responses, in a nucleus accumbens subregion, following a postnatal inactivation of the left PFC (infralimbic/prelimbic region). During the neurodevelopmental period, impulse electrical activity appears to be crucial for shaping connections once developing axons reach the target structure. Therefore, reversible functional inactivation of the left PFC was carried out by local Tetrodotoxin (TTX) microinjection in 8-day-old rats. DA variations were recorded in the core subregion of the nucleus accumbens using *in vivo* voltammetry in freely moving adult rats (11 weeks). Ketamine was administered s.c. with different doses.

The obtained results were the following : 1) A clear dose effect was observed for the two conditions (PBS and TTX microinjected at PND8); 2) DA increase in the core part of the nucleus accumbens in adult animals after the administration of the highest ketamine dose (20 mg/kg) was more elevated in TTX microinjected animals than in PBS microinjected animals.

These data suggest that animals microinjected with TTX in the left PFC at PND8 present a more important reactivity to ketamine than control animals. To conclude, these findings suggest that early functional impairment of PFC induced by TTX is a valid approach to modeling the pathophysiology of schizophrenia in animals.



P025

IMPACT OF EXPOSURE TO A CHRONIC SOCIAL STRESS PROCEDURE DURING ADOLESCENCE ON THE ANXIETY RESPONSE IN NMRI MALE MICE

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Problem statement: Exposure to chronic stress during adolescence could have important consequences on the neurodevelopment of animals. A plausible hypothesis is that social stress increases anxiety levels in NMRI mice, although data relating to animals exposed to social stress through unstable social environments is as yet scarce.

Approach: With the aim of evaluating emotional response to an unstable social environment, 32 male NMRI mice were randomly assigned to either social stress (SS) or no stress conditions (NS) on PND 28. The procedure consisted of a disruption of the social hierarchy by altering the group's composition (4 animals per cage) twice per week for seven weeks. After this period (PND 77), the mice were evaluated in the elevated plus-maze (EPM).

Results: Exposure to social stress induced statistical differences in frequencies and percentage of entries into the open arms ($p < 0.05$) and in the percentage of time that animals spent in the closed arms of the EPM ($p < 0.05$). The SS group displayed a lower number and percentage of entries into the open arms (34.79 ± 4.76) and increased time in the closed arms (34.30 ± 2.44) with respect to the NS group, suggesting increased anxiety levels in adolescence-stressed mice.

Conclusions/Recommendations: Exposure at early ages to social stress caused by an unstable environment induces an emotional response in NMRI male mice similar to that reported with other stress procedures. Future studies are needed in order to establish pharmacological or behavioral interventions (e.g. environmental enrichment) which prevent or revert these effects.

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P026

EPIDEMIOLOGICAL STUDY OF PSYCHIATRIC DISORDER IN THE REGION OF GHARB CHERARDA BENI HSEN (MOROCCO)

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The objectives of our work was to realize an inventory of psychiatric disorders in the region of Gharb Cherarda Beni Hsen to highlight the most common diseases and to make hypothesis about the possible influence that some risk factors might have on the development of psychopathologies. In one hand, we conducted a retrospective study used archived data of a population of 3680 patients. In the other hand, we led an epidemiological study, which focused on major depression (MD) and examined 192 patients. The first axis revealed the vulnerability of women aged between 18 and 39, from urban area, with no grade and unemployed to psychiatric disorders in general and MD in particular. It revealed the dominance of MD (27, 4%), compared to other disorders in the survey population. The second axis has confirmed the susceptibility of women (70.8%) pre-adults and adults from urban areas and unemployed towards MD. It showed that it is women in the last position among siblings (38%), married with more than two children, who received an authoritarian parenting, under the influence of disruptive events such as family abandon (28%) or mourning (27%) and judging bad their standard of living (44.27%) who are more likely to develop MD. Also, 60.41% have a family history of MD. Moreover, through this second axis, emerges the hypothesis of a possible influence of a deficient diet in certain nutrients whose antidepressant virtues are proven (tryptophan, polyunsaturated fatty acids n-3, B vitamins) in the development of MD.



P027

EVALUATION OF SERUM INTERLEUKIN-23 AND INTERLEUKIN-6 IN SCHIZOPHRENIC PATIENTS VERSUS HEALTHY CONTROL SUBJECTS

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Due to several reports regarding abnormal cytokine production, abnormal cytokine concentrations and their receptors in the peripheral blood and cerebrospinal fluid, activation of the inflammatory response system and altered levels of different cytokines in acute schizophrenia have been much considered during recent years. Cytokines which acting as chemical messengers between immune cells are able to modify metabolism of neurotransmitters and neuroendocrine hormones, and influence neural development and behavioral changes. There are also evidences that revealed the existence of antibrain antibodies in the serum of schizophrenic patients. The purpose of this study was to determine IL-23 and IL-6 levels in schizophrenic patients versus healthy control subjects. We measured the serum levels of IL-23 and IL-6 of 30 schizophrenic patients and 20 age and gender matched healthy controls by using ELISA assay. We measured serum levels of IL-23 in schizophrenic patients for the first time. Our results showed that serum levels of IL-23 were significantly higher in patients 696 ± 132 (pg/ml) than in controls 313 ± 33 (pg/ml). The serum IL-6 levels of the schizophrenic patients 5.28 ± 1.1 (pg/ml) were significantly higher the control group 2.54 ± 0.32 (pg/ml). These findings indicate that immune system activation involved in the pathophysiology of schizophrenia and increased IL-23 levels demonstrate that autoimmune process might be involved in certain groups of schizophrenic patients.



P028

CAUSES OF PSYCHIATRIC PATIENTS' AGGRESSION AND VIOLENCE: NURSING STAFF AND PATIENTS PERSPECTIVES

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Aggression and violence have always been difficult behaviors for any society to manage, and when such behaviors present in psychiatric patients, special approaches and interventions need to be considered. The incidence and nature of patient aggression and violence in health care has been a neglected area of investigation, the psychiatric nurse has a crucial role in preventing aggressive behaviors, results of this study will increase nurse's knowledge related to causes of aggression and violence among psychiatric patients. Therefore, this study was conducted to assess and compare causes of aggression and violence among psychiatric patients as perceived both by nursing staff and patients. A descriptive comparative design was utilized in this study. A sample of convenience of 200 psychiatric patients and nurses were recruited from the inpatient departments and outpatient clinic of EL-Abbassia Mental Health Hospital in Cairo. Sociodemographic/medical data sheet and causes of aggression and violence attitude scale were used to achieve the purpose of this study. A semi-structured interview was used to collect the data from both the studied patients and nurses. Findings of this study indicate that, psychological, interactional and environmental factors are the most frequent causes for aggression and violence among psychiatric patients, there were statistically significant differences were found between nurses and patients responses in relation to poor impulse control and delusions as psychological factors for aggression and violence among patients. To conclude it is important for nurses to remember that aggression and violence may not be solely a result of patient pathology but may be also a reaction to the situation in which patient find himself/herself. Periodical in-service training programs should be designed and implemented for nursing staff in prediction and management of aggressive and violent behaviors in psychiatric settings. More attention should be paid to educate patient alternative coping methods, by encouraging them to participate in group teaching stress management activities through the day treatment program.



P029

PREVALENCE OF EPILEPSY IN ETHIOPIAN COMMUNITY

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Chronic non-communicable diseases, such as epilepsy, are increasingly recognized as important health care problems in developing countries. Despite cheap effective treatment, the majority of people with epilepsy remain untreated. Community-based epidemiological studies of neurological disorders were performed in different part of Ethiopia. The most prevalent neurological disorder identified was epilepsy. It was estimated 360 to 400 thousand epileptic Ethiopians are living with poor medication. The prevalence of epilepsy was 5.2/1000 inhabitants at risk, 5.8 for males, and 4.6 for females.



P030

QUANTITATIVE ELECTROENCEPHALOGRAPHIC MONITORING OF THE ELECTRICAL ACTIVITY OF THE BRAIN IN ELDERLY DEMENTED PATIENTS IN COMPARISON TO NORMAL AGED SUBJECTS

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Introduction & rationale: Neurometric QEEG features are sensitive to the earliest presence of subjective cognitive dysfunction and might be useful in the initial evaluation of patients with suspected dementia and can increase diagnostic accuracy when used with other imaging techniques. Agreement on the parameters that are best measured on QEEG is still awaited. **Aim of the work:** was to identify the EEG changes in patients with dementia of Alzheimer type in comparison to normal subjects. **Subjects & methods:** A Case- control study was done to record the changes that occur in the electrical activity of the brain in patients with dementia of Alzheimer's type in comparison to a control group. Ten demented and ten normal age- matched subjects underwent EEG recording. **Results:** The disturbance of cognitive function in dementia was associated with electrical activity changes of the brain in the form of increase in the peak power frequency of theta and alpha 1, 2 frequency bands, while there was a decrease in the mean power of the delta and beta 1, 2 frequency bands in the demented group compared to the control group (P value > 0.05) over Fp2, and Fz electrode sites. QEEG and the MMSE scores in demented group using Spearman's rho correlation revealed no correlation between the mean of relative power of the frequency bands and the scores of MMSE in all frequency bands except for the alpha 1 frequency band which was positively correlated to the MMSE results (P value > 0.05 ; $r: 0.7$). **Conclusion:** QEEG is a non-invasive inexpensive tool for monitoring the changes that occur in brain activity in the dementia of Alzheimer's type in clinical practice, yet further studies to identify standardized criteria are still awaited.



P031

THE EFFICACY OF “INSIGHT ENHANCEMENT PROGRAM” ON IMPROVING THE PERCEPTION OF INTERNALIZED STIGMA AND LOCUS OF CONTROL AMONG SCHIZOPHRENIC PATIENTS

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lacking insight constitutes one of the major obstacles facing recovery among schizophrenic patients. This study aimed to investigate the efficacy of “Insight Enhancement Program” (IEP) on improving the perception of internalized stigma and locus of control among schizophrenic patients at “Agiad” psychiatry hospital “ at “ El-Mansoura” city .To verify this aim, 30 participants were recruited for this study using a quasi experimental research design (15 participants as a study group and 15 participants in the control group). Patients undergone the program while being in the inpatient unit, they were followed up 6 months after their discharge. Data was collected using both semi structured interviews and self rating scales. This study recommends the implementation Insight Enhancement program with psychiatric patients to improve their orientation of the nature of psychiatric illness, and the management of psychotic patients should move beyond symptomatic treatment to the integration between all forms of treatments, specially the insight oriented psychotherapies. Results of this study showed positive correlation between lacking insight and the positive history of aggression or violent behavior, also findings showed that lacking insight is mostly prevalent in single subjects compared to married subjects.(93.3%) of subjects in the study group after implementation of the program are totally insightful, compared to (46.7%) in the control group, also it was observed that (73.3%) of patients in the study group developed internal locus of control compared to (26.7%) in the control group after implementing the study. 6 months after patients’ discharge; it was observed that: (57.1) of patients who had internal locus of control felt low level of internalized perception of stigma, while (66.7) of patients who had external locus of control felt moderate level of internalized perception of stigma.



P032

ANALYSIS OF ASSOCIATION BETWEEN DOPAMINE RECEPTORS GENES METHYLATION RISK OF SCHIZOPHRENIA

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Dopamine is one of major neurotransmitters in brain and its receptors are associated with number of psychotic disorders such as schizophrenia. The aims of the present study were to analyze methylation of Dopamine receptor D1, DRD2, DRD4 and DRD5 genes in patients with SCZ. Methods: Promoter methylation of DRD1, DRD2, DRD4 and DRD5 genes was assayed by methylation-specific polymerase chain reaction (MS-PCR) in blood samples obtained from 88 SCZ cases and 71 healthy controls. Results: Promoter methylation of DRD4 and DRD5 genes were statistically different ($p < 0.05$) in cases when compared to healthy controls in blood samples, and a non significant association was found for methylation status of DRD1 and DRD2 genes between patients and healthy controls. Conclusion: Significant association were found in methylation profiles between schizophrenic patients and healthy controls for DRD4 ($p=0.002$) and a near significant association for DRD5 ($p=0.06$).



P033

STUDIES ON EFFECT OF STRESS PARADIGM IN STRESS-INDUCED BEHAVIORAL ALTERATIONS

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The stress is generally considered as the functional adaptation of the organism in order to cope with a changing and challenging environment. Thus, exposure to a stressor is immediately followed by somatic and neuro-physiological reactions involving peripheral organs and brain areas. In laboratory conditions, the most commonly used stressors are restraint or immobilization and forced swim. Although it is not easy to determine stressor intensity, which seems to be determinant in the level of the induced stress reactions, themselves made of short and long-lasting alterations. Behavioural consequences of different stressors applied chronically (90 min of restraint, 60 min of immobilization or 20 min of forced swim stress) were assessed in using two behavioural tests: after the stressor exposure in order to explore the psychomotor ability and a 10 min open field session after the stressor exposure to estimate the emotional status and the locomotor activity of the rat. Different behavioural responses were observed depending on the nature of the applied stressor. In the light extinction test, the rodents submitted to forced swim and restraint exhibited an activity level depending on the species. Moreover, restrained rats had a higher transient activity than forced swim rats under light condition. In the open field test, none of the stressed rats did develop differences in behavior compared to mice. The application of olfactive discrimination test shows many differences between the stress paradigms applied and between rats and mice. Taken together, the data obtained show, the behavioural response to a stressor exposure depends on the species, the intensity of the applied stressor and the behavioural demands.



P034

ASSESSMENT OF OBSESSIVE COMPULSIVE DISORDERS BEFORE AND AFTER TREATMENT USING MAGNETIC RESONANCE IMAGING APPROACH

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We suggest studying never treated OCD patients. This would contribute to better understanding of the OCD pathological aspects as well as clarifying indices of prognosis and final outcome after SIRS and/or behavioral psychotherapy treatments. In addition, evolving profiles of OCD patients still are not enough studied, and fewer studies interested in the predictive factors of a good evolution and no correlative neuroimaging study for objectifying the prognosis evolution. The goal of our work is to investigate the structural brain imaging abnormalities of never treated OCD patients, then find out correlations between the imaging abnormalities and the clinical profile of studied patients such the duration of the OCD, the severity and the prognosis of the disease after SIRS treatment. Never treated OCD patients were assessed using DMS IV. Patients were also assessed for OCD, depression and anxiety. All patients underwent MRI protocol of T1, T2, FLAIR and diffusion MRI before treatment. The initial assessment was achieved before treatment; then on third, sixth and 12 months of treatments. Meanwhile, a psychometric assessment was considered 2, 4 and 8 weeks of treatments. MRI data was postprocessed and results were correlated with clinical findings. Results showed correlations between the duration of the OCD before treatment, the gravity of the YBOCCS scores; and on the other hand the presence of brain MRI abnormalities, the size of depicted lesions and their regression after the treatment. The clinical improvement, absence of brain MRI abnormalities and the good prognosis were correlated. This indicated that MRI would be important predictive of answering to pharmacological treatments of OCD patients.



P035

INTERLEUKIN-1 BETA AND MICRORNA-146A IN AN IMMATURE RAT MODEL AND CHILDREN WITH MESIAL TEMPORAL LOBE EPILEPSY

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Problem statement: Increasing evidence indicates the critical role of neuroinflammation in the pathogenesis of mesial temporal lobe epilepsy (MTLE) which represents one of the most common and intractable forms of seizure disorders. The aim of this study was to investigate the dynamic expression of interleukin (IL)-1 β and microRNA (miR)-146a in the hippocampi of an immature rats and children with MTLE **Approach:** We studied the expression of IL-1 β and miR-146a through performing a RT-PCR, WB and qPCR on the hippocampi of immature rats PN (11). Expression was monitored in the acute, latent and chronic stages of disease (2 hours, 3 weeks and 8 weeks after induction of lithium–pilocarpine status epilepticus (SE), respectively), and in control hippocampal tissues. Similar expression methods were applied to hippocampi obtained from children with MTLE and normal controls **Results:** The expression of IL-1 β and miR-146a in both children and immature rats with MTLE differs according to the stage of MTLE development. Both IL-1 β and miR-146a are significantly upregulated, but in opposite ways: IL-1 β expression is highest in the acute stage (mean 0.36 ± 0.01), when expression of miR-146a is at its lowest level (mean 1 ± 0.1); miR-146a expression is highest in the latent stage (mean 2.8 ± 0.2), when IL-1 β expression is at its lowest level (mean 0.27 ± 0.08). Both IL-1 β and miR-146a are upregulated in the chronic stage, but not as much as in the other stages **Conclusion & Recommendation:** The different expression pattern of both IL-1 β and miR-146a at different stages suggests an interactive relationship. Our findings elucidate the role of inflammation in the pathogenesis of MTLE. Therefore, modulation of the IL-1 β –miR-146a axis may be a novel therapeutic target in the treatment of MTLE, working on the other inflammation related microRNAs will open a new avenue in the MTLE research



P036

DOPAMINE MANIPULATION LIMITED TO PRE-EXPOSURE SESSION IS SUFFICIENT TO MODULATE LATENT INHIBITION.

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Animals with a neonatal ventral hippocampal (nVH) lesion develop abnormal behaviors during or after adolescence, suggesting that early insults can have delayed consequences. Both the amygdala and hippocampus are implicated in psychiatric disorders as autism, attention-deficit, hyperactivity and schizophrenia. The present study was undertaken in order to test whether the latent inhibition (LI) is disrupted in postnatal lesioned rats using bilateral injection of Lidocaine into the ventral hippocampus.

A neonatal ventral hippocampal lesion was made in 7 days old pups. Two groups were formed, the first one received Lidocaine and the second was constituted by Sham operated control animals. At postnatal day 56, both groups were tested for social contact and the locomotor activity in an open field to confirm the establishment of schizophrenia symptoms. The LI was studied using the conditioned taste aversion paradigm before and after injection of D2 antagonist of dopamine receptors, Haloperidol prior pre-exposition phase sessions.

In behavioral study, we reported that the lesion of nVH induced several changes that mimic schizophrenia symptoms. Indeed, at the pubertal age, animals showed a significant decrease in the number of social interactions and highly increase in the locomotor compared to controls. Conditioned aversion taste showed that the nVH lesion significantly alters the LI which was more reduced compared to the control. However, we showed that the injection of haloperidol, 45 min before each of pre-exposure session in lesioned animals can recover substantially the latent inhibition to values around those of control.

Thus, these experiments demonstrated that nVH lesion using Lidocaine cause many behavioral changes related to Schizophrenia: disruption of LI, hyperactivity, anxiety... Furthermore our results showed that injection of Haloperidol restricted only to the three days of the pre-exposure phase is sufficient to facilitate LI of conditioned taste aversion.



P037

ANTIDEPRESSANT EFFECT OF BARLEY GRAINS INCOMPARE WITH PROZAC DRUG: BIOCHEMICAL AND CYTOLOGICAL STUDIES ON SKELETAL MUSCLES OF MICE

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Problem Statement The dysfunction of serotonin, norepinephrine &/or dopamine systems might contribute to depression. Many antidepressant drugs work by modulating these neurotransmission systems as Prozac drug but with adverse effects. The purpose of this study was comparing between the antidepressant effects of Barley grains with antidepressant drug (Prozac) on skeletal muscle of depressed mouse model, as Barley had been referred in Arabian traditional medicine for the treatment of depression. **Approach:** Forty adult mice assigned into four groups: -ve control (normal social environment), +ve control (socially isolated), Prozac (socially isolated) received an intraperitoneal injection (0.06 mg. Prozac/mouse/day-1) and Barley (socially isolated) supplemented with Barley grains instead the usual food (5g. Barley/mouse/day-1) for 30 days. Comparative observations included biochemical and cytological changes were recorded. **Results** In +ve control group exhibited hyperglycemia, had peripheral nerve with small accessory ending, short sarcomeres, accumulation of huge mitochondria, nerve terminals devoided of mitochondria but with electron-dense synaptic vesicles. Barley group exhibited hypoglycemia, low concentrations of lactate dehydrogenase, had side motor nerve trunk and neuromuscular junction demonstrating normative appearance. In the other hand, Prozac group attained the maximum level of creatinine kinase & total cholesterol, lower level of creatinine had degenerated axon terminal which failed to reach the subneural apparatus, myofillaments autolysis, incidence of mitochondrial cristolysis, diminished neuromuscular junction and demyelinated peripheral axons. **Conclusions** from the results obtained in this work, it was concluded that Barley reduce risk factors & might be therapeutic in preventing or treating many psychiatric & emotional disorders leading to more healthy life. **Key words:** Prozac Drug, Barley Grains, Biochemical, Cytology, skeletal muscles, neuromuscular junction, peripheral axon.



P038

CENTRAL NEUROPLASTICITY AND LOWER LIMBS FUNCTIONAL OUTCOME FOLLOWING REPETITIVE LOCOMOTOR TRAINING IN CHRONIC STROKE PATIENTS

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Background: Gait rehabilitation via task-specific repetitive training may induce central neuroplasticity in chronic hemiparetic stroke. Aims: explore central neuroplasticity underlying lower limbs functional improvement following repetitive locomotor training by electromechanical gait trainer (EMGT) compared to treadmill with partial body weight support (PBWS) in chronic hemiparetic stroke. Methods: Fifty chronic hemiparetic stroke patients allocated into 2 groups. Group 1 trained on EMGT of Hesse and group 2 trained on treadmill with PBWS. Fugel-Meyer lower extremity motor performance test (FM) and motor evoked potential (MEP) of paretic rectus femoris (RF), tibialis anterior (TA) and gastrocnemius (GC) muscles were assessed at beginning, end of eight-week training, and three months. Results: Group 1 scored higher postrehabilitation FM. In group 1, MEP variables showed postrehabilitation improvement (lower resting threshold, shorter latency and higher amplitude). Group 2 showed improvement in MEP variables except for MEP latency of TA and GC. Higher percentage of group 1 patients had obtainable MEP at study end. Percent changes in FM score and MEP variables were higher in group 1. In group 1, percent change of FM correlated positively with percent change of MEP amplitude of TA and RF and negatively with percent change of MEP latency of GC. In group 2, percent change of FM score correlated positively with percent change of MEP amplitude of RF and GC. Conclusion: EMGT is effective in promoting lower limb functional recovery in chronic hemiparetic stroke and central neural plasticity is underlying this recovery. This can help optimizing the therapeutic approach in chronic stroke rehabilitation with less number and facilitated work of the therapist.



P039

CENTRAL NEUROPLASTICITY AND UPPER LIMBS FUNCTIONAL OUTCOME FOLLOWING REPETITIVE LOWER LIMB LOCOMOTOR TRAINING IN CHRONIC STROKE PATIENTS

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Background: locomotor training may improve upper limb motor function in chronic hemiparetic stroke. Aims: explore the neurophysiological mechanism underlying the effect of long term repetitive locomotor training on treadmill with partial body weight support (PBWS) in improving swinging and supported paretic upper limb motor function. Methods: Thirty chronic hemiparetic stroke patients were assigned to either one of 2 experimental conditions while trained for 20 minutes on PBWS treadmill for 8 weeks. Patients under condition one received verbal cueing to perform bilateral upper limb swinging. In condition 2, patients were instructed to support both upper limbs on treadmill handrails. Fugel-Meyer upper extremity motor performance test (FM) and motor evoked potentials (MEP) of paretic deltoid (D), biceps brachii (BB) and abductor pollicis brevis (APB) were assessed before, immediately at end of program and at three months. Results: both conditions resulted in increase of FM score. Group 1 showed significant improvement of MEP variables (lower resting threshold, shorter central motor conduction time and higher amplitude ratio) in the 3 muscles. Group 2 showed significant improvement in MEP variables of APB muscle and increase of MEP amplitude of BB muscle only. Change of MEP threshold and amplitude of D and BB muscles were significantly higher in group 1 patients than in group 2. Conclusion: During treadmill training, active bilateral upper limb swinging improves effectively paretic upper limb motor function than supported upper limbs training. Central neural plasticity is underlying this improvement. Task-dependent neuronal coupling between lower and upper limbs could be beneficial in stroke rehabilitation.



P040

IMPLICATION OF CALCIUM-STIMULATED ADENYLATE CYCLASE 1 IN THE FUNCTIONAL RECOVERY OF AC1 KO MICE INJURED CORTICOSPINAL TRACT.

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cAMP is a major signalling pathway in axonal growth and regeneration. The enzymes that produce cAMP, the adenylates cyclases, could carry out different functions at different times in development and in the different domains of neurons. We recently showed that one isoform of the calcium-stimulated adenylate cyclase (AC1) is crucial in the fine patterning of the retinal maps and is required to modulate the response of retinal axons to ephrinA5. This indicates that cAMP signal is an important factor for modulating the responses of axons to molecular guidance in axon growth and regeneration.

We evaluated in the present study the implication of AC1 in the development of the corticospinal tract in vivo by investigating the anatomical organization of these pathways in the barreless (brl) mouse strain which carry a spontaneous mutation of the AC1 gene (anterograde tracing with BDA), and by examining whether this adenylate cyclase is implicated in vivo during the plastic remodeling of the corticospinal tract after injury (dorsal hemi-sections at the thoracic cord (T8-T10) in brl and WT mice.

Results of behavioral tests showed that brl mice exhibit better functional recovery over time compared to WT mice. 90% of brl mice recover after the 5th week vs 70% in WT using BDA tracing analysis of adult brl mice did not reveal obvious abnormalities in CST formation, but showed an increase in the number of ipsilateral fibers in the dorsal finuculis of the cervical cord.

Our study shows that the brl mice display greater functional improvement compared to WT. This suggests that the targeting defects could be linked to activity dependent remodeling of the CST and maintenance of exuberant axonal branches. Increase in the number of projections may explain the enhanced functional recovery after a spinal cord injury.



P041

ALTERATIONS IN INHIBITORY SYNAPTIC TRANSMISSION TO LUMBAR MOTONEURONS AFTER SPINAL CORD INJURY AND STEPPING RECOVERY IN ADULT RATS

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After spinal cord injury, the disruption of flexion/extension and left-right alternations has been attributed to an alteration of inhibitory circuitry. The aim of this study was to: 1) measure the alteration of the GABA and glycinergic synaptic transmission on lumbar Mns after spinal cord transection (SCT) in the adult rat, and 2) evaluate the benefit of manual training and stepping recovery on the changes of inhibitory networks. Changes in the expression of GABAA and Glycine receptors (GABAAR and GlyRA1) were investigated by immunohistochemistry in Mns innervating gastrocnemius (GS : ankle extensor) or tibialis anterior (Tib : ankle flexor). One month after SCT, GABAAR were significantly up-regulated on both GS and Tib Mns, while GlyR expression significantly increased in GS MNs, but remained stable on Tib MNs. Two months after SCT, a decreased expression of both types of receptors was observed in GS and Tib MNs. This decrease was highly significant four months after SCT. We developed a manual training procedure, based on daily alternate phases of imposed stepping and free walking in enriched environment. The recovery of stepping and standing was assessed using the CATWALK system (Noldus). Pharmacological treatment with 5-HT2 receptor agonists allowed a standing recovery and alternate stepping. Modifications of GABAergic and Glycinergic axonal terminals (ATs) on lumbar Mns were studied by immunohistochemistry. After SCT, a significant decrease of the density of glycinergic inputs was observed, whereas the density of GABAergic and mixed ATs was increased. In SCT-trained animals, the density of the three types of inhibitory ATs remained similar to those of controls. However, the mean length of all types of inhibitory ATs was significantly reduced in SCT-trained rats as compared to both SCT- and control rats. These results indicate that the training of SCT rats partially preserves a normal inhibitory afferent input to lumbar Mns.



P042

NEUROGLIAL ORGANIZATION OF THE HYPOTHALAMO-NEUROHYPOPHYSIAL SYSTEM OF PSAMMOMYS OBESUS

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The desert rodent *Psammomys obesus* lives under extreme conditions and overcome food and water shortage by modes of food and fluid intake. The hypothalamo-neurohypophysial system (HNS) is composed of magnocellular neurons that secrete vasopressin which is important in osmotic and cardiovascular regulation or oxytocin that intervenes essentially in the control of parturition and lactation. The axons of these neurons project to the neurohypophysis where the hormones are released into perivascular spaces. In the present study, we analysed the HNS of the diurnal desert rodent, *Psammomys obesus*. Using an immunocytochemistry and the electron microscopy, we revealed that the magnocellular neurons in this specie appear far more numerous than those in the rat, and vasopressinergic neurons clearly predominated. As dehydrated rat, in desert rodent, we also observed a coexistence of oxytocin and vasopressin in the same neurons. The HNS of *Psammomys obesus* showed neuro-glial organisation that characterized the HNS whose neuropeptides secretion is stimulated. Thus, as in the rat, during prolonged dehydration, there is a significant reduction in glial coverage of neuronal surfaces, and they are left directly juxtaposed and contacted by an increased number of synapses. Concurrently, in the neurohypophysis, there is an increased neurovascular contact zone. The neuro-glial remodeling in HNS must be mediated by cell-cell and cell-matrix interactions and the making and breaking of cell adhesion. Thus, it has been demonstrated that the expression of PSA-NCAM in the adult rat HNS is indispensable to its capacity for activity-dependent morphological neuronal-glial and synaptic plasticity. We showed that PSA-NCAM is strongly expressed in all portions of the SHN of *Psammomys*.



P043

NEURON-GLIA INTERACTIONS IN THE HYPOTHALAMIC MAGNOCELLULAR NEUROSECRETORY NUCLEI AN IMMUNOHISTOCHEMICAL STUDY IN THE SAHARAN LIZARD, UROMASTYX ACANTHINURUS BELL, 1825

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The morphological interactions between astroglial and neuronal elements were elucidated in the hypothalamic magnocellular neurosecretory nuclei of the Saharan lizard *Uromastix acanthinurus* by immunohistochemistry using polyclonal antibodies against Arginine vasotocin (AVT), glial fibrillary acidic protein (GFAP) and polysialic form of cellular adhesion molecule (PSA-NCAM) which intervenes in neuronal-glia interactions changes. In this Saharan lizard the hypothalamo-neurohypophysial system (HNS) was developed and riche in AVT magnocellular neurones involved in water balance. The capacity of neurones and astrocytes of the HNS to undergo reversible morphological changes in response to environmental stress intervenes in the perfect adaptation of this species to the dry area. Under conditions of low demand for AVT synthesis and release, astrocyte processes were interposed between adjacent neurones bodies. These astrocyte processes tightly covered much of each soma controlling the neuronal microenvironment and reduced neuronal excitability. In increasing demand for AVT synthesis and release due to the effects of dehydration, astrocyte-neurone interactions were modified by neuronal activity. Juxtaposed neuronal surfaces were induced by retraction of astrocytic processes. Astrocytic-neuronal remodelling participates to modulation and control of neurosecretion synthesis by the hypothalamic magnocellular nuclei.



P044

FRONTAL CONNECTIONS OF THE MEDIAL POSTERIOR-PARIETAL CORTEX IN THE MACAQUE

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Here we present the frontal connectivity pattern of the medial posterior-parietal cortex in macaque monkeys, a cortical region that contains the cytoarchitecturally-defined areas V6, V6Av, V6Ad, and PEc. Area V6 is an extrastriate pure visual area which lies in the fundus of the parieto-occipital sulcus. The two cytoarchitectonic sectors of V6A and area PEc are visuomotor areas lying in the caudalmost part of the superior parietal lobule. Contrary to V6, V6A and PEc receive and elaborate visual and somatosensory signals from the arms (V6A, PEc) and legs (PEc). Both areas contain arm reaching neurons strongly activated during reach-to-grasp movements. In the present work, horse-radish peroxidase and retrograde fluorescent tracers were injected within the cytoarchitectonic limits of areas V6, V6Av, V6Ad, PEc in 16 cynomolgus monkeys (*Macaca fascicularis*). No labeled cells were found in the frontal lobe after V6 injections and a few cells, confined within frontal eye fields and dorsal premotor area F7, were found after V6Av injections. Tracer injections in V6Ad resulted in a main projection originating from area F2 and a weaker projection originating from F7. After PEc injections, the large majority of labelled cells in the frontal lobe were found in area F2, with fewer cells in F1 and F3. About 75% of F2 projection cells were in the part of the area representing the leg. The remaining 25% were located in the visually responsive ventro-rostral portion of F2, the same part of F2 which is connected with V6Ad. If we take into account the relative emphasis of leg-field projections to PEc and of arm-field projections to the adjacent V6Ad, it could be suggested that the caudal pole of the superior parietal lobule, taken as a whole, contains the neuronal machinery to help control in locomotion and coordinated limb movements in the environment.



P138

THE MEDIAL POSTERIOR PARIETAL AREA V6A AND THE CONTROL OF ARM ACTIONS IN DEPTH

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A crucial region of the brain involved in controlling visually guided arm actions in both human and non-human primates is the medial part of posterior parietal cortex. Within this cortical sector, V6A represents a node of the parieto-frontal network involved in arm movement control. Here we show that V6A neurons are involved in several aspects of ocular and arm action control, together with the encoding of sensory signals dealing with somatosensory and visual monitoring of prehensile actions. The encoding of action-in-depth by single cells had not been studied till recently in V6A. Here we show that the activity of many V6A neurons is modulated by vergence eye movements aimed at fixating visual targets in depth. These signals are integrated, often at the level of single cells, with information about the direction of gaze, thus encoding spatial locations in 3D space. Moreover, 3D eye position signals seem to be further exploited at two additional levels of neural processing: a) in determining whether targets are located in the peripersonal or extrapersonal space, and b) in shaping the spatial tuning of arm movement related activity towards reachable targets. In the majority of the cells, a significant effect of both target direction and depth was found in all epochs of an instructed-delay reaching task performed in darkness. Spatial modulations of fixation activity were generally maintained across planning and subsequent reach-related epochs. Spatial preferences were kept across epochs and were evenly distributed throughout the reachable space. These findings are in line with studies in putative homologous regions in human medial posterior parietal cortex and point to a role of this cortical sector in the processing of eye position signals in order to jointly encode spatial location and hand movement information.



P112

EFFECT OF HAEMORRHAGE ON THE CATECHOLINDOLAMINERGIC ACTIVITY OF NEUROHYPOPHYSIS IN MAL WISTAR RAT, RATTUS NORVEGICUS.

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Catecholindolamines in the brain participate in drinking behavior control in response to hypovolemia, release of vasopressin and angiotensin-II induced thirst. The aim of the present work is to determine the evolution of blood parameters, and the catecholaminergic activity in the neurohypophysis of rats, subjected to bleeding for 10% of total blood volume and their implication in the physiological mechanisms controlling body fluid balance and neuroplasticity. The experiment focused on: 1) The study of physiological parameters of the water balance. 2) The study of catecholaminergic activity in the neurohypophysis. The bleeding has caused a significant changes in the plasma parameters. In the second part of our work, neurochemical study which concerns the determination of catecholindolamines rates (DA dopamine, norepinephrine NA and serotonin 5-HT) and their metabolites on neurohypophysial tissue, after separation by HPLC-DEC, showed an increase of DA and 5-HT, but rate of NA decreases. The increase in the DA and the decrease in its turnover reveal an increase of anabolism of this neurotransmitter. The significant decline recorded in the HVA and the ratio HVA to DA, indicate that there is a release of DA. Thus, the accumulation of DOPAC, resulting from the increased activity of tuberohypophysial dopaminergic neurons. Norepinephrine released is presumed to have peripheral effects, acting on the redistribution of fluids. In conclusion, our results suggested that changes in neurochemical and haematological parameters could result from a failure of hydromineral homeostasis which activates several neuroendocrine mechanisms including the release of catecholindolamines, ANG II and VP. These pituitary hormones work with the autonomic nervous system to decrease water and sodium loss, adjust the distribution of water between intra and extracellular fluid compartments.



P045

LEAD TOXICITY AND THE HYPOTHALAMIC - PITUITARY -TESTICULAR AXIS

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Environmental exposure to toxic levels of lead occurs in a number of industries with potential adverse effects on the reproductive capacity of exposed men. Clinical and animal studies indicate that abnormalities of spermatogenesis result from toxic lead exposure, but the pathogenetic mechanisms involved have not been identified.

In order to ascertain what reproductive abnormalities occur in experimental animals when exposed to low levels of lead, 65 days old animals were treated with water containing 0,0 mg (control), 10mg Pb /Kg/day and 15mg Pb /Kg/day intraperitoneally for 20 days. At the end of the 20 days, the animals were sacrificed and the blood collected and analyzed for luteinizing hormone (LH) and testosterone using standard procedures. The testis were collected and studied for histopathology.

Results showed high serum LH concentration in control animals and low concentration in test animals. The testosterone concentration also follows similar result. Histological examination of testis showed deformities in morphology of testis in test animals with gross damage within the somniferous tubules.

A strong correlation was established between LH and testosterone ($r=0,873$) suggesting that both biomarkers were synthesized at the same site. Changes in levels and stored hormone levels of LH and testosterone may be a mechanism by which the organism can adapt to Pb's toxic effects. We hypothesize that this is the mechanism by which Pb exposure during the critical time of sexual differentiation induces reproductive axis abnormalities in adulthood. From the results of these experiments we will develop a general model which accounts for the disruption by Pb of biologic function at specific metal dependent site. It was conclude that lead is a gonadotoxic with tendency of suppressing LH and testosterone levels of animals.



P046

EFFECTS OF EARLY IRON DEFICIENCY ON CATECHOLAMINERGIC TRANSPORTERS IN RAT BRAIN

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Iron deficiency (ID) is the most common single nutrient disorder worldwide. In this study, we investigated the possible effects of infantile ID on catecholaminergic membrane transporter densities in the brain. At postnatal day-4 (PND4), all pups were out-fostered. Animals were sacrificed at 21, 45 and 75 days of age. We examined individual brain regions specific for DAT; striatum, nucleus accumbens (NA), substantia nigra (SN), and olfactory tubercle (OT); and others specific for NET; frontal cortex (FC), dentate gyrus (DG), and locus coeruleus (LC). DA transporter ligand binding was performed using [¹²⁵I]-RTI-55 while NET transporter ligand binding was performed using Nisoxetine HCl [N-Methyl-³H]. Results reveal a significant age effect on DAT levels in NA, OT, and SN respectively but not in the striatum. Specifically, 21-day-old rats had greater DAT levels compared to 45-day-old rats in the NA, OT and SN as well as in the OT compared to 75-day-old rats. There was no main effect for diet and no diet-age interactions. Furthermore, there was a significant age difference on NET levels in the dentate gyrus but not in the frontal cortex or the locus coeruleus. Specifically, NET levels were increased among 45-day-old rats compared to 75-day-old rats. There was no main effect for diet and no diet-age interaction on any of the dependent variables. In summary, early ID in rats alters many monoaminergic-mediated behaviors. Such changes might be irreversible despite the fact that there is a restoration of peripheral and/or central iron. Future studies measuring monoamine transporter activities may highlight the effects of brain iron deficiency on various neural pathways with further defining the functional ramifications.



P047

BEHAVIORAL AND NEUROCOGNITIVE STATUS OF IRON DEFICIENT SCHOOLCHILDREN IN KENITRA NORTH WEST OF MOROCCO

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Objective: This work aims study the problem of iron deficiency and its implication on neurocognitive regulations and their impact on neurocognitive development and schoolchildren performances in Kenitra north west of Morocco. Iron deficiency remains an important public health trouble on a global scale, regional and local levels. The relations between iron deficiency and cognitive performance exist but the biochemical and physiological mechanisms linking it to an altered neurocognitive function are not yet clear.

Methods: We reviewed the studies relating IDA to Neurocognition especially on hippocampus functions alteration and consequently on learning abilities and memory. Then a set of cross sectional observational studies carried out in the city of Kenitra and its region will be presented. A total of 600 pupils were observed in different settings in rural periurban and urban. After validation and adaptation of cognitive tools, extracted batteries were used to assess cognitive status (Raven Progressive matrix, Bell tests, WISC extracts etc.). Iron status was assessed by Hemoglobin and serum ferritin.

Results: The main results confirm that anemia is very important in schoolchildren and its prevalence varies from 20 to 30 %. A strong association was found between iron deficiency alone and iron deficiency anemia with a global induced intelligence and visual attention performances.

Conclusion: Scientists rely on the use of new exploration techniques and behavioral neurocognitive (fMRI, EEG evoked potentials) to enlighten in the near future. The ongoing research is with infants in collaboration with Pediatric hospitals and research on animal models in relation to Long term potentating.



P048

NEUROHEPATIC TOXICITY OF SUBACUTE MANGANESE CHLORIDE EXPOSURE AND POTENTIAL CHEMOPROTECTIVE EFFECTS OF LYCOPENE

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Excess manganese (Mn) is potentially toxic resulting in a permanent neurodegenerative disorder, clinically known as “manganism” that is distinctive for hepaticencephalopathy. The present study was designed to explore the toxic impacts of subacute Mn exposure on brain and liver tissues, and the relative abilities of lycopene in averting such neurohepatic damage. Rats were daily injected with MnCl₂ (0 or 6 mg/kg, i.p.) 20 days after lycopene administration (0 or 10 mg/kg, p.o.), and killed 4 weeks after MnCl₂ exposure. MnCl₂-induced lipid peroxidation and perturbation in antioxidant system, increase of acetylcholinesterase, aminotransferases, and decrease alkaline phosphatase, and lactate dehydrogenase activities with hyperglycemia as demonstrated by Alzheimer type II astrocytosis, and periportal hepatic necrosis and apoptosis were prevented by lycopene. However, lycopene did not prevent the increased body burden of Mn and the altered Fe and Cu homeostasis induced by MnCl₂. Glutathione S-transferase and catalase activities, and glutathione content were reduced in MnCl₂-challenged rats, and sustained by lycopene. Our results indicate that although lycopene failed to reduce Mn concentration or retain disturbed elemental status; it appears to be a highly effective in alleviating its neurohepatic deleterious effects by preventing lipid peroxidation, hyperglycemia and changes in the activity of acetylcholinesterase and hepatobiliary enzymes, and antioxidant pathways.



P049

RESVERATROL ATTENUATES ALUMINUM-INDUCED NEUROINFLAMMATION: ROLE OF APURINIC / APYRIMIDINIC ENDONUCLEASE1 (APE1) AND CEREBRAL OXIDATIVE STRESS

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Chronic administration of Aluminum is proposed as an environmental factor that may affect several enzymes and other biomolecules related to neurotoxicity and Alzheimer's disease (AD). APE1 is a multifunctional protein that plays a key role in cell survival versus cell death upon stimulation with cytotoxic agent. The promising protective effect of resveratrol (RES), which is known to exert potent anti-inflammatory effects on neurotoxicity induced by aluminum chloride (AlCl₃), may be derived from its own antioxidant properties. In the present work we investigated the modulation of APE1 expression during AlCl₃-induced neuroinflammation (500 mg/kg body weight by oral gavages) in experimental rats. We tested the hypothesis that a reactive oxygen species (ROS)-scavenger, resveratrol (RES) at 200 mg/kg body weight, which is known to exert potent anti-inflammatory effects, would attenuate central inflammation and improve behavior condition in AlCl₃-fed rats. Neuroinflammation-induced genes including B-secretase, amyloid-B, PSEN-1, PSEN-2 and sirt-2 were determined by RT-PCR. APE1 is determined at mRNA and protein levels. Our results indicate that resveratrol may attenuate AlCl₃-induced direct neuroinflammation in rats, and its mechanisms are, at least partly, due to maintaining high APE1 level. Resveratrol co-administration with aluminum chloride exerted more protective effect than pre-administration or treatment of induced rats. A significant elevation of APE1 at both mRNA and protein levels was observed in addition to a marked reduction in B-secretase and amyloid-B. We conclude that the biochemical and molecular studies showed the neurotoxicity of AlCl₃ in the brains of rats. In addition, there was an ameliorative change with resveratrol against AlCl₃ neurotoxicity. This work was supported by Science-REP-2011, BA/CSSP-2010 and N€uromed FP7 project number 245807



P050

THE ANTI- NOCICEPTIVE ACTIVITIE AND TOXICITY OF PISTACIA LENTISCUS OF MOROCCO.

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INTRODUCTION: Pistacia lentiscus L., an evergreen shrub of the family Anacardiaceae, can reach 3 m in height, grows wild in arid areas and is characteristic of Mediterranean countries(1). The aerial part has traditionally been used as a stimulant, for its diuretic properties, and to treat hypertension, coughs, sore throats, eczema, stomach aches, kidney stones and jaundice (Bentley and Trimen, 1980(2); Palevitch and Yaniv, 2000(3)).

Objective: The aim is to study the toxicity and a nociceptive activity to leaves of Moroccan P. lentiscus

Materiel and method: We use in this study a male Swiss mouse weight between 24g and 30 g, and male Sprague –dawley rats weighting between 200-300g. And the decoction of leaves of Pistacia lentiscus obtained in the province of oulad zeyyad in beni mellal region-morocco. We use the aqueous extract.

Results: Any toxicity as shown in our doses, and the time of resistance to pain is less to the treated group than a control group in the hot plate test. And the number of stretching's very less to the group treated than a controlled group.

Conclusion: The leaves of our tree have an effect anti-ulcer that mean a propriety anti peripheral pain.

Bibliography: 1. The European Garden Flora, V: Dicotyledons, III. Cambridge University Press: Cambridge, 2.Bentley RY, Trimen H (1980). Medicinal plants. In Gardeli et al. (eds) Essential oil composition of Pistacia lentiscus L. and Myrtus communis L.: Evaluation of antioxidant capacity of methanolic extracts. Food Chem. pp. 1-11. 3.Palevitch D, Yaniv Z (2000). Medicinal Plants of the Holy Land. Modan Publishing House, Tel Aviv, Israel. In Ljubuncic et al. The effects of aqueous extracts prepared from the leaves of Pistacia lentiscus in experimental liver disease. J. Ethnopharmacol pp. 198–204.



P051

POTENTIAL NEUROPROTECTIVE EFFECTS OF HESPERIDIN ON 3-NITROPROPIONIC ACID-INDUCED NEUROTOXICITY IN RATS

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Huntington's disease (HD) is a progressive neurodegenerative disorder with a spectrum of cognitive, behavioral, and motor abnormalities. The mitochondrial toxin 3-nitropropionic acid (3-NP) effectively induces specific behavioral changes, primarily manifested as prepulse inhibition (PPI) deficit of acoustic startle stimuli, and selective striatal lesions in rats and primates mimicking those in HD. The implications of nitric oxide in a variety of neurodegenerative diseases attracts attention to study the possible role of flavonoids in interaction with nitric oxide pathways involved in HD. The present study investigates the potential effect of hesperidin, a flavanone group member, on 3-NP-induced behavioral, neurochemical, histopathological and cellular changes. Systemic administration of 3-NP to rats for 5 days (20 mg/kg) caused reduction of locomotor activity by days 2 and 5, 55% deficit of PPI response, elevation of cortical, striatal and hippocampal malondialdehyde (MDA) levels by 63%, 41% and 56%, reduction of respective catalase activity by 50%. Immunohistochemical staining of cortices, striata and hippocampi showed patches of iNOS positive cells. Electron microscopy ultrastructural examination showed marked mitochondrial swelling, perivascular edema and shrunken nerve cells. Pretreatment with hesperidin (100 mg/kg) ahead of 3-NP prevented any changes of locomotor activity or PPI response, slightly increased cortical, striatal and hippocampal MDA levels by 10% and reduced respective catalase activity by 22%, 20% and 5%. Only few iNOS positive cells were detected in sections from rats pretreated with hesperidin. This study suggests a potential neuroprotective role of hesperidin against 3-NP-induced Huntington's disease-like manifestations. Such neuroprotection can be referred to its antioxidant and anti-inflammatory activities.



P052

EFFECTS OF NICOTINE AND ALKALOIDS OF TOBACCO PLANT ON EXTRACELLULAR LEVEL OF DOPAMINE IN SUBCORTICAL REGIONS AND BEHAVIOR

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Nicotine, the main alkaloid found in tobacco plant, is generally accepted as the chemical responsible for the addictive properties of tobacco. Other alkaloids in the plant have been suggested to participate in the biological action of nicotine. Here, we hypothesized that these molecules modulate the effect of nicotine on the activity of central dopamine (DA) neurons, one of the main cellular target in addiction to drug abuse, as well as on behaviors addressing locomotor activity and anxiety.

Effects of single injection of nicotine and alkaloids of tobacco plant at dose (i.p., 0.5 mg/kg) were investigated behaviorally on locomotor activity in the “open field” (monitored 10 min and 35 min post injection), and on anxiety-like status on digging and marble burying test and neurochemically on the efflux of DA monitored in vivo by intracerebral microdialysis in the striatum and the nucleus accumbens of freely-moving Sprague-dawley rats.

Results show that locomotor activity was significantly enhanced and reduced by nicotine and the extract, respectively, when compared to vehicle-treated rats (number of lines crossed in vehicle-, extract-, nicotine-treated rats: 56 ± 6 , 27 ± 3 , 106 ± 13). In the digging and marble test, the number of marbles buried in the sawdust in controls (3 ± 0.1) was significantly enhanced in extract-treated (5.8 ± 0.2 , $p < 0.01$) only. Neurochemically, nicotine (0.5 mg/kg) enhanced accumbal and striatal DA extracellular levels (+47 and 20% above baseline, respectively). The extract (0.5 mg/kg, ip) evoked also a significant increase in DA extracellular levels in both regions (+33 and +38% above baseline). However, this effect was significantly higher compared to nicotine in the striatum ($p < 0.05$) only.

In conclusion, we provide behavioral and neurochemical evidence that the tobacco extract induces distinct effects compared to sole nicotine as it favors anxiolytic-like behaviors and normalizes the impact of nicotine on the nigrostriatal and mesoaccumbal pathway.



P053

PROTECTIVE EFFECT OF ARTEMISIA ABSINTHIUM L. EXTRACT ON LEAD INDUCED NEUROTOXICITY DISORDER IN RATS.

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Introduction: Lead poisoning is a potential factor in brain damage causes several neurophysiological and behavioral alterations.

Objectives: This study was undertaken to investigate the effect of wormwood plant *Artemisia Absinthium* L (A.AB) on lipids profile, redox status and neurobehavioral parameters of male rats intoxicated by lead.

Methods: rats (n=36) weighing 36 ± 6 g were assigned into 3 groups: (1) control group, (2) group was exposed to 1g of lead acetate (Pb) in drinking water treated for 11 weeks, (3) group was exposed of (Pb) who later received aqueous *Artemisia absinthium* extract (A.AB) (300mg/kg body weight) for 4-weeks (Pb(-)+A.AB). Thiobarbituric reactive substances (TBARS), carbonyls, catalase, phosphatase alkaline, phospholipids, cholesterol and triacylglycerol were determined on brain. Locomotors activities were performed in all groups.

Results: The intoxicated group (Pb) has a significantly increased the levels of TBARS, carbonyl proteins, phospholipids, cholesterol, triacylglycerol whereas a significant reduction was noted in the activity of catalase, phosphatase alkaline compared with the control group, hyperactivity by behavioral test, compared with control group. After treatment with *Artemisia Absinthium* L extract during 4 week, the group (Pb(-)+A.AB) indicate a significant decrease of TBARS, carbonyl, phospholipids, cholesterol and triacylglycerol ($p < 0,05$) compared with Pb group, the phosphatase alkaline, catalase activity increased significantly ($p < 0.05$) compared with Pb. The behavioral test (locomotors and grooming, sniffing, biting test) indicates a lower activity compared the group Pb.

Conclusion: These data suggest that administration of wormwood extract for 4 weeks ameliorate the damage neurotoxicological and neurobehavioral against lead exposure. Thus, aqueous extract wormwood might be effective to improve some disorders induced by lead.



P054

EFFECT OF ACUTE AND REPEATED NICOTINE ADMINISTRATION ON THE ELECTRICAL ACTIVITY OF THE LATERAL HABENULAR NEURONS IN RATS

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The lateral habenular (LHb) of the epithalamus is involved in a number of behaviours such as pain, stress, anxiety, learning and reward and drugs of abuse.

Here, we have investigated whether the LHb neurons are affected by nicotine treatment and whether they express nicotinic receptors.

First, the expression alpha4 and alpha7-containing nicotinic receptors (nAChRs) in the rat LHb was verified by western blot. The expression of these receptors by LHb neurons was further confirmed by immunofluorescence using confocal microscopy. Spontaneous activity of 34 LHb neurons was then extracellularly recorded in vivo in chloral anesthetized Sprague-Dawley rats. Spontaneous discharge rates of the recorded neurons displayed a range within 0.2-30.0Hz, with most of the neurons showing irregular firing patterns. The effect of acute i.v. injection of nicotine (200ug/kg) was tested on spontaneously active neurons. Only one cell per rat was tested with nicotine. 5 min before nicotine administration, an equal volume of vehicle was injected i.v. as a control. Nicotine induced an increase in firing rate in 40% of neurons characterized by a relatively slow onset, long duration and a peak effect of 200% compared to the baseline. A second group of neurons (40%) responded to nicotine injection with an increase characterized by a very short latency onset, an average peak effect of about 300% compared to the baseline and duration of about 20-30 sec, with spikes of decreasing amplitude leading to a total silencing of the neuron. Only 20% of the recorded neurons were unresponsive to nicotine.

The present study demonstrates that spontaneous activity of neurons within the LHb is strongly affected by systemic activation of nicotinic receptors. These data support previous evidence revealing an important role for LHb in nicotine addiction brain circuitry. The excitation of LHb neurons might mediate aversive events and indirectly inhibit midbrain dopamine neurons.



P055

THE POTENTIAL ROLE OF ARETEMISIA ABSINTHIUM EXTRACT AFTER CHRONIC LEAD TOXICITY IN ADULT WISTAR RATS

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Lead (Pb) is a heavy metal with no apparent biological function. It is recognized as a dangerous neurotoxic, since it induces morphological and functional abnormalities in the brain. Several studies reported, in the rat brain, the antioxidant and anti-inflammatory effect of aqueous extracts of *Aretemisia absinthium*.

In this study, we investigated the potential role of *Aretemisia absinthium* extract in protecting brain against the effect of chronic lead exposure on the dopaminergic neurons together with the glial system, using immunohistochemistry of tyrosine hydroxylase (TH).

The number of dopaminergic neurons in substantia nigra pars compacta (SNpc) was found to decrease by 50% in lead-treated group, while the glial fibrillary acidic protein (GFAP) immunohistochemistry shows hypertrophic immunoreactive astrocytes in the frontal cortex. The quantification of immunolabelled astrocytes shows an increase by 48% in comparison with controls. Treatment with *A. absinthium* extract restores most of the changes in the glial and dopaminergic systems which occur in lead intoxicated rats.

Our findings suggest that *A. absinthium* might be beneficial for the treatment of the glial and neuronal alterations observed during chronic lead intoxication in adult rat.



P056

PERSISTENCE OF LEAD NEUROTOXICITY IN MALE F2 GENERATION WISTAR RATS: BEHAVIORAL AND HISTOLOGICAL ASPECTS

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Lead (Pb), a non-essential trace metal, is ubiquitous in our environment, yet it has no physiologic role in biological systems and it is recognized as a toxic environment pollutant which the primary target of its toxicity is the nervous system. Even if it is supposed to be excreted by the urine, it was shown that the inorganic lead crosses the placental barrier and accumulates in fetal tissues including the brain. It is known that its toxicity causes structural, neurochemical and/or behavioral brain impairments. The aim of this study is to investigate the effect of lead persistence on memory and some nervous structures (hippocampus and entorhinal cortex) responsible of memorization process of male F2 generation Wistar rats. The intoxication lasted ten months and the stopping of treatment was for six weeks. Object Recognition memory test and histological study of different cited brain structures are conducted. The results show that significant decrease is shown in the index of short and long term recognition memory ($p < 0.05$) of intoxicated rats, compared to the control ones. Indeed, the hippocampus and the entorhinal cortex of intoxicated rats are too affected even the administration of toxic was stopped; the histological study demonstrate the presence of nuclear pyknosis, cell shrinkage and eosinophilic cytoplasm, in both structures of these groups of rats compared to the controls ones. Lead toxicity remains harmful to nervous system's structures and to behavioral performances, even the exposure is stopped.



P057

ALUMINIUM ALTERS THE CENTRAL NERVOUS SYSTEM IN RAT AND HUMAN: EPIDEMIOLOGICAL AND EXPERIMENTAL APPROACHES

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Heavy metals such as Aluminum (Al) constitute a category of metals that can elicit multiples Impairments in numerous tissues including the central nervous system, in fact, Al exposure have been mostly associated with neurological dysfunctions that occur in Alzheimer disease (AD). Indeed, we underwent an epidemiological investigation in the area of Marrakesh to assess the potential causes of AD in a sample of patients collected in the hospital of Mohammed VI)CHU MVI(. Our data showed that men as well women are affected with a same probability of 50%. Furthermore, the age of patients with AD may also be involved as a possible factor that can enhance the probability to have the illness. Regarding the environmental components of the illness, we suspected the consumption water treated with Al)during the process of water purification(highly consummated by most patients . Experimentally, we assessed in the wistar rat the effect of chronic exposure to Al in a dose of 3 g/L for 3 months from the intrauterine to adult age. By means of Immunohistochemistry of serotonin)5HT (in the dorsal raphe nucleus)DRN(, we showed a significant loss of 5HT immunoreactivity within the whole nucleus. Such alteration of serotonin expression was accompanied by noticeable changes in anxiety behavior in the intoxicated rats observed using the Dark Light Box apparatus in which animals spend more time in the light box, suggesting obvious anxiogenic-like effects of chronic Al exposure in rat. According to our epidemiological and experimental investigations, Aluminum may be an important risk factor involved in the pathophysiology of Alzheimer disease in humans as well as animals, while the precise mechanisms of Al neurotoxicity are still not well established, further questions should be addressed.



P058

IMPACT OF EXPOSURE TO MALATHION ON LOCOMOTOR ACTIVITY IN F2 GENERATION OF MALE WISTAR RAT

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Background: Organophosphorus pesticides (OP) are widely used in agriculture to pest control, thus improving quantity and quality of Human nutrition. So, their persistence in environment causes pollution and Human health hazards. Chronic exposure to low-level dose can interfere with normal development of central nervous system; this is leading to brain developmental neurotoxicity. Aim: The aim of this study is to evaluate the effect of exposition to malathion (pesticide less toxic but widely used in agriculture) during brain development, on motor activities in young rats. Methods: Four groups of female rats are bred with one non-pesticide exposed male. At gestation days six (GD6), groups1 is force-fed daily with Malathion (100 mg/kg (b.w.) "Mal 100"), group2 with 200 mg/kg (b.w.) and group3 with 300 mg/kg (bw), dissolved in corn oil. Control female group receive only vehicle "VEH" and they give control pup groups. At postnatal 12 (PND12), pups of each group are force-fed by the same dose until the stage of young adult (PND 60). Open field test (OF) is used to assess locomotor activity of rats in PND 60 stage. Results: The obtained results show that Malathion "Mal 300" is toxic to pregnant dam and causes stillbirth of pups. Both "Mal 200" and "Mal 100" induce high significant decrease in number of squares crossed ($p<0.001$ and $p<0.01$, respectively) and in numbers of rearing ($p<0.01$), compared to "VEH" ones ($p<0.001$). Conclusion: Malathion exposure during brain development can cause stillbirth at high doses, and decreases locomotor activity in young age, at lower doses.



P059

PROTECTIVE EFFECT OF ZINC AGAINST CADMIUM CYTOTOXICITY IN ADULT HIPPOCAMPAL NEURONS OF MERIONES SHAWI

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Purpose: Cadmium is a well-known environmental pollutant that leads to several neurodegenerative diseases during adulthood. The role of zinc in cadmium toxicity has been controversial and there are reports suggesting its synergistic as well as antagonistic effects. The current study was conducted to determinate the effect of zinc on cadmium-induced toxicity in the brain of a semi desert rodent *Meriones shawi* and to explore the role of metallothioneins in response to cadmium exposure. **Methods:** To imitate human environmental exposure and to produce adequate in vivo condition, we target a neuronal hippocampal culture model from adult rodent that supports the long-term survival and physiological regeneration of mature cells. The viability of neurons was assessed by TUNEL assay. The expression of metallothioneins (MT-I and-II) on neuron culture was examined by immunohistochemistry. **Results:** Cadmium induces neuronal death as Cd concentration increases with IC50 of 2.5 μ M, following 5 days of treatment. The present innovative data support that low concentrations of zinc protect against cadmium cytotoxicity via nuclear metallothionein induction by hippocampal neurons following heavy metals exposure. **Conclusion:** zinc may be used to module neuron for metallothionein release and provide therapeutic potential for brain lesions.



P060

TOXIC EFFECTS OF CADMIUM ON RETINAL NEURONS OF MERIONES SHAWI- A BIOINDICATOR OF CADMIUM POLLUTION

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Purpose: Cadmium (Cd) is a highly toxic environmental heavy metal. Cd accumulates in human tissues with a long biological half-life. Thus, the effects of Cd in human and animal eye are still under investigations. In this study, we report the effects of Cd on the retina of a nocturnal rodent *Meriones shawi* **Methods:** 24 adult males *Meriones shawi*, were divided into three groups: the first group received contaminated diet with Cd in the form of CdCl₂, (administered at 1g Cd/1 L H₂O/1.5 kg of granule flour) for two weeks; the second group received contaminated diet with Zinc (Zn) and Cd with the same doses as the first group for two weeks; finally, a control group received standard rat chow in identical manner. After two weeks, Cd and Zn levels were measured in retina using inductively coupled plasma mass spectrometry and graphite furnace spectrophotometry, with values normalized to protein levels. Immunohistochemistry and western blot analysis were performed to assess the structural effects of Cd on all retinal layers. **Results:** Higher Cd levels were found in the neural retina of treated animals compared to controls. Cd induced statistically significant decreases in retinal cell layers thickness and density accompanied by profound alterations in glial cells (down-regulation of glutamine synthetase, up-regulation of glial fibrillar acidic protein). Cone photoreceptors were particularly affected, with reduced expression of cone opsins and transducin. Apoptotic nuclei were observed in all retinal layers of CdCl₂-treated animals. Contrarily, Zn restored initial retina state. Treatment with Zn exhibited a protective role against Cd toxicity. This fact may be explained by the role of Zn in metallothionein synthesis, a Cd detoxification agent. **Conclusion:** The retinal exposure to Cd caused apoptotic changes in *Meriones* retina after two weeks of CdCl₂ treatment, and shows the toxic effect of Cd and possible protective effects of Zn.



P061

IMPACT OF LEAD (PB) ON CEREBRAL ENZYMES AND BEHAVIORAL CHANGES IN YOUNG WISTAR RATS

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This study was carried out to investigate the neurotoxic effects of lead acetate (1g/L) in wistar rats. Enzymatic Alkaline phosphatase (ALP), acetylcholinesterase (AChE), monoamine oxidase (MAO) activity was determined in offspring rats (day 21) issues from Pb treated females during lactation period. Our results showed that lead affects certain enzymes involved in brain development such as AChE, the PAL and MAO. We observed that the administration of lead acetate at a dose of 1g / L for 4 weeks in drinking water to young rats aged 21 days préablement intoxicated in lactation period , causes changes in physiological, biochemical and neurobehavioural parameters. In fact, this exposure to lead causes a significant reduction in body weight, water consumption and the relative weight of different organs (liver, kidney and brain). This shows that lead has an anorexigenic effect through its involvement in the neural pathways responsible for regulating satiety. We also observed a significant decrease in locomotor activity in young rats intoxicated compared with controls. This hypolocomoteur is accompanied by a decrease in stereotypic behavior of the animal (curiosity, sniffing, biting and grooming) . Locomotor hypoactivity is the consequence of disruption of the synthesis of catecholamines or their release at the synaptic by an implication on the voltage-dependent Ca channels. This series of behavioral tests also allowed us to observe the installation of a state of despair and anxiety .Histological study showed alterations in the cerebellum and a separation of cerebella cortex layers. In conclusion, lead is dangerous neurotoxic metal , it induce alteration of development and neuronal differentiation by modified activity of cerebral enzymes witch play a critical role in brain development and behavior.



P062

PHYSIOLOGICAL VARIATIONS OF MONOAMINE TISSUE CONTENT DURING THE REPRODUCTIVE CYCLE IN *PERNA PERNA* AND THEIR OUTCOME IN MARINE POLLUTED SITES.

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Monoamines are present in bivalvia where they are thought to control reproduction functions. Reproduction of *Perna perna* is disrupted in polluted sites, altering gametogenesis, invidious laying or atresia. Although these modifications could involve changes in monoamines function in those mussels, the distribution and the putative seasonal variations of monoamines are lacking in *Perna perna*. In this study we determined noradrenaline (NA), dopamine (DA), and 5-hydroxytryptamine (5-HT) tissue content in three organs (gonads, cerebral and pedal ganglia) of 3 mussel populations at 4 reproductive stages (resting, developing, maturing and egg-laying). Samples of *Perna perna* were collected from an unpolluted site (Bouknadel) and two polluted sites (Hay al-Fath, Mohammedia) localized alongside the Atlantic coast of Morocco. The distinct stages of reproductive cycle of *Perna perna* were identified histologically on gonads in each population. Monoamine contents were determined by HPLC coupled to electrochemical detection. The results show in the unpolluted site a distinct distribution of monoamines in selected organs (NA, DA and 5-HT in pg/mg respectively: 128±10, 15±1, 8±1 in gonads; 96±19, 75±9, 85±14 in pedal ganglia; 91±12, 158±13; 51±7 in cerebral ganglia). NA concentrations sharply increased during maturing stages and declined during spawning. DA and 5-HT concentrations increased during egg-laying (> threefold increase). Pollution altered the seasonal variations of monoamines. In particular, NA content did not fluctuate in polluted sites. Differences between polluted sites were observed mostly during laying for DA or 5-HT contents. This study extends previous data in bivalve mollusks to the situation of *Perna perna* that monoamines contents fluctuate with respect to organs and seasons. It further shows clear-cut variations for each monoamine during the stages of the sexual cycle highlighting their distinct functional role. The disruption of reproductive functions in polluted sites could be therefore underlined by alterations of monoaminergic systems and notably NA.



P063

BENEFICIAL EFFECTS OF PECTIN AGAINST LEAD INTOXICATION

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The aim of the present study was to investigate the beneficial action, *in vivo*, of pectin against subacute lead acetate (350 mg/l) intoxication. The adverse effects of lead on the haematological disturbances that concerned, more precisely, the decrease of red blood corpuscle life duration and on the appearance of ever granulated basophilic haematites by inhibiting an enzyme responsible for haeme synthesis have been demonstrated after 1 month of oral lead administration to female Wistar rats. Also, this caused an elevation of the blood lead level as compared with the control group. The introduction of carrot pectin to a level of 3% in the feeding of intoxicated rats has shown a chelating and correcting effect on haematological disturbances caused by lead toxicity, which is reflected by a significant decrease ($P < 0.05$) of blood lead (from 117 to 65 to 19 $\mu\text{g/l}$), zinc protoporphyrine (portoporphyrine-zinc from 7.7 to 5.1 to 3.5 $\mu\text{g/g}$ of Hb), increase in haemoglobin to 27% (from 5.09 to 6.05 to 7.79%) and iron to 8% (from 1.34 to 0.9 to 0.5%) of the treated rats by pectin as compared with the untreated groups. Differences in blood lead were significant between the control diet and the addition of pectin therefore suggesting that pectin fiber ingestion in diets decreases the risk of lead poisoning.



P064

INNATE IMMUNE RESPONSES TO AFRICAN TRYPANOSOME BRAIN INVASION

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The central nervous system is adapted to down-regulation of immune responses that could inflict injury to the system, but has preserved less harmful responses to combat infections. To study the immune response to a microbe in the brain we use mice infected with trypanosome brucei (Tb; extracellular parasites, which have developed complex interactions with the immune system to favor their survival. We study mechanisms by which parasites pass across the BBB and how growth of the parasite can be controlled in the immunoprivileged brain. In particular, we have studied the role played by the chemokine CXCL10 in the cross-talk between the innate and adaptive immune responses. Here we ask whether a control of parasite growth in the brain exists distinct from that of neuroinvasion. In order to distinguish these processes the role of nitric oxide (NO) in the outcome of Tb infections is have been analyzed. A direct trypanocidal role of NO is unlikely since Tb and different mammalian cell lines were similarly susceptible to NO donors in vitro. In the brain of Tb-infected mice, iNOS was induced, but surprisingly localized in perivascular macrophages, but not in activated microglia. iNOS^{-/-} and control mice (WT) showed similar parasitemia levels. However iNOS^{-/-} infected mice showed accelerated loss of weight and mortality than WT controls. Unexpectedly, iNOS^{-/-} mice showed dramatically increased numbers of Tb, CD4⁺ and CD8⁺ T cells in the brain. In line with this, Tb. infected iNOS^{-/-} mice showed increased levels of endothelial cell adhesion molecules. Moreover, iNOS^{-/-}, but not WT, mice showed increased vascular permeability in the brain, reversed by treatment with an NO donor. Thus, NO plays an unanticipated anti-inflammatory role in Tb infection by negatively regulating expression of adhesion molecules, inhibiting vascular permeability and protecting the brain from penetration of parasites and T cells.



P065

ACUTE LEAD ACETATE ADMINISTRATION AFFECTS MOTOR COORDINATION IN MALE MICE

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Lead (Pb) is widespread toxic metals found in the environment and potential danger to human health due to its multifaceted action with a broad range of physiological and biochemical dysfunctions. Exposure to low-levels of Lead leads to the behavioral abnormalities, learning impairment, decreased hearing, and impaired cognitive functions in humans and in also reported in laboratory animals. In this study, the effect of acute lead administration on motor coordination was evaluated using beam walk test in male mice. Animals were administered lead acetate in graded doses of 7.5 – 60 mg/kg. There was a statistically significant increase in the number of foot slips at doses 30 and 15 mg/kg when compared with control. This finding suggested that acute lead administration at lower doses produces motor coordination deficits in the male mice. Key words: lead, beam walk test, motor coordination *Corresponding author: Dr. Rabiu AbduSSALAM Magaji. E-mail: rabiumagaji@yahoo.co.uk, phone No. +2348023558721



P066

ESSENTIAL HEAVY METALS STATUS IN THE BRAIN OF STRESSED RATS

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GABAA receptors are ligand-gated ion channels, mediating fast synaptic inhibition in the central nervous system (CNS). They are the targets of a variety of pharmacologically and clinically important drugs such as benzodiazepines, depressant barbiturates and hypnotic steroids. Beside these major modulators, some metal cations inhibited the GABA response of neurons in a variety of organisms. Among them zinc and at a lesser extent iron, have been reported to be the most potent. GABAA receptors have been shown to increase in density following the application of acute stress. Furthermore, their modulation has been reported to be altered. These alterations in density and modulation have been explained by an alteration of the content of these endogenous modulators. For this, we aim to exam in the present investigation the concentrations of Zn²⁺ and Fe²⁺ in the brains of stressed rats and compare them to unstressed animals, to assess eventual differences. GABAA receptors level in several stress-sensitive areas investigated for the assessment of endogenous heavy metals following acute immobilization stress. The mean concentrations of Zn²⁺ are significantly decreased in whole cerebral cortex, whereas they are not changed in the whole brainstem. It seems that the forebrain structures were relatively highly sensitive to stress effect, principally hippocampus. Interestingly, the topography of these alterations correlates well with the stress sensitive brain areas we reported previously. Taken together, these results support the alteration of the modulatory function occurring at the GABAA receptor level induced by stress. The concentration of the heavy metals investigated is not sufficient to modulate with efficacy the GABAA receptor. This could explain the higher densities of GABAA receptors observed after acute stress. Indeed, the concentrations are not still sufficient to inhibit with efficacy these receptors.



P067

MANGANESE NEUROTOXICITY INDUCES ATYPICAL PARKINSONISM IN THE RAT

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Manganese (Mn) neurotoxicity is associated with progressive disturbances in motor and cognitive functions. However, the exact mechanisms underlying these deficits remain unknown. The present study aimed to investigate the effects of Mn intoxication on: locomotor activity using an open field actimeter; motor coordination using rotarod; anxiety behavior using elevated plus maze; “depression-like” behavior using sucrose preference and forced swim test; Globus Pallidus (GP) and Subthalamic Nucleus (STN) neuronal activities by using extracellular electrophysiology. Male Sprague–Dawley rats were daily treated with MnCl₂ (10 mg/kg/ i.p.) for 5 weeks. Subsequently, we determined the impact of Mn on the postmortem tissue level of monoamines in different brain regions. The results show that Mn induced a gradual decrease of exploratory and locomotor activities, of motor coordination, together with anxiety and “depressive-like” behaviors. Electrophysiological results show that while majority of GP and STN neurons discharged regularly in controls, Mn induced an increase in the number of GP and STN neurons discharging irregularly and/or with bursty pattern. Moreover, Mn decreased the firing rate of GP and STN neurons. HPLC analyses show that Mn significantly decreased tissue levels of noradrenalin and serotonin in the prefrontal cortex, while an increase in the level of dopamine and its metabolite 3,4-dihydroxyphenylacetic acid was found in the striatum. This work shows for the first time that Mn resulted in motor and non motor deficits as well as changes in the activity of GP and STN neurons. These changes were paralleled by noradrenaline and serotonin depletion, in addition to an increase of dopamine metabolism. Together, these data provide evidence that Mn is responsible of pathophysiological changes similar to those observed in atypical parkinsonism. This work is supported by “Université Bordeaux Segalen”; French-Morocco International Program (GDRI N198: CNRS and INSERM, France and CNRST, Morocco), Volubilis No 20565ZM, and NEUROMED 7th PCRD-FP7 REGPOT-245807.



P068

EFFECTS OF DATES EXTRACTS ON LEARNING AND MEMORY IN MICE

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The role of phytomicronutrients such as polyphenols is now highly studied and appreciated in the control of such degenerative diseases. Dietary polyphenols have been widely touted as antioxidants, and numerous studies have attributed the potential health beneficial effects of these compounds to their antioxidative activities. The present study was undertaken to assess the protective effects of dates extracts on behaviour and memory of mice.

Mice were randomly assigned to one control group and three groups orally administered 25, 50 and 100 mg/kg/day dates extract for a period of eight weeks. The animals of the control group received only physiological saline solution during this period. After cessation of treatment, locomotor activity, hole-board test, forced swimming, black and white test box and Morris water maze were evaluated to assess anxiety, responses to stress and learning memory of animals.

In anxiety-related behaviors, dates extracts exposed mice were more active in the locomotor activity and holeboard tests with significantly higher activity scores ($p < 0.05$), and they did not become hyperactive in the porsolt's swimming test. They were less affected by the light conditions in the central area of black and white test box. Dates extracts treated mice had improved spatial working memory, with high performance scores ($p < 0.01$) at Morris water maze. Dates extracts treatment dose-dependently ameliorates spatial learning and memory in mice.

This study demonstrates that dates polyphenols are effective in improving the spatial learning and memory of mice. These findings strongly implicate that dates has potential to protect brain from oxidative damage resulting from such environmental factors.



P069

A NEW COGNITIVE THERAPEUTIC PROGRAM OF APHASIC IMPAIRMENTS IN PLURILINGUAL CASES

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Problem Statement The main challenge in neuropsycholinguistic field was, since 1915, the creation of theoretical models. In this proposal, we'll synthesize our 30 year experience in neuropsychological clinical-theoretical approach. We started our researches in neuropsychology in 1977 (Paris VI, Faculty of Medicine). We have worked in description, then classification (N. Z., Glossa, n° 23, 1991), then interpretation (N. Z., IALP, Septembre 1998), then rehabilitation (N. Z., I.A.L.P, Cairo, 1995) of aphasic syndroms.

Approach We have used a program - the first Algerian neuropsychological full battery plurilingual tasks : the "MTA"2002, the elaboration and technical realization have been financed in the frame of a French-Algerian agreement project (CMEP - Algiers and Toulouse Le Mirail Universities - 91MDU 177). The observation concerned 17 motor and sensory cases of 50-60 years old. The cerebral injury was caused by a physical traumatism. Starting from our neurolinguistic typology and cognitive interpretation of aphasic impairments, we'll present a cognitive theoretical model of aphasia based upon temporo-spatial structuration concepts. **Results** A therapeutic program deduced from this model gives positive results, promising new perspectives in neurosciences (N. Z., ANAE, 111, Paris, 2011). We have directed a research team of Sciences of Language and Cognitive Neurosciences of Algiers 2 University Laboratory experience during these two last years. The team propose here 02 case studies results : a motor and a sensory cases followed in a group work, on the basis of the use of this model. Patients are trilingual : arabophone, berberophone and francophone, what means that our therapeutic program is applicable whatever the aphasic language is.

Conclusions/Recommendations Our results will concern two points : - the theoretical implication of our approach upon anosognosia notion ; - proposal of recommendations about the approach of the tests performances, based upon our conceptual model of aphasic impairments explanation model.



P070

THE EFFECT OF ECSTASY IN LONG MEMORY AND D1,D4 AND D5 DOPAMINE GENE EXPRESSION OF HIPPOCAMPUS IN MALE VISTAR RAT

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Introduction: The demand for MDMA is so concerning and consumers have problems in learning, verbal memory, cognitive disorders, behavioral problems, orientation and learning templates, frequently in neurophysiological tests, which can be a sign for neurodegenerative disorders. So the aim of this research is to study the effect of MDMA on long memory and gene expression of D1, D4 and D5 dopamine receptor in hippocampus of rat. **Materials and Methods:** In this research, forty male rats from vistar race were used. Animals were divided into four groups including control, sham (saline) and experimental doses (2.5, 5 and 10 mg/kg). Rats in experimental group were received MDMA each seven days, three times in a day, during four weeks and the memory were assessed by shuttle box. 12 hours after the last injection and the test, the brain of rats were dissected. After total RNA extraction and cDNA synthesis, we used real-time RT-PCR to determine the gene expression of dopamine D1, D4, D5 receptors in hippocampus. **RESULT:** Our study have shown that low and middle doses of ecstasy interfere with memory but in high doses, MDMA doesn't show the same result. In the other hand, all the doses of MDMA will increase the expression of dopamine receptor and the peak of this elevation is in the middle dose group. **CONCLUSION:** We suggest that MDMA can destroy memory (dose depended) and this may increase the gene expression of dopamine receptor in hippocampus. **KEY WORDS:** MDMA, passive avoidance memory, dopamine receptor, hippocampus



P071

NUMBER PROCESSING IN ARABIC AND HEBREW BILINGUALS: EVIDENCE FOR THE DISTANCE AND COMPATIBILITY EFFECT

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Previous studies on numbers processing conducted in Indo-European languages have suggested that there are differences in performing different number tasks. In this study we used two-digit numbers in Arabic (Hindi) and Hebrew (Arabic) that differ in both lexical and syntactic structure to test the hypothesis that the lexical-syntactic presentation of the Arabic numbers has an effect on the task of comparing numbers and especially on the distance effect and the compatibility effect.

Native Arab bilingual subjects who participated in choice paradigm of numerical comparison in Arabic and Hebrew, showed differences in the compatibility effect between the different numerical-digital numbers. We argue that the magnitude of two-digit numbers has not been exclusively represented on the mental-semantic number line, but it may be represented by additional separate representations of unit-digits and decade-digits.

The findings extend previous results on other languages with regard to the syntactic structure of the language number system and support the notion that there is a differential weight assigned for the decades-digits comparison (in Hebrew) and the units-digits comparison (in Arabic). A theory to account for how representations depend on the numerical amount is proposed based on the study results and previous findings.



P072

DYNAMICS OF DECISION-RELATED ACTIVITY IN PROSPECTIVE HIPPOCAMPAL PLACE CELLS

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The hippocampus is involved in spatial navigation and contextual memory. Hippocampal principal cells fire when a rat is in a specific place in its environment and this “place cell” activity can be prospectively modulated by the rat’s imminent trajectory.

To examine whether there is a link between prospective coding and navigational decision processing, we recorded place cells in rats performing a task involving a sudden decisional switch and assessed the latency of the prospective activity onset. Rats learned to alternate (ALT) in a continuous T-maze task. Every 5 to 7 trials, a visual cue (VC) was presented as the rat crossed a photodetector at the middle of the central arm. This instructed the rat to repeat a visit to the previous arm rather than to continue alternating. This permitted measurement of the delay required for place cell responses to started to change in accordance with the changed intention of the animal. We recorded 866 cells in 4 rats in 26 sessions and measured prospective activity onset in the VC and ALT trials employing a bootstrap method.

In all prospective 19 neurons activity never appeared earlier in cued trials than in alternation trials. A linear regression (t-test for slope $p=0.0128$) of the onset times of activity in ALT trials plotted as a function of the time difference between the activity onsets of VC and ALT trials yielded a value of $T\sim 420$ ms.

This relatively long delay for prospective activity to arise (compared to on the order of 100-150 ms in other brain areas) indicates that the navigational behavioral choice signal is likely elaborated elsewhere before reaching the hippocampus, perhaps in pathways involving cortico-striatal loops and are then transmitted to the hippocampus for prospective activity. The hippocampus would then engage this for contextual processing of memories in time and space.



P073

STUDY OF CHANGES IN THE NEURONAL NETWORKS RESPONSIBLE FOR MEMORY IN RESPONSE TO STRESS IN DIFFERENT ENVIRONMENTAL CONDITIONS IN RAT

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Stress can produce pathologically strong and intrusive memories, and also impair concentration and increase forgetfulness. Chronic stress causes neurons to shrink or retract their connections, which may have important behavioral consequences. The present study was performed to determine the effect of series of stressors in different brain parts especially hippo-campus, amygdala and basal ganglia focusing on the change in synaptic connections. This effect was also correlated to the changes in rat memory after living alone and/or in society using a light-dark box.

Three rat groups were included as follows: Group C (controls which did not exercise), Group A (40 days exposed to an unfamiliar environment with irregular light-dark cycle along the day) and Group B (65 days exposed to an unfamiliar environment with irregular light-dark cycle along the day).

Our preliminary results showed average changes in rat weight from great increase to stability with a constant in nourishment dose. Animal behavior changed rapidly and unpredictably from quiet and gentle mode to more nervous and aggressive mode with absence of balance in their movement. Our complement research suggests that the hippocampal volume will be reduced due to the loss of nerve cells and change in dendritic morphology which might alter synaptic connections in response to chronic stress.

Those changes may cause a defect in encoding new memory or recovery of the old one stored in the rat brain.



P074

CROSS-MODAL PLASTICITY ASSOCIATED WITH ARG3.1/ARC GENE EXPRESSION WITHIN THE OCCIPITAL CORTEX OF ANOPHTHALMIC ZRDCT/AN MUTANT MICE FOLLOWING AUDITORY OR SOMATOSENSORY STIMULATION

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The immediate-early gene *arg3.1/arc* has been shown to directly modulate synaptic properties underlying long-term memory. In recognition memory, a stimulus is compared to previously encoded stimuli for it to be perceived as novel.

Immunohistochemical techniques were employed to map *arg3.1/arc*-immunoreactive (-ir) neurons in superficial (II-IV: SL) and deep (V-VI:DL) laminae of occipital (OC) and either auditory (AC) or somatosensory (barrel field:SC) cortices in anophthalmic ZRDCT/An mutant mice after either novel unilateral auditory (white noise bursts) or somatosensory (air puff) stimulation (groups ZA and ZS, respectively). The same experiments were carried out in normal-sighted C57BL/6 mice (respectively groups CA and CS).

Arg3.1/arc-ir neurons were always more numerous in DL than SL of stimulated cortices and maximum mean numbers (\pm S.E.) recorded in single brain sections in the AC of ZA animals were $94\pm 11/63\pm 8$ and in the SC of ZS mice were $180\pm 45/49\pm 16$. Significant numbers of immunoreactive neurons indicating cross-modal plasticity were also observed in the OC of both ZA ($92\pm 30/21\pm 9$) and ZS ($157\pm 46/36\pm 7$) groups. In CA and CS mice, *arg3.1/arc* immunoreactive neurons were found within the respective stimulated AC ($76\pm 11/45\pm 1$) and SC ($265\pm 68/107\pm 37$) and their numbers did not differ significantly from those observed in ZRDCT/An mice. However, compared to the latter, very few labeled cells were identified within the OC (visual cortex) of C57BL/6 mice.

Cross-modal plasticity to both auditory and somatosensory stimulation was demonstrated in ZRDCT/An mice. Moreover, the data indicated that the topographical distribution of *arg3.1/arc* neuronal expression to both the auditory and somatosensory stimuli overlapped within the different layers of the occipital cortex. It remains to be determined how, in the blind mice, such transferred input from these two different sensory modalities is simultaneously processed within what is normally a unimodal primary occipital cortical centre.



P075

SPATIAL MEMORY AND LEARNING DEFICIT FOLLOWING PRENATAL EXPOSURE TO FENUGREEK SEEDS IN ADOLESCENT MICE

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Disturbance of endogenous hormones actions by chemicals, have been implicated in birth defects associated with hormone-dependent development. Phytoestrogens are a class of endocrine disruptors found in plants. In the current study we examined the effects of prenatal exposure to Fenugreek seeds, a phytoestrogen plant; on learning and memory ability of the offspring mice. Female swiss mice were randomized into 3 groups and subjected to daily oral gavage of Fenugreek seeds aqueous extract at the doses of 500 mg/kg (group A), 1000 mg/kg (group B), or distilled water (group C, as control). Pups body weight was measured at 1, 7, 14, 21 and 28 day of age. From each group, 20 male weaning mice of the first generation were randomly selected to examine their spatial memory (3 weeks) using continuous alternation in T-maze task and to assess associative learning ability by the shuttle-box- avoidance learning test (14 weeks). The brain of the offspring was removed and cut for histological evaluation.

The progeny of exposed mice displayed reduced body weight at birth (1000 mg/kg group: 27%; 500 mg/kg group: 32%) and reduced brain weight (10% in both treated groups). Assessment on a continuous alternation T-maze test showed a significant reduction in successful spontaneous alternations in exposed mice but only in the 1000 mg/kg group. In the shuttle-box, the avoidance performance of the treated groups was significantly inferior to that of controls in the 2nd, 3rd and 4th days of the test.

These results allow us to conclude that maternal fenugreek seeds exposure induces growth retardation and disturbance of the learning and memorizing abilities in the offspring mice.



P076

RIGHT-HEMISPHERIC DOMINANCE OF DENTATE GRANULE CELL ACTIVITY AFTER SPATIAL EXPLORATION IN SPLIT-BRAIN MICE BUT NOT IN ACALLOSAL MUTANT MICE

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In the last decade, left/right brain asymmetry studies have been focused on the molecular level of the hippocampus. First, left/right asymmetry has been reported in GluN2B-NMDA subunit distribution and synaptic plasticity in hippocampal pyramidal cell synapses depending on the side of input (Kawakami et al, 2003). Furthermore, Shinohara et al (2008) found that GluA1-AMPA receptor subunit density, PSD size and spine head volume are larger in CA1 radiatum synapses contacting with presynaptic fibers from right than left CA3. Second, right isomerism in terms of the GluN2B asymmetry was found in *inversus viscerum* (iv) mice (Kawakami et al, 2008). Third, right-side dominance in spatial learning was reported in split-brain mouse (Shinohara et al, 2012).

In the present study, we investigated asymmetry of hippocampal neural activity in wild-type, iv, Arc-Venus transgenic and acallosal mutant mice. Arc-Venus mice have the ability to produce destabilized form of Venus (derivative of green fluorescent protein) controlled by Arc-promoter which is activated by neural stimulation. These mice received transection of ventral hippocampal commissure and corpus callosum with unilateral eye deprivation to force each mice use predominantly either left or right hippocampus during spatial learning. Both left and right eye deprived wild-type mice showed right-side dominance of c-Fos expression in dentate gyrus with a similar tendency in CA1. Venus expression and Venus-immunopositive cells in left eye deprived Arc-Venus mice also showed right-side dominance confirming the dominance of neural activity in right hippocampus. Interestingly, c-Fos positive cells in left eye deprived iv mice also showed right-side dominance regardless of normal or inverted asymmetry in internal organs. On the other hand, left and right eye deprived acallosal mutant mice showed lack of left/right asymmetry in neural activity.

These results suggest right-hemispheric dominance in spatial learning in mice and a critical role of corpus callosum for the development of this asymmetry.



P077

DEEP BRAIN STIMULATION OF THE FORNIX AND ENTORHINAL CORTEX IN AN EXPERIMENTAL MODEL OF MEMORY IMPAIRMENT

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Deep brain stimulation (DBS) is a surgical treatment involving the implantation of electrodes which give electrical impulses to specific parts of the brain. Recently, DBS in the region of the fornix has been applied in Alzheimer's disease with the purpose of improving or reducing the progression of memory loss. When structures of the memory circuitry are stimulated, DBS is thought to enhance neural activity and thus improves performance on memory tasks.

In the following study, we implanted bilateral electrodes at the site of the fornix and entorhinal cortex in order to detect which stimulation parameters provide beneficial effects in spatial memory. Rats were then tested in the Object Location Task with the following conditions: (i) with attachment of stimulation cable (off stimulation), and (ii) with DBS at various amplitudes (50 μ A, 100 μ A and 200 μ A), 100 μ s pulse width and 100 Hz or 10 Hz stimulation frequency. Intraperitoneal scopolamine injections 30 min before the first trial were given to imitate memory impairment.

DBS of both regions reversed the scopolamine effects in high current densities and showed superior memory performance when compared to sham rats. With the most efficient stimulation parameter rats did not show anxiety-like behaviour in the Open Field and Elevated Zero Maze, suggesting no potential side effects regarding anxiety levels or general motor activity.



P078

EFFECTS OF COLD EXPOSURE ON BEHAVIORAL AND ELECTROPHYSIOLOGICAL PARAMETERS RELATED WITH HIPPOCAMPAL FUNCTION IN RATS

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Physical or psychological stress induces a rapid reaction activating of the autonomous nervous system leading to release of adrenaline from the adrenal medulla; and slower response activating of the hypothalamus–pituitary–adrenal (HPA) axis leading to secretion of glucocorticoids. Our experiments were designed to investigate and to compare the effects of high ACTH levels, achieved by cold stress application, on spatial memory performance and synaptic plasticity in the dentate gyrus.

In this study male Wistar rats were divided into 3 groups: the control, 15 min and 2h cold stress groups. The animals in the cold-stress group were placed in a cold room (ambient temperature of 4°C) for 15 minutes/day or 2 hours/day for 5 days between 8:00 a.m. and 10:00 a.m. to avoid corticosterone circadian rhythm. Control animals were acclimatized to standard animal laboratory conditions (temperature 22°C). All rats were housed in a room under a 12/12 h light–dark cycle. Light period lasted from 7:00 a.m. to 7:00 p.m. Morris water maze and long-term potentiation (LTP) recordings were taken and blood was obtained for ACTH measurements.

The ACTH levels of the cold stress groups were significantly higher than the control group. The results for the MWM testing demonstrate that escape latency and distance moved were not significantly different in the cold stressed groups from the control group at the end of training period. However cold stressed rats spent more less time in target quadrants than the control rats in probe trial. The LTP responses obtained by perforant path stimulation were found to be more depressed in the cold stressed rats than those in the control rats.

These findings indicate that the exposure to cold stress affects aspects of local circuit activity and plasticity in the dentate gyrus. It is possible that these alterations underlie some of the behavioral consequences of the stress experience.



P079

SPECIFIC AND REGIONALLY RESTRICTED CORRELATIONS BETWEEN MONOAMINE TISSUE CONTENT IN CEREBRAL STRUCTURES INVOLVED IN COGNITION

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Cognitive treatment of information involves the cooperation and integration of numerous cortical and sub-cortical regions whose relations are modulated by the dopamine (DA), noradrenalin (NA) and serotonin (5-HT) monoaminergic systems. The widely spread nature of these monoaminergic networks is the main difficulty to foresee their functions and their interactions.

We sought to undertake the functional relationships between brain areas within a particular monoamine system network and between distinct monoaminergic systems in various brain areas involved in decision-making, through a global correlational approach of the monoamine tissue content. Bilateral punches of twenty brain regions were taken on a cryostat from each frozen Sprague-Dawley rat brains (n=35). NA, DA and 5-HT tissue contents were measured using a sensitive HPLC/electrochemistry system. Significant correlations were searched for between the monoamine content of brain regions.

NA and 5-HT were present in all brain regions, ranging respectively from 0.1 (anterior insula) to 0.38 ng/mg of tissue (hippocampus) and 0.07 (posterior cingular cortex) to 0.94 ng/mg (posterior insula). DA tissue content, less homogeneous, was higher in dorsomedial striatum (8.6 ng/mg) compared to extrastriatal tissues (<0.5 ng/mg). We found some significant correlations between paired regions within a particular monoamine system (22/190 possible correlations for 5-HT; 16/190 for NA and 12/152 for DA). Correlations were exclusively positive for intracortical relationships. Negative correlations emerged from few cortico-subcortical and subcortical associations (4/6 and 3/9 for DA or 5-HT, respectively). We did not find any correlation between some adjacent brain regions for any monoamine (prelimbic/infralimbic cortex; core/shell accumbens; basolateral/central amygdala).

When looking at the correlations between monoamines tissue content within brain areas, we found a higher degree of significant associations. This approach of monoaminergic function reveals intriguing anatomical correlations that corroborate and extend functional relationships described in the literature of decision-making. These patterns could sustain large inter-individual differences in behavior and adaptability.



P080

A COMPARISON BETWEEN BEHAVIORAL EFFECTS OF THE CHOLINERGIC AGONIST PNU282987 IN MICE MAINTAINED IN ENRICHED ENVIRONMENTS AND IN MARLAU CAGES

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Problem statement: PNU-282987 is an A7 nicotinic acetylcholine receptor agonist with antidepressant-like activity, although its effects on cognition and anxiety-like behavior are not clearly established. In rodents, enriched environments clearly reduce anxiety in the elevated plus-mice (EPM). Given that there are few reports concerning the effects of PNU282987 in mice reared in different housing conditions, our aim was to carry out a comparative study in these animals.

Approach: 96 male NMRI mice were maintained in different housing conditions (environmental enrichment (EE), Marlau cages (MC), standard housing (SE)) for 4 months. After this period, the animals received an i.p. injection of PNU282987 (2.5, 5, 10 mg/kg) and were evaluated in the EPM. The time spent in the open and closed arms by each group was compared. An increase in the percentage of time spent in the open areas of the maze is generally interpreted as reflecting decreased anxiety.

Results: PNU282987 did not induce changes in the behavior displayed in the EPM at any of the doses tested. Complex housing conditions had significant anxiolytic-like effects on EPM measures: animals maintained in EE spent a higher percentage of time (27.72 ± 16.41) in the open arms than MC (20.33 ± 10.3) or SE (16.24 ± 11.85) groups ($p < 0.01$), which is in accordance with results reported in prior studies.

Conclusions/Recommendations: EE induces a more pronounced decrease in anxiety levels than more complex MC housing (which includes cognitive stimulation through labyrinths). These results may have implications for longitudinal studies and highlight the need for standardization of EE paradigms.

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P081

ASSESSMENT OF NEURO-COGNITIVE IMPAIRMENTS AMONG PATIENTS WITH GLIOMA BRAIN TUMORS

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ABSTRACT BACKGROUND: Most of patients with glioma brain tumors are encountered with cognitive impairments and coping with such challenges is intolerable for them. **Objective:** This study tries to determine the diagnostic role of cognitive tests of CPT, Stroop and TOL in assessing neuro-cognitive impairments of sustained, selective attention and planning among patients with brain tumor and healthy participants. **MATERIALS and METHODS:** A cross-sectional study was done on a sample of 15 to 65 years old of 84 patients with glioma brain tumors and 84 healthy Iranians. Participants of both groups were physically and mentally examined and approved by neurosurgeons, neurologists and psychiatrists and they all entered the study after completing the questionnaires by being referred and introduced to the neuroscientist for performing the tests. **RESULTS:** According to CPT, Stroop and TOL tests a significant difference was observed between the performance of both groups of patients and healthy ones in age, sex and education variables ($P < 0.05$). **CONCLUSION:** patients with glioma brain tumors in comparison to healthy participants met more cognitive changes relating to sustained, selective attention and planning. Therefore, diagnosis and assessment of these cognitive changes before and after the surgery can help to rehabilitate their brains considerably and improve their lives quality.



P082

APPLICATION OF COGNITIVE COMPUTERIZED TEST IN ASSESSMENT OF SELECTIVE ATTENTION

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Background: The Stroop Color-Word test is a common and quick tool for assessing selective attention. The aim of study was Stroop cognitive test application in assessment of selective attention. Method: A cross-sectional study was implemented during 6 months from June to November, 2010 on 84 healthy adults (42 male and 42 female). The whole participants performed computerized STROOP test after being content, examination, health confirmation and trained. Results: The obtained data indicate that there is a significant correlation coefficient between age, sex and education variables ($p < 0.05$). Conclusion: The above-mentioned test can be used to assess cognitive domain of selective attention in healthy persons.



P083

REHABILITATION WITH EYE MOVEMENT DESENSITIZATION AND REPROCESSING

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ABSTRACT A variety of nervous system components such as medulla, pons, midbrain, cerebellum, basal ganglia, and parietal, frontal and occipital lobes have roles in EMDR process. The eye movement is done simultaneously for gaining client's attention to an external stimulus when he is concentrating on a certain internal subject. Eye movement guided by therapist is the most common attention stimulus. The role of eye movement has been documented previously in relation with cognitive processing mechanisms. A series of systemic experiments have shown that the eyes spontaneous movement is associated with emotional and cognitive changes and results into decreased excitement, flexibility in attention, memory processing, enhanced semantic recalling. Eye movement also decreases the memory's image clarity and the accompanying excitement. By using EMDR we can reach some parts of memory which were inaccessible before and also emotionally intolerable. Various researches emphasize on the effectiveness of EMDR in treating and curing phobias, pains, personality disorders, and dependent personality disorders. Consequently, due to the involvement of multiple neural system components, this palliative method of treatment can also help to rehabilitate the neuro-cognitive system.



P084

ACYLATED GHRELIN AMELIORATES LEARNING AND MEMORY IMPAIRMENTS INDUCED BY TRANSIENT GLOBAL CEREBRAL ISCHEMIA IN RATS

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Cerebral ischemia is the third leading cause of death and first cause of morbidity worldwide. Hundreds of thousands of people suffer from cerebral ischemia reperfusion injury each year. Since the most striking result of cerebral ischemia reperfusion injury is learning and memory impairment, we focused on mechanisms relating cerebral ischemia reperfusion injury to hippocampal damage. Ghrelin, so called hunger hormone, is used as a therapeutic agent in our study because of its antioxidant and memory enhancing effects. Sixty adult male Wistar rats were divided randomly into Sham (SHAM), Ischemia/Reperfusion (I/R) and Ischemia/Reperfusion+Ghrelin (I/R+GHR) groups. SHAM group rats only underwent sham surgery, i.e. without any vessel occlusion, and received saline daily for three reperfusion days. I/R group rats were exposed to global cerebral ischemia/reperfusion and given saline daily for three days of reperfusion. I/R+GHR group rats, however, both underwent global cerebral ischemia/reperfusion surgery and received ghrelin daily for three days of reperfusion. Y-Maze and Open Field tests were carried out at postischemic 24th and 48th hours. On the third reperfusion day, blood samples and brains of the animals were collected. Total oxidant status (TOS) and nitrate+nitrite levels in the hippocampi were analysed. Y-maze and Open Field test results revealed that cerebral ischemia/reperfusion caused learning and memory impairment due to hippocampal damage. Additionally, ghrelin administration ameliorated ischemia/reperfusion induced cognitive impairment. Higher TOS and nitrite+nitrate levels of I/R group with respect to SHAM group were in consistency with hippocampal damage. In conclusion, our study showed that cerebral ischemia/reperfusion resulted in TOS and nitrite+nitrate increase coupled with cognitive impairment and ghrelin can be proposed as a therapeutic agent for learning and memory impairments induced by cerebral ischemia/reperfusion injury.



P085

MELATONIN ANTIDEPRESSANT EFFECTS ARE REGULATED BY GONADECTOMY IN WISTAR RATS: A POSSIBLE IMPLICATION OF SEX HORMONES.

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The main objective of this study was to analyze the effects of sex, ovariectomy (Ovx) and orchidectomy (Orx) on antidepressant effect of melatonin in forced swimming test.

Initially, 4mg/kg of melatonin was daily administered, at 4:00 pm, to intact male and female rats during 8 weeks.

Our results have shown that the effect of chronic injection of Mel is sex dependent in the forced swimming test. Females rats have responded better than males in behavior test study after administration of melatonin, this difference between the sexes may be related to the action of sex hormones (androgens and estrogens) on behavior in males as well as in females.

Secondly, to determine the possible interaction between Melatonin and steroid hormones, Ovx/sham female received Mel at dose of 4mg/kg alone or NaCl (0.9 %) alone daily and during 8 weeks of treatment at 4:00 pm. All animals were tested in the forced swimming test for depression behavior study.

Results revealed that Mel exerts antidepressant effects in the orchidectomized males and in intact females, confirming that the suppression of androgens by orchidectomy improved antidepressant effects of melatonin in males. However in females, the suppression of estrogen by ovariectomy masked the antidepressant and anxiolytic effects of melatonin.

Our results demonstrated that the antidepressant effects of melatonin are linked to sex hormones.



P086

THE NEUROPEPTIDE PCAPA AND THE GLIOPEPTIDE ODN PREVENT 6-HYDROXYDOPAMINE-INDUCED APOPTOSIS OF CEREBELLAR GRANULE NEURONS

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It is well documented that pituitary adenylate cyclase-activating polypeptide(PACAP) exerts potent neuroprotective effects in models of neurodegenerative diseases,traumatic brain injury and stroke.Besides its direct neuroprotective action,PACAP may also acts indirectly on astrocytes to stimulate the release of neurotrophic factors that prevent neuron death.We have previously shown that PACAP stimulate the biosynthesis and the release of endozepines,a family of biologically active peptides that are exclusively produced by astroglial cell.Since the endozepine octadecanuropeptide(ODN) is a neurotrophic factor regulating proliferation and/or survival of neuronal cells,we have investigated the ability of PACAP alone or in association with ODN to counteract the neurotoxic effects of 6-hydroxydopamine(6-OHDA) on cerebellar granule neurons. Incubation of cerebellar granule neurons cells with graded oncentrations of PACAP(10-11M-10-6M) for 72h dose-dependently prevented cell death induced by 6-OHDA(30µM).Kinetic studies revealed that PACAP inhibited 6-OHDA-evoked cell apoptosis within 24h with a maximal effect occurring 72h after the onset of treatment.Thereafter,the neurprotective action effect of PACAP gradually declined and vanished after 96h.Addition of the gliopeptide ODN(10-14M) in the culture medium prolonged the neuroprotective effect of PACAP that lasted for more than 120h.By using selective blockers,we showed that the neuroprotective action of PACAP up on 6-OHDA-induced neuron death was PKC- and ERK MAP kinase,but PLC/PKC-independent.These results suggest that the anti-apoptotic effect of PACAP and ODN are additive and this effect is attributable,at least in part,to activation of two distinct transduction pathways.Moreover,6-OHDA treatment induced an accumulation of reactive oxygen species(ROS) levels and a stimulation of caspase-3 activity.Addition of PACAP alone or in combination with ODN to 6-OHDA-treated cells,blocked all these deleterious effects.On the other hand,we have demonstrated that PACAP stimulated both superoxide dismutases(SOD) and catalase antioxidant enzymatic activities and blocked the inhibitory effect of 6-OHDA on SOD and catalase activities. Taken together these data indicate tha exert a potent neuroprotective action against 6-OHDA-induced cerebellar granule neurons apoptosis.



P087

NEUROGENESIS INDUCTION BY GRAPE SEED EXTRACT AND ITS NEUROPROTECTIVE ACTIVITY

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Background: Neurogenesis occurs in the adult mammalian brain throughout life in limited areas like the subgranular zone (SGZ) in the hippocampus. Recently, polyphenolic compounds enhance brain healthy so, the dietary consumption of grape seed extract (GSE) is associated with a lower incidence of neurodegenerative diseases. Aim of the work: In vitro study the effect of GSE and its major polyphenolic components (e.g., (-)-epicatechin, (+)-catechin and gallic acid) on proliferation and differentiation of cultured adult hippocampal neural cells, and the protective activity of such treatments on glutamate neurotoxicity. Methods: Preisolated Hippocampal cells from (10 weeks old) mice were used as target neural cells. Antioxidant activity of treatments on neural cells was measured using DPPH free radical assay. Neuroproliferation was assessed by neutral red protocol using serial dilution of each treatment along 3 days incubation. The gene expression of Doublecortin (DCX, a neural proliferation and differentiation gene marker) was quantified by RT-qPCR. Neuroprotective activity of treatments against (2mM) glutamate induction for 30 min was measured via RT-qPCR of caspase 3 gene. Results: GSE (2mg/ml) was the most potent agent for neuroproliferation, it represented the highest free radical scavenging activity and raised DCX gene expression up to $175 \pm 0.5\%$, ($p < 0.05$) followed by (-)-epicatechin, (+)-catechin and gallic acid, respectively. (-)-Epicatechin (0.6mg/ml) stands as the most neuroprotective agent, against glutamate neurotoxicity, reducing caspase3 expression with ratio $93 \pm 0.8\%$, ($p < 0.05$) then GSE, gallic acid and (+)-catechin, respectively. Conclusion: GSE and its polyphenolic components have high affinity to molecular targets in hippocampal neural cells for proliferation, differentiation and protection.



P088

AN EVALUATION OF NEUROPROTECTIVE EFFECTS OF MELATONIN, AGAINST ADVERSE EFFECTS OF PRENATAL EXPOSURE TO A NON-STEROIDAL ANTI INFLAMMATORY DRUG, DURING THE PERIPHERAL NERVE DEVELOPMENT

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Neuroprotective effect of melatonin was investigated to decrease the impairment of the fetal peripheral nerve system due to maternal consumption of diclofenac sodium (DS). Eighty four pregnant rats were divided to 7 groups as control group (Group 1), saline administered group (Group 2), DS administered group (Group 3), DS with low dose melatonin administered group (Group 4), DS with high dose melatonin administered group (Group 5), low dose melatonin administered group (Group 6), and high dose melatonin administered group (Group 7). After pregnancy period, six male newborn rats that reached to 4 weeks of age from each group were sacrificed. Sciatic nerves were harvested and mean axon numbers, diameter, and myelin thicknesses were estimated with stereological techniques. The mean myelinated axon numbers are counted as 7520; 7180; 4537; 5777; 6479; 7221 and 7288 for the Groups 1 through Group 7 respectively. The mean myelinated axon areas are estimated as 9.98; 9.42; 7.11; 8.60; 9.76; 9.88 and 10.75 for the Groups 1-7 respectively. Mean myelin sheet thickness are found as 1.19; 1.15; 1.00; 1.11; 1.12; 1.15 and 1.14 for Groups 1-7 respectively. According to these results prenatal DS exposed rats had significantly fewer axon numbers, small sized of the myelinated axon diameter and thin myelin sheath compared to the control groups ($p < 0.05$). Although melatonin in both doses significantly increased the axon numbers, but only high dose of melatonin significantly increased myelinated axon diameter ($p < 0.05$). Melatonin did not increase the myelin thickness ($p > 0.05$). Current study proves that the prenatal exposure to DS decreases axon number and diameter and these effects can be reversed with melatonin prophylaxis. The mechanisms for such effect are believed to be by the apoptotic effect and inhibition of differentiation of DS on embryonic neuronal stem cells is either prevented from the beginning or reversed afterwards.

Keywords: nerve melatonin diclofenac neuroprotection

Stereological analysis results of the 4 week old rats

	axon numbers	axon areas	sheet thickness
group 1	7520±165	9,98±0,47	1,19±0,04
group 2	7180±69	9,42±0,47	1,15±0,02
group 3	4537±278	7,11±0,32	1,00±0,01
group 4	5777±136	8,60±0,84	1,11±0,03
group 5	6479±366	9,76±0,47	1,12±0,03
group 6	7221±225	9,88±0,52	1,15±0,04
group 7	7288±235	10,75±0,71	1,14±0,03



P089

THE EFFECTS OF SPERMINE ON NEUROGENESIS AND THE PASSIVE AVOIDANCE LEARNING AFTER TRANSIENT CEREBRAL ISCHEMIA IN THE CHICKS

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P090

PROTECTIVE EFFECTS OF ALPHA LIPOIC-ACID AND N-ACETYL CYSTEINE AGAINST ACRYLAMIDE-INDUCED PERIPHERIC NEUROPATHY

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Acrylamide (ACR) is a vinyl monomer with a significantly high chemical reactivity. It is easily absorbed by all routes of administration and peripheral nervous system is a selective target for its toxicity. The early clinical symptoms to ACR results in degeneration of nerves causing distal axonopathy. ACR has been reported to cause disturbances in oxidative stress. The aim of this study is to determine the effects of alpha lipoic-acid (LA) and n-acetyl cysteine (NAC) against acrylamide-induced peripheral neuropathy in rats. Male Sprague-Dawley rats were included in the study. ACR was given i.p. at a dose of 45mg/kg/day. LA group received additionally 35mg/kg/day LA, and NAC group received 150mg/kg/day NAC for 10 days. Controls were injected saline at the same dose. After the time rats were sacrificed and sciatic nerves were removed. For free radical determination luminol (selective for hydroxyl radical, hydrogen peroxide and hypochlorous acid) and lucigenin (selective for superoxide radical) enhanced chemiluminescence (CL) method was used. Additionally histopathological examination was also made. Our luminol enhanced CL results was in ACR group higher than control group ($21,6 \pm 7,1$ rlu/mg tissue vs. $11,2 \pm 1,9$ rlu/mg tissue; $p < 0,001$). LA and NAC reduces luminol enhanced CL ($8,6 \pm 1,7$ rlu/mg tissue vs. $9,5 \pm 2,2$ rlu/mg tissue) measurements significantly ($p < 0,001$). Lucigenin enhanced CL measurements did not change between ACR, control and NAC received group ($p > 0,05$). LA has a low reducing effect but was also not significant. Histopathological examination has shown normal myelination in peripheral neurons. In ACR group myelin organization was damaged and the count of disturbed myelinated nerve fibers was increased with respect to the control group. NAC and LA groups have shown a moderate reducing effect against myelin damage. ACR toxicity increased oxidative stress in peripheral neurons, which results in myelin damage. NAC and LA can reduce this damage. In conclusion, LA and NAC have protective effects against ACR induced peripheral neuropathy.



P091

PROTECTIVE EFFECTS OF NIGELLA SATIVA OIL CONTROL ASTROGLIOSIS AND REDUCE HALOPERIDOL-INDUCED DEFICIT IN RATS.

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The neuropathological status of Haloperidol (HAL)-induced Extrapyrmidal Symptoms (EPS) remains unclear. Evidence suggested persistent neuronal alterations in the basal ganglia produce oxidative stress. Studies supporting a potential toxic role of HAL on Astrocytes at exposure of oxidative stress and glial viability contribute in neuronal degeneration. This study evaluates the possible protective effects of the antioxidative agent “Nigella sativa (NS) oil” on HAL-induced neuronal alterations and motor symptoms. EPS was monitored in HAL treated groups with and without NS oil and with placebo. HAL treated group displayed ($p < 0.01$) high degree of motor deficits with late appearing Tardive Dyskinesia (TD). Striatum shown grossly disturbed large fraction of cytoarchitectonic pattern with nerve cell depletion concomitant shrunken cytoplasm, nuclear membrane breakdown and chromatin disorganization. Scarring was prominent feature owing profusion of astrogliosis in the dorso-ventro lateral regions of the caudate putamen and in the core of nucleus accumbens. Halo and pyknotic neurons were moderate ($p < 0.05$). HAL-induced neuronal changes were almost absent ($p < 0.01$) in the HAL plus NS oil treated groups. However minor astrogliosis with no indication of cell loss and 82% normal neuronal densities were observed. We conclude that NS oil may prevent HAL-induced neuronal degeneration. We believe that further preclinical research into the utility of NS oil may indicate its usefulness as a protective agent from irreversible EPS.



P092

ASSESSMENT OF THE HEMODIALYSIS IMPACT ON BRAIN PLASTICITY USING BOLD-FMRI

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INTRODUCTION The oxidative stress is a known factor contributing to long-term complications of dialysis. Studies have shown the involvement of hemodialysis “HD” membrane in the genesis of oxidative stress (OS). Hence the goal of this study is to assess the impact of HD by the Helixone membrane using BOLD-fMRI and serological approaches. **MATERIALS AND METHODS** 12 male volunteers following chronic HD for more than 6 months were recruited. Diabetic, smoking and patients with episodes of infection or treatment with iron or erythropoietin injection were excluded. The MDA marker of OS was assessed in the blood using TBARS method before and after HD sessions. Similarly, the BOLD-fMRI was performed before and after HD using motor paradigm immediately before and after HD sessions; the fMRI data was processed using SPM8 package. **RESULTS AND CONCLUSION** The biological results showed that HD increases the OS in these patients. [MDA before HD= $3,550 \pm 0,580\mu\text{M}$ vs. MDA after HD = $9,899 \pm 8,367\mu\text{M}$; $p=0,002$]. BOLD-fMRI revealed significant activation of the motor cortex, the BOLD signal in the activated site is inversely correlated with level of OS. The HD seems to rise the inflammatory state of the brain tissue reflecting increased OS, while it was expected to decrease considering the removal of free radicals responsible of OS by HD procedure. Hence, particular care must be paid to HD patients considering the long term impact on general health and brain tissues in particular.



P093

CORD BLOOD BRAIN DERIVED NEUROTROPHIC FACTOR: DIAGNOSTIC AND PROGNOSTIC MARKER IN FULLTERM NEWBORNS WITH PERINATAL ASPHYXIA

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Backgrounds: This prospective case control study was designed to evaluate cord blood brain derived neurotrophic factor level in full term newborns with perinatal asphyxia as a marker of central nervous system insult and predictor of severity of hypoxic ischemic encephalopathy, with follow up of its level during the reperfusion phase. **Material and Methods:** The study included twenty fullterm neonates with perinatal asphyxia (cases) and twenty controls. Cord blood samples were obtained at birth and peripheral blood samples at 72 h postnatal from cases only. Plasma brain derived neurotrophic factor level was measured using enzyme linked immunosorbent assay. The clinical severity of encephalopathy was graded based on Sarnat and Sarnat staging. **Results:** Cord Plasma brain derived neurotrophic factor level was significantly increased among cases compared to controls. Among cases, brain derived neurotrophic factor level at delivery and after 72 h significantly correlated with the severity of encephalopathy according to Sarnat staging being higher as severity increases. Brain derived neurotrophic factor level significantly increased after 72 h of life compared to its level at delivery among cases. Brain derived neurotrophic factor levels at delivery and at 72 h postnatal were predictors of severe Sarnat stage and poor outcome. **Conclusion:** We concluded that brain derived neurotrophic factor level as a marker of central nervous system insult is increased in full term newborns with perinatal asphyxia. It can serve as an indicator for the severity of encephalopathy and adverse outcomes.



P094

SIMPLE BONE CYST TREATED WITH ASPIRATION AND A SINGLE BONE MARROW INJECTION. A CASE STUDY.

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A young and fit child (Omar Mohamed Ramadan Mohamed Abdelgawad) of age 4.5yrs and weighting about 23kg was administered to Suez Canal university hospital in 13/1/2008 suffering from pain limping in his right leg. After clinical, radiological and laboratory examinations a huge bone cyst of about 5cm³ was determined in upper neck femur bone right leg and needs an operation. A simple bone cyst treated by percutaneous autologous bone marrow grafting was studied prospectively to evaluate the radiographic healing of the cyst, complications, and clinical outcome. The procedure included percutaneous aspiration of the cyst's fluid and the injection of the autologous bone marrow into the cyst cavity, which was aspirated from the posterior iliac crest. The mean volume of the lesion was about 10 cubic centimeters (10cc). The follow-up time was 16weeks.

Complete healing occurred in the patient within about 16weeks with a large callus. Unfortunately, during the bone marrow injection the patient had cardiac arrest for 33minutes. Since then he has followed by orthopedists, psychologist and physical therapist. He is now improving speak well, some trouble in walking (falls during walking). Learning troubles in writing



P095

EFFECT OF PERIPUBERTAL CHRONIC STRESS ON EXPRESSION OF HYPOTHALAMIC KISS-1 MRNA AND HISTOLOGICAL CHANGES OF THE REPRODUCTIVE TRACT IN FEMALE RAT.

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Aim of the work: Kiss-1 gene is involved in the regulation of gonadotropin secretion and in puberty onset. Kiss-1 mRNA expressing neurons are located in the hypothalamus. Our question is whether exposure of female rats to repetitive stressors, while growing from weaning to adolescence, would affect the expression of hypothalamic kiss-1 mRNA and accordingly alter the histology of the reproductive tract.

Methods: 2 groups of Sprague-Dawley female pups (at age of 25 days) were assigned as control group (CR; n=10) that housed as usual and stressed group (SR; n=10) that was subjected to daily different stressors for 12 weeks. At the end of stress period, blood samples were taken for plasma cortisol, FSH and LH level determination. The brains, ovaries and uterine horns were dissected out for Kiss-1 mRNA determination and histopathological examination.

Results: Quantitative RT-PCR of hypothalamic kiss-1 mRNA revealed a significantly lower level in SR than in CR ($p < 0.0001$). Serum cortisol was significantly higher in SR than in CR ($p < 0.001$), while FSH and LH levels were significantly less in SR than in CR ($p < 0.01$, 0.0001 respectively). The ovarian sections of SR showed significantly increased number of preantral and atretic follicles. The uterine sections of SR showed hyperplasia of the endometrium with polyps formation while some sections showed thinning and atrophy of the uterine wall.

Conclusion: the present results suggest that peripubertal exposure to repetitive stressors, seems to markedly reduce the hypothalamic Kiss-1 mRNA expression that was associated with altered hormonal secretion, polycystic ovary changes and dysorganised uterine proliferative changes. Such findings attract our attention to study, in future work, the relation between exposure to chronic stress and polycystic ovary syndrome in human.



P096

PILOT STUDY: VALPROIC ACID EFFECTIVENESS IN MINIMIZING INCIDENCE OF SEIZURES IN POSTOPERATIVE PEDIATRIC BRAIN TUMOR PATIENTS

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Valproic acid (VPA) has found clinical use as an antiepileptic (AED), primarily in the treatment of epilepsy. The risk of seizures varies by tumor type and its location in the brain. It was believed that preventing seizures with AED was effective and necessary, but it was later concluded that seizure prophylaxis was ineffective in people with brain tumors. However, postoperative seizure prophylaxis after brain tumor resection is still controversial. Aim of the Study To assess VPA Effectiveness in postoperative seizure prophylaxis in pediatric brain tumor patients Methods A retrospective review of pediatric brain tumor patients was performed to evaluate the effect of VPA on postoperative seizure prophylaxis. The patients were monitored for a period of 3 months postoperatively to determine whether VPA was effective in prophylaxis from seizures. The data collected included the patients' age, sex, weight, platelet count, albumin, liver enzymes, serum VPA concentration and any other medications the patients were receiving. Any clinical intervention and any drug interaction were recorded. Results Sixty patients were eligible for this study, 27 patients received VPA and 33 received no AED. Seven patients from the VPA group had a history of seizures compared to 2 patients only in the non-VPA group. Postoperatively, a total of 8 patients had seizures, two patient in the VPA group with an onset of 36 days and 7 days (associated with VP shunt) respectively, and 6 patients in the non-VPA group with an average onset of 32 days. Comparing the incidence of seizures postoperatively using Fisher's exact test, the difference between the two groups was not statistically significantly different ($p=0.11$). Conclusion Although VPA tended to reduce the incidence of seizure events and to delay the onset of seizures postoperatively in brain tumor patients, the difference did not reach statistical significance.)



P097

EFFECT OF LONG-TERM NOISE ON FOOD INTAKE AND ENDOCRINE RESPONSE (ACTH) IN WISTAR RATS.

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Summary: Stress is thought to influence the feeding behaviour. Several studies in animal and human have shown that stress influence the eating behaviour. Human and animals exposed to repeated stressful noise show a change in physiologic homeostasis and general behaviour. Although the effects of stress are clearly established, it is interesting to see how the body responds to stress even if the homotypic stress is performed for an extended period.

In our work we evaluated the effect of a noise stress (95 dB, 2,64 KHz, 30 minutes/j) during 28 days on feeding and HPA axis responds.

Our results shows that the repetition of auditory stress for 2 weeks contained no significant variation in the plasma levels of ACTH ($84,3 \pm 11,59$ vs $94 \pm 6,32$), in the feeding behaviour ($22,5 \pm 0,25$ g vs $22,4 \pm 0,19$ g) and in body weight ($317,2 \pm 0,87$ g vs $315,9 \pm 0,53$ g). After 3 and 4 weeks of homotypic stress, we observed a decrease in food intake ($22,3 \pm 0,21$ vs $21,1 \pm 0,2$ g/j) associated with a decreased body weight ($329,6 \pm 0,53$ g vs $323,5 \pm 0,37$ g). The decrease in food intake is concomitant with an augmentation in the levels of plasmatic ACTH. ($77 \pm 12,44$ pg/ml vs $144,3 \pm 31,53$ pg/ml).

Our results suggest a presence of relationship between the HPA axis activity and the central regulation of feeding behaviour. Further studies will be necessary in order to understanding the physiologic and molecular mechanism underlying the responses observed.



P098

ASSESSMENT OF THE ROLE OF L-CARNITINE IN IMPROVING HEPATIC ENCEPHALOPATHY USING MR SPECTROSCOPY

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Abstract: Background and aim: Hepatic encephalopathy (HE) is related to the presence of abnormal cerebral metabolites. MR Spectroscopy (MRS) can demonstrate neuro-metabolite changes associated with therapy. The aim of this study was to evaluate the influence of L-carnitine on mental conditions, serum ammonia and neurometabolite levels in patients with HE using MRS. Patients and methods: Ten control subjects and 54 patients with grades II to III HE, were randomized into (GI) receiving lactulose 30ml/t.d.s as standard therapy and (GII) receiving L-Carnitine 350mg t.d.s in addition to the lactulose. Clinical assessment, fasting serum ammonia levels, and measurement of neurometabolite levels using proton MRS were recorded and compared at base line and after one week. Results: After one week, 25% of HE patients were reversed in group I versus 42.3% in group II. Fasting ammonia levels were significantly decreased in both groups compared to pretreatment levels and significantly lower in the L-carnitine and lactulose treated group compared to the lactulose group ($P=0.041$). Neurometabolites mI/Cre, Cho/Cre, Glx/Cre, and (Cho+mI)/Glx ratios were significantly improved in both groups compared to pre treatment levels, but the L Carnitine added group (II), showed a significant increase in mI/Cre, and (Cho+mI)/Glx ratios and decrease in Glx/Cre ratio in comparison to the lactulose group ($p=0.002$ - $p=0.003$ - $p=0.002$ respectively). Conclusion: Adding L Carnitine to lactulose for treatment of hepatic encephalopathy hastened the clinical improvement and was associated with significant improvements in serum ammonia and neurometabolites specially mI/Cre, and (Cho+ mI)/Glx and Glx/Cre ratios. Abbreviations: (HE) hepatic encephalopathy, (MRS) Magnetic Resonance Spectroscopy, (Cho) Choline, (Cre) creatine, (NAA) N-acetylaspartate, (Glx)glutamine+glutamate, and(mI) myo-inositol



P099

TYPE 2 DIABETES AFFECTS M AND S CONE OPSIN EXPRESSION IN THE DIURNAL SAND RAT PSAMMOMYS OBESUS

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Problem statement: Understanding of cone pathophysiology is central to human vision. The progressive loss of cones is the leading cause of visual impairment in several retinal diseases, and is involved in diabetic retinopathy (DR).

Approach: Young adult Psammomys obesus, a diurnal animal model of human type 2 diabetes, were captured and maintained under captivity during 7 months and fed either a natural vegetation-based diet (control group, ND), or standard rat chow (test group, HDD). Retinas were analyzed by immunohistochemistry and western blotting using a range of antibodies.

Results: Whereas the intensity and distribution of rhodopsin expression (specific to rod photoreceptors) did not differ significantly between the two groups, immunostaining of cone mid wavelength opsin (MOp) and short wavelength opsin (SOp) was greatly reduced in the retinas of HDD compared with ND retinas. These observations were confirmed by western blotting, showing similar rhodopsin levels in both groups while MOp and SOp levels were reduced by about 50% in the HDD compared to ND group. We examined several other markers specific for rods and cones in the two different experimental conditions. Immunolabeling of peripherin/RDS, arrestin, transducin and recoverin of cones and rods was similar in normal and diabetic conditions. The differential susceptibility of rods and cones under conditions of hyperglycemia could be due to cones being more dependent on glycemetic regulation

Conclusion: P.obesus represents an original animal model of type 2 DR with an etiology resembling humans, and should facilitate unravelling the pathogenic mechanisms involved in cone loss.



P100

ANTERIOR REPOSITIONING SPLINT VERSUS LASER THERAPY FOR TREATMENT TMDs WITH ANTERIOR DISC DISPLACEMENT

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State of problem: Continues using ARS for treatment TMDs especially anterior disk displacement lead to muscle strain. Laser has power effect for removal muscle strain Aim of work: The aim of this study was to evaluated the effectiveness of laser application and anterior repositioning splint on TMDs in patient with anterior disc displacement. Materials& methods: Thirty patients were randomly divided into Three equal groups, for group I the patient treated with anterior repositioning appliance while for group II the patient treated with alternative application of anterior repositioning splint (ARS) and low-level laser therapy (LLLT). For group III the patient treated with low-level laser therapy (LLLT). The evaluations were done by clinical finding and MRI. Three evaluations were performed: before, two and five months after therapy. Results: Results of clinical finding and symptoms and MRI of group II was significantly reduced compare to group I and III. Conclusion: It can be concluded that laser application can be a supportive therapy in the treatment of TMJ with anterior disk displacement in conjunction with ARS, since it resulted in the immediate decrease of painful symptoms of clinical finding.



P101

THE IMPACT OF EXPRESSION PROFILING USING PCR TECHNOLOGY ON DIAGNOSTIC AND PROGNOSTIC TESTING IN GLIOMA

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Background: Advances in the biological sciences and technology are providing molecular targets for diagnosing and treating cancer. Current classifications in surgical pathology for staging malignancies are based primarily on anatomic features (e.g., tumor-node-metastasis) and histopathology (e.g., grade). The challenge for pathology will be the development and implementation of these molecular classifications for routine clinical practice. Approach: Study of the benefits, challenges, and possibilities for solid-tumor profiling in the clinical laboratory with an emphasis on DNA-based PCR techniques. Content: Some new molecular classifications of tumors are based on gene expression, requiring a paradigm shift in specimen processing to preserve the integrity of RNA for analysis. More stable markers (i.e., DNA and protein) are readily handled in the clinical laboratory. These techniques are becoming easier and faster and can be multiplexed. PCR methods are a favorable option for the analysis of cancer markers. Summary: There is a need to translate recent discoveries in oncology research into clinical practice. This requires objective, and cost-effective molecular techniques for clinical trials and, eventually, routine use. PCR has attractive features for tumor profiling in the clinical laboratory.



P102

MODULATION OF EXCITATORY POSTSYNAPTIC CURRENTS IN MEDIUM SPINY NEURONS PRODUCED BY THE SYNAPTIC ACTIVATION OF CHOLINERGIC INTERNEURONS IN RAT NUCLEUS ACCUMBENS.

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The nucleus accumbens (nAcb) contains a small population of large aspiny (LA) cholinergic interneurons. LA neurons are the only source of acetylcholine (ACh) in the nAcb and ACh has been shown to modulate both excitatory and inhibitory inputs in medium spiny (MS) projecting neurons. The source of excitation of LA neurons is largely unknown and their role in modulating excitatory inputs in MS neurons is not well understood.

We have recorded from both LA and MS neurons in nAcb slice preparation from 2-6 week-old rats in which the connectivity between the medial prefrontal cortex (mPFC) and the nAcb was preserved.

In LA neurons (n=23), stimulus train of mPFC afferents consistently produced a long depolarization (up to 6 seconds) that was overridden by a burst of 9 to 23 action potentials. In voltage clamp recordings, the slow inward current evoked by mPFC afferent stimulation was largely attenuated by E4CPG suggesting it was mediated by the activation of metabotropic glutamate receptor. In MS neurons (n=59), similar stimulus train produced an increase in both the frequency and the amplitude of spontaneous postsynaptic excitatory currents (sEPSCs) and these effects were antagonized by nicotinic receptor antagonists or by E4CPG. The increase in sEPSCs frequency was antagonized by a specific A7 nicotinic receptor antagonist whereas the increase in their amplitude was blocked by a non-A7 nicotinic receptor antagonist. The addition of nicotine to the superfusing medium mimicked the effect of train stimulus on the amplitude of sEPSCs but not those on the frequency.

The present results suggest that mPFC afferent constitute an important excitatory input activating LA neurons which in turn modulate different characteristics of glutamatergic neurotransmission in MS neurons through the activation of different subtypes of nicotinic receptors.



P103

DIFFERENT PATTERNS OF DYSTROPHIN GENE EXPRESSION IN AN EGYPTIAN FAMILY SUFFERING FROM MUSCULAR DYSTROPHY

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Abstract :Background:The gold-standard in the diagnosis of multiple syndromes of muscle dystrophy, is the immunohistochemical study of muscle biopsies obtained from patients, as it helps distinguishing between the different types efficiently. Aim: The aim was to clinicopathologically study an Egyptian family of a non-consanguineous couple, with 5 (3 males and 2 females) out of 7 siblings suspected clinically to have muscular dystrophyMaterial and Methods: Four siblings were subjected to biochemical and electrophysiological investigations. The family pedigree was constructed to study the mode of inheritance and recommended to undergo quadriceps muscle biopsy for histopathological examination. Furthermore, immunohistochemical staining of the paraffin embedded tissue sections of three of them with dystrophin stain was undertaken. Results: The biochemical study of these patients showed high value of serum CPK exceeding 1000 IU/L. The electrophysiological studies revealed myopathic changes. Histopathological examination of their muscle biopsies confirmed the diagnosis of muscular dystrophy and the immunohistochemical staining using dystrophin, revealed different patterns of gene expression, ranging from totally absent membranous staining in the female patient, to weak staining and interrupted staining in the other two male patients. Conclusion: The immunohistochemical staining technique confirmed the diagnosis of DMD/BMD dystrophinopathy and showed different patterns of the expression and distribution of dystrophin protein. Although DMD/BMD are both X-link, but in our study, a female expression in diseases with X-linked recessive inheritance pattern was found , which may suggest possible and different explanations .



P104

KISSPEPTIN-10 STIMULATES THE SECRETION OF TESTOSTERONE IN PREPUBERTAL MALE CATTLE

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Kisspeptin, a hypothalamic neuropeptide, is a functional ligand of the GPR54 receptors which are expressed by the gonadotropin-releasing hormone (GnRH)-secreting neurons. Thus, kisspeptin was found to stimulate the secretion of the pituitary gonadotropins which control the process of spermatogenesis and testosterone (T) secretion in the male.

Our study clarifies the secretion of T in response to injection of kisspeptin-10 (Kp10) in prepubertal male cattle, and compares the characteristics of any response with those of the response to GnRH. The experiments were performed in Morioka city, Iwate, Japan, using five male (4-6 month old) Japanese Black calves. On experimental days, calves were not fed before or during the experiment; they were fed only after the experiment while water was available continuously. The calves were given a single intravenous (i.v.) injection of Kp10 (5 µg/kg body weight (b.w.): 3.85 nmol/kg b.w.) or GnRH (5 µg/kg b.w.: 4.23 nmol/kg b.w.). Injections and blood sampling were performed via indwelling catheter previously inserted into one of the external jugular veins. All animals received all treatments and each treatment was carried out at 3-day intervals. Blood samples were drawn at – 60 and 0 min before injection, and 10-, 30-, 60-, 120- and 180-min interval after injections.

Plasma T concentrations significantly increased from pre-injection levels of 0.56 - 0.78 ng/ml following injection of both Kp10 and GnRH ($P < 0.05$) (Fig. 1). Maximum values were observed 120–180 min after each injection of both peptides. The maximum values of T within 120 min after the injection of Kp10 and GnRH were 4.01 ± 1.40 and 4.62 ± 1.70 ng/ml, respectively. However, injection of both peptides couldn't initiate the spermatogenesis in the histological sections of testes obtained from the treated calves at that age.

Conclusion; kisspeptin and GnRH injection stimulate the T secretion equally but no effect on spermatogenesis at prepubertal age.



P105

ALTERATION OF DOPAMINERGIC INNERVATION AND VOLUNTARY MOVEMENTS AFTER LONG PERIOD OF THIRST IN A SEMI-DESERT RODENT, MERIONES SHAWI: BEHAVIORAL AND IMMUNOHISTOCHEMICAL STUDIES.

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Problem Statement: Dehydration is a powerful stimulus causing disequilibrium in homeostasis of water and electrolytes resulting from depletion in total body water. Most studies have focused on domestic and laboratory animals; however, the study of desert animals allows improved understanding about water balance and resistance to dehydration and associated behavioral changes, including those related to voluntary movements. The aim of this study was to evaluate the effect of dehydration on both dopaminergic innervation and locomotor activity.

Approach: *Meriones shawi* is a desert rodent characterized by its resistance to long periods of thirst that can extend for several months. In the present study, *M. shawi* were subjected to water deprivation for one month. We used tyrosine hydroxylase immunohistochemistry (TH: the key enzyme of chetecholamine biosynthesis) to evaluate the effects of prolonged dehydration on the dopaminergic system in both substantia nigra pars compacta and ventral tegmental area (SNpc and VTA), which are the main sources of dopamine input to several brain areas, the immunolabelling was performed also in both the medial forebrain bundle and the caudate putamen (striatum). In addition, the open field test was used to evaluate the effect of dehydration on locomotor activity on *M. shawi*.

Results: Our results showed an increase in TH immunolabelling in both SNpc and VTA following one month of dehydration compared to controls level. The same results were obtained with fibers in both MFB and striatum. This augmentation of TH immunoreactivity was accompanied by changes in locomotor activity behavior of *Meriones*, the recording test shows the hyperactivity of animals which is probably caused by dehydration.

Conclusions: Our results indicate that this osmotic stress by dehydration is able to increase dopaminergic neurotransmission, which might be involved in generating hyperactivity in this desert animal.



P106

CHRONIC HYPERAMMONEMIA INDUCES TONIC ACTIVATION OF NMDA RECEPTORS IN CEREBELLUM LEADING TO A DECREASE ACTIVITY OF NEURONAL NITRIC OXIDE SYNTHASE

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Impaired function of the glutamate-nitric oxide-cGMP pathway contributes to cognitive impairment in hyperammonemia and hepatic encephalopathy. The mechanisms by which hyperammonemia impairs this pathway remain unclear. Understanding these mechanisms would allow designing clinical treatments for cognitive deficits in hepatic encephalopathy.

The aims of this work were: 1- to assess whether chronic hyperammonemia *in vivo* alters basal activity of neuronal nitric oxide synthase (nNOS) in cerebellum and/or its activation in response to NMDA receptor activation; 2- to analyse the molecular mechanisms by which hyperammonemia induces these alterations; 3- to investigate whether tonic NMDA activation is increased in cerebellum in chronic hyperammonemia *in vivo*, and 4- whether this tonic activation is responsible for nNOS alterations in cerebellum.

The findings show that hyperammonemia reduces both basal activity of nNOS and its activation following NMDA receptor activation. Reduced basal activity is due to increased phosphorylation of Ser847 by calcium-calmodulin-dependent protein kinases (CaMKII), which in turn is due to increased phosphorylation of Thr286. Reduced activation of nNOS in response to NMDA receptor activation in hyperammonemia is due to altered subcellular localization of nNOS, with reduced amount in post-synaptic membranes and increased amount in the cytosol. Blocking NMDA receptors with MK-801 increases cGMP and NO metabolites in cerebellum *in vivo* and in slices from hyperammonemic rats, reduces phosphorylation and activity of CaMKII and normalizes nNOS phosphorylation and activity. MK-801 also increases nNOS in synaptic membranes and reduces it in cytosol.

This indicates that hyperammonemia increases tonic activation of NMDA receptors leading to reduced activity of nNOS and of the glutamate–NO–cGMP pathway.



P107

NUCLEAR RECEPTOR REV-ERB ALPHA AND RETINAL FUNCTION

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The nuclear hormone receptor Rev-ErbA has been widely studied for its role in the circadian rhythms and cell metabolism. However its role in the retina remains elusive. The aim of the present study was to understand the role of Rev-ErbA in the retina and evaluated the effects of its loss on retinal structure and function. Methods: Rev-ErbA^{-/-} and Rev-ErbA^{+/+} mice were examined by scanning laser ophthalmoscopy (SLO) and electroretinography (ERG) (scotopic and photopic tests). Retinas were processed for histology and immunohistochemistry using rod and cone-specific antibodies (anti -rhodopsin, -MW and -SW opsin). For the analysis of the phagocytosis rhythm, eyes were sampled every 3 hours during a 24 h LD cycle (12 light: 12 h dark) and quantified using a morphometric method. Finally, animals were subjected to circadian photoentrainment under different lighting (100, 70, <1lux).and jet lag (6h delay) conditions.

Results: Depletion of RevErbA did not induce structural modifications in the mouse retina. However, ERG studies showed that the rod b-wave, the post-receptor electrical response, was distinctly abnormal in Rev-ErbA^{-/-} mice. Phagocytosis study showed a ~50% reduction in the peak 1 h after light onset in the null mice. Also, actimetry recordings showed a faster response to the jet lag and light intensity changes comparing to wild type littermates.

Conclusion: Rev-ErbA^{-/-} mice show dramatic changes in rhythmic shedding although the general structure of the retina is not affected. Our data show that the entrainment to a light/dark cycle with decreased light levels is different in both genotypes We conclude that RevErbA plays an important role in retina physiology.



P108

STROKE AWARENESS IN THE SAUDI COMMUNITY: PROMPT PUBLIC HEALTH MEASURES MUST BE IMPLEMENTED

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Background: Stroke is very prevalent in the Kingdom of Saudi Arabia, approaching 43.8 per 100,000 population. Stroke outcome is known to be affected by the level of stroke awareness in the community. We conducted this study to assess the level of stroke awareness in the Saudi population.

Methods: A survey of 21 questions, pertaining to stroke awareness (stroke symptoms, and signs and stroke risk factors), was distributed to Saudi population (aged 15-70) in malls, super markets, health clubs, mosques, universities and schools. R

Results: 2862 (82% response rate) completed the questionnaire. 1844 (64%) were able to define stroke correctly. 1428 (49.9%) named mass media as the source of their knowledge. 1301 (45.9%) believe stroke and brain death share the same pathological mechanism and outcome, particularly those under the age of 40 ($p < 0.05$). Only a small proportion was able to identify stroke risk factors (hypertension 957 (33.4%), diabetes mellitus 482 (16.8%), tobacco smoking 1065 (37.2%), dyslipidemia 889 (31.1%), old age 971 (33.9%), heart disease 1161 (40.6%), ethnicity 109 (3.8%), obesity 718 (25.1%) Additionally, a smaller proportion was able to recognize stroke symptoms and signs (speech difficulty 1321 (46.2%), blurred vision 1114 (38.9%), dizziness 759 (26.5%), numbness 534 (18.7%), focal weakness 1303 (45.5%).

Conclusion: There is an alarming deficit in the level of stroke awareness in the Saudi population. Urgent public health measures to correct this deficiency, that will match the rate of similar countries, is promptly needed.



P109

POSTNATAL UNDERNUTRITION AND BRAIN DEVELOPMENT: BEHAVIORAL AND NEUROCHEMICAL STUDY.

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Problem statement: Undernutrition can result in abnormal development of the brain. Depending on age at onset different functional deficits can be observed. Most of the previous studies focused on the effects of prenatal and perinatal period while there is evidence that the effects may persist later in life.

Approach: The effects of undernutrition were examined on rat at weaning and in adult. Rats were provided either an ad libidum diet (control group) or maintained at 80% of the weight of their control littermate (undernourished group). After three weeks into diet, rats were tested in an open field. HPLC analysis was conducted in rats undernourished at weaning in order to assess dopamine and metabolites in the striatum. Rats were tested in radial maze in order to assess acquisition and retention. For both group, undernourished at weaning and in adult, locomotor and exploratory activities was recorded after intra-peritoneal amphetamine injection. Sensory reactivity was measured in a tail flick test.

Results: Undernutrition induced a decrease in dopamine concentration in the striatum of rats undernourished at weaning with an increase in DOPAC and HVA. No effect was observed in acquisition and retention in the radial maze but intra-peritoneal haloperidol injection impaired retention by control but not undernourished rats. Undernourished rats exhibited hyperactivity when the diet was imposed at weaning with increased locomotor and exploratory activities, while no effect was observed in adult rat. Amphetamine injection did not induce any effect in rats undernourished at weaning but increased locomotor and exploratory activities in adults. Both groups showed hyperreactivity to heat in the tail flick test.

Conclusions: In spite of the attention devoted in the literature to prenatal effects of undernutrition, behavioral deficits were more serious after weaning. We thus clearly establish a special vulnerability of this period in rats.



P110

DYSFUNCTION OF VOLTAGE-GATED K⁺ CHANNELS KV1.1 IN SCIATIC NERVE CAUSES SPONTANEOUS AND STRESS-INDUCED NEUROMUSCULAR HYPEREXCITABILITY

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Episodic ataxia type 1 (EA1) is an autosomal dominant neurological disorder characterized by myokymia and attacks of ataxic gait often precipitated by stress. Several genetic mutations have been identified in the Shaker-like K⁺ channel Kv1.1 (KCNA1) of EA1 individuals, including V408A which result in remarkable channel dysfunction. By inserting the heterozygous V408A mutation in one Kv1.1 allele, a mouse model of EA1 has been generated (Kv1.1V408A/+).

Here, we investigated the neuromuscular transmission of Kv1.1V408A/+ ataxic mice and their susceptibility to physiologically relevant stressors. By using *in vivo* preparations of lateral gastrocnemius (LG) nerve-muscle from Kv1.1+/+ and Kv1.1V408A/+ mice, we show that the mutant animals exhibit spontaneous myokymic discharges consisting of repeated singlets, duplets or multiplets, despite motor nerve axotomy. Two-photon laser scanning microscopy from the motor nerve, *ex vivo*, revealed spontaneous Ca²⁺ signals that occurred abnormally only in preparations dissected from Kv1.1V408A/+ mice. Spontaneous bursting activity, as well as that evoked by sciatic nerve stimulation, was exacerbated by muscle fatigue, ischemia and low temperatures. These stressors also increased the amplitude of compound muscle action potential. Such abnormal neuromuscular transmission did not alter fiber type composition, neuromuscular junction and vascularization of LG muscle, analyzed by light and electron microscopy.

Taken together these findings provide direct evidence that identifies the motor nerve as an important generator of myokymic activity, that dysfunction of Kv1.1 channels alters Ca²⁺ homeostasis in motor axons, and also strongly suggest that muscle fatigue contributes more than PNS fatigue to exacerbate the myokymia/neuromyotonia phenotype. More broadly, this study points out that juxtaparanodal K⁺ channels composed of Kv1.1 subunits exert an important role in dampening the excitability of motor nerve axons during fatigue or ischemic insult.



P111

PERIPHERAL OPTIC-FLOW INVOLVEMENT IN THE MULTISENSORY CONSTRUCTION OF THE 3D PERCEPT IN HUMANS

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Problem statement. Optical flow in the peripheral field of view changes the assessment of distances (Watanabe et al., 2004, *Systems and Computers in Japan*, 35(8), 107-116) and we showed that peripheral motion influenced the foveal 3D percept of a stimulus situated 1m away from the subject (Maggia et al, 2009, 3rd Med Conf of Neuroscience. doi 10.3389/conf.neuro.01.2009.16.112). Removing the fixation point that restrained vergence eye movements during the stimuli presentation strengthened the effect (Séverac Cauquil et al., 2010, AVA Christmas meeting). In this work, we investigated how 3D perception is modulated by peripheral optic flow when the stimulus is in the reaching space. Indeed it is in the near space that vergence and stereopsis predominate. **Approach.** 13 healthy subjects indicated via a joystick the depth of circular random dot stereograms presented in the centre of a PC monitor 40-cm away from the subject, while dots scrolled on two, lateral monitors. 5 peripheral conditions were tested: divergent and convergent flow, Brownian motion, static dots and blank. Error rate and reaction times were measured. **Results.** The optic flow changed the error rate in 3D perception: convergent flow clearly facilitated near perception and decreased far and, conversely, divergent flow elicited a better far perception and impaired near perception ($\pm 30\%$; repeated measures ANOVA, $p < 0.05$). Controls (Brownian, static and blank) did not change the error rate ($p = 0.684$). **Conclusion.** This demonstrates that peripheral flow participates to 3D percept construction based on disparity in the reaching space. Convergent and divergent flows mimicking a backward or forward self-motion lead to a better 3D perception either in the near or far plane. Whether this effect is mediated by vergence remains possible and deserves further investigation.



P113

FORENSICALLY FLIES DETECT THE NUTRITIONAL VALUE OF CORPSES THROUGH NEURO-CHEMORECEPTIVE CELLS.

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Animals have evolved several chemosensory systems for detecting potentially dangerous foods in the environment. Activation of specific sensory cells within these chemosensory systems usually elicits an aversive behavioral response, leading to avoidance of the noxious foods. Using forensically important flies (blowflies) as a model organism, the question was if these flies have the ability to detect the nutritional value of corpses when injected with different doses of morphine. Blowflies respond to sugars, salts and water through the activation of specific chemoreceptor neurons in the antennal, labellar and tarsal chemosensilla. These insects also detect deterrent stimuli with the so called fifth or deterrent cell. In the attempt to gain information on the mechanisms underlying reception of noxious and repellent compounds, electrophysiological and behavioral experiments have been performed to confirm the hypothesis that morphine sulfate has a repellent effect on fly attraction to corpse. This finding is in good agreement the spike frequency elevation observed for the fifth cell activity. The prevailing activation of the deterrent cell by morphine sulfate is directly coupled with a coherent behavioral output. Therefore, comparison of behavioral and electrophysiological data, affirm that blowfly identify morphine sulfate as a deterrent stimuli by activation of the fifth cell.



P114

COMPARATIVE STUDY BETWEEN MOROCCAN BLACK PROPOLIS AND FRENCH RED PROPOLIS

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Propolis is a resinous natural hive product derived from plant exudates collected by honey bees. Due to biological and pharmacological activities, it has been extensively used in folk medicine since ancient times. The chemical composition varies qualitatively and quantitatively with the geographical and botanical origins. In the present study, we attempted to verify the possible antinociceptive action of water extract obtained from Moroccan propolis and French propolis. Two experimental models were used (acetic acid, and hot-plate tests) in order to characterize the analgesic effect. The extracts of black propolis reduced the pain induced by intraperitoneal injection of acetic acid and have also a significant effect in the hot plate test. But the extract of red propolis has an opposite effect. These results suggest that the compounds present in the extract of Moroccan propolis activated both central and peripheral mechanisms to elicit the analgesic effect. but the extract of French propolis has an algogenic effect.



P115

THE RAT SCO RESPONSIVENESS TO PROLONGED WATER DEPRIVATION: IMPLICATION OF REISSNER'S FIBER AND SEROTONIN SYSTEM

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The osmotic stress is a potent stimulus that can trigger several peripheral as well as central impairments. The brain is a vulnerable target of the osmotic stress and particularly circumventricular organs (CVOs) regarding their strategic localization as sensory organs of biochemical changes in the blood and cerebrospinal fluid circulations. The subcommissural organ (SCO) is a CVO which releases doubly in the CSF and blood circulation a glycoprotein called Reissner's fiber (RF) that has been associated to several functions including electrolyte and water balances. The present work was aimed on the assessment of the secretory activity of the SCO and its serotonergic innervation following 2 weeks of total water restriction in Wistar rat. Using the immunohistochemistry of RF and serotonin (5HT), our data showed a significant overall reduction of RF immunoreactivity within both ependymal and hypendymal cells of the SCO of dehydrated rats compared to their corresponding controls, this decrease was concomitant with an enhancement of fibers 5HT immunoreactivity in the SCO as well as in the classical ependyma and in the dorsal raphe nucleus (DRN), constituting the origin of this innervation. The present findings support the possible involvement of the SCO in the response to prolonged water deprivation by decreasing its secretory materials which may result from either a direct peripheral hormonal control and/or the consequence of the enhanced 5HT innervation of the SCO.



P116

L-TYPE CHANNEL MODULATION BY CB1 RECEPTORS IS MEDIATED BY PTX-SENSITIVE G PROTEINS AND CAMP IN HYPOTHALAMIC IMMORTALIZED GT1-7 CELLS

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Using immortalized hypothalamic GT1-7 neurons, which express the CB1 receptor (CB1R) and three Ca²⁺ channel subtypes (T-, R- and L-type), we found that the CB1R agonist WIN55,212-2 inhibited the voltage-gated Ca²⁺ currents by about 35%. The inhibition by WIN55, 212-2 (10 μ M) was reversible and prevented by nifedipine (3 μ M), suggesting a selective action on L-type Ca²⁺ channels (LTCCs). WIN55, 212-2 action exhibited all the features of voltage-independent Ca²⁺ channel modulation: 1) no changes of the activation kinetics, 2) equal depressive action at all potentials and 3) no facilitation using strong prepulses. At variance with WIN55, 212-2, the CB1R inverse-agonist AM-251 (5 μ M) caused 20% increase of Ca²⁺ currents. The inhibition of LTCCs by WIN55, 212-2 was prevented by overnight PTX-incubation and by intracellular perfusion with GDP-B-S. The latter caused also a 20% Ca²⁺ current up-regulation. WIN55, 212-2 action was also prevented by application of the PKA-blocker H89 or by loading neurons with 8-CPT-cAMP. Our results suggest that LTCCs in GT1-7 neurons are partially inhibited at rest due to a constitutive CB1R activity removed by AM-251 and GDP-B-S. Activation of CB1R via PTX-sensitive G-proteins and cAMP/PKA pathway selectively depresses LTCCs that critically control the synchronized spontaneous firing and pulsatile release of gonadotropin-releasing hormone in GT1-7 neurons.



P117

THE EFFECT OF EARLY AGE HEAT CONDITIONING AND SOME FEEDING PROGRAMS FOR HEAT-STRESSED BROILER CHICKS ON: (3). IMMUNOPHYSIOLOGICAL RESPONSE.

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A total of 144 one day old commercial broiler chicks were used in the present study to investigate the effects of early heat conditioning and some feeding programs on some physiological responses of broiler chicks reared under heat stress conditions. They were divided into two groups of 72 birds each. The first group was subjected to $38^{\circ}\text{C} \pm 1^{\circ}$ for 24hrs at day 5 post-hatching (heat conditioning group, H.C) while the second group was kept as a control (non heat conditioning group, N.H.C). Two days later (day 7) birds of each group were subdivided into four sub groups including control group, feed withdrawal (F.W.D) on day 9 for 24hrs, qualitative feed restriction (70%) on days 7, 8 and 9 (F.R) and vitamin C 20% (Vit.C) (1g/Kg diet) at 21 to 42 days. Chickens exposed to early heat conditioning, showed significant ($P < 0.05$) decrease in heterophils to lymphocytes ratio (H/L ratio) compared with non the early age heat conditioning treatments. Haematocrit value (Ht%) and haemoglobin (Hb) level were insignificantly changed with all experimental treatments during 3 and 6 week of the age. Early age heat conditioning have significant effects, ($p < 0.05$) on antibody production against NDV 20 days post vaccination. The best value was recorded for early age heat conditioning group. At 5 day of the age broiler chicks subjected to early age heat conditioning recorded significantly higher HSP 70 level 5h post heat episode. Early age heat conditioning recorded significantly lower values for HSP 70 at 21 and 42 day of the age. Feeding programs have significant effects on HSP 70 at 21 and 42 day of the age. The lowest values were recorded for all feeding programs especially the FR and FWD treatments respectively, while at 42 day of the age Vit.C supplementation, FR and FWD treatments recorded the best levels, respectively. The economic evaluation showed that the benefits of using early heat conditioning and some feeding programs.



P118

STRUCTURE AND FUNCTION OF NEUROSECRETORY CELLS IN THE BIVALVE PERNA PERNA

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Light and electron microscopic investigations on the nerve ganglia of *Perna perna* were carried out to study the development of neurosecretion and to determine quantitative variations of neurosecretory cells (NSC) during the different phases of the sexual cycle. These studies were performed in two mussel populations (unpolluted, or contaminated with domestic and industrial wastewater). Considering the size, form, density of cytoplasm, and the size and position of the nucleus, four types of NSCs were identified: a1 (about 80% of the total population), a2, a3, and a4. The fine structure demonstrated that NSCs were often unipolar or sometimes bipolar, and could be distinguished by their form. The a1 NSCs were small-sized, unipolar, and their nuclear chromatin was homogeneous or heterogeneous in relation to the state of cell activity. Five types of elementary granules and three types of large granules, formed by crinophagy or by condensation, were identified in the perikarya of NSCs. The neuroendocrine control by NSCs was demonstrated by following findings: i) the number of NSCs was significantly correlated with the sexual cycle and the cycle of reserves; ii) the numerical increase of NSCs comprised two phases, the first period preceding gonial mitoses and spawning (while the storage tissue decreased in volume) and the second characterized by a greater increase in NSC numbers. The GnRH-like NSCs of cerebroid and pedal ganglia showed the same development in relation to the different phases of the sexual cycle or the storage tissue. In contrast, insulin-like NSCs present in both types of ganglia showed a different development from December to July. Pollution estimated mainly by inhibition of acetylcholinesterase showed cell neurotoxicity. This factor disrupted the sexual cycle, by reducing the number of gametogenetic waves and their length. In addition, it reduced the number of immunoreactive NSCs in the cerebroid ganglia of mussels.



P119

DESYNCHRONIZED RHYTHMS AND MORPHOLOGICAL CHANGES OF THE RETINA IN AGEING: A STUDY IN CROCIDURA RUSSULA

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Biological rhythms are controlled by the circadian system. Retina is the input structure of this system. It is implicated in the transmission of photic information to the central pacemaker, leading finally to the release of melatonin by night. This hormone synchronizes endogenous rhythm to rate environmental. This rhythmicity is lost in aged animals. Shrew (*Crocidura russula*) is a micropthalmic small mammal, exhibiting very marked daily and seasonal rhythmic physiological and behavioural activities. Indices of this rhythmicity are lost in aged shrews suggesting a link between desynchronization and ageing. This study aims to elucidate the involvement of retina in this desynchronisation. A total of 12 shrews, young (1-4mois) and aged (25-28 mois) were sacrificed; the eyes removed were prepared by techniques of light and electron microscopy. The morphometric, histochemical and ultrastructural analyses indicate impaired photoreceptor and ganglion cells function in older individuals suggesting altered reception and transmission mechanisms in aged retina. Our results strongly propose a direct correlation between the disturbance of retinal function and desynchronized rhythms in this species.



P120

NEURONAL NITRIC OXIDE SYNTHASE EXPRESSION AND ACTIVITY IN SUPRAOPTIC AND PARAVENTRICULAR NUCLEI OF NORMAL AND DP71 DEFICIT MICE

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Next to their osmoreceptive function, the supraoptic and paraventricular nuclei (SON/PVN) exert their major role in osmoregulation as the effector pole by adapting the synthesis and the release of vasopressin neuro-peptide to the variation of the plasmatic osmolality. This needs a fine tuning of the magnocellular neuron (MCN) activity and among the different modulatory pathways, nitric oxide (NO) is of particular importance. Previous study of our group demonstrated that mice knock-out for Dp71 exhibit a perturbed osmoregulatory axis, characterized by a lower plasma osmolality under normal conditions. To go further in the understanding of the mechanisms underlying this result, in the SON and PVN, we analysed nNOS, and NADPH-diaphorase, the histochemical marker of NOS activity, because these proteins represent an index of the osmoregulatory axis activation. Indeed, NO is an important modulator of vasopressin synthesis. In normal mice, we found nNOS in magnocellular neurons in the dorsal part of the SON and in the lateral part of the PVN. In the SON and PVN of Dp71-null mice, nNOS expression was upregulated and in the same way, the NADPH-diaphorase staining was increased. Since NADPH-diaphorase activity correlates with the distribution of NOS expression and activity, it could be deduced that the enhancement of nNOS expression was accompanied with a rise of its activity and presumably with an increase of the NO production. Such a modification in the NO pathway activity could also, at least partially, explain the modified osmolality of the Dp71-null mice.



P121

MELANOPSPIN EXPRESSION IS ALTERED IN A MOUSE MODEL OF DIABETIC RETINOPATHY

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The mammalian retina contains an endogenous pacemaker that regulates retinal physiology and adjusts daily the temporal phase of the central circadian timing system with environmental time. This entrainment process involves rods, cones and melanopsin-expressing retinal ganglion cells. Diabetic retinopathy is a major cause of blindness and visual impairment that affects up to 90% of patients with diabetes. Although vascular damage is considered the first clinical sign of retinopathy, several studies suggest that alterations in retinal neurons and glial cells precede these vascular symptoms. Based on findings that retinal ganglion cells and photoreceptors degenerate during the development of diabetic retinopathy, we addressed the question to what extent this neuronal loss impacts on the molecular machinery of the retinal clock (clock and clock-controlled genes) and opsin mRNA expression (melanopsin, MW, SW and rhodopsin). Diabetes was induced in 3-week-old C57/BL6 wild-type mice by injection of three successive doses of streptozotocin (SZT), which damages pancreatic B-insulin-producing cells. At 12 weeks post-injection, freshly dissected mice retinas (n=24 diabetic mice and n=24 control mice) were collected from animals at different circadian times (CT0, CT4, CT8, CT12, CT16 and CT20). The expression of clock and clock-controlled genes and opsin mRNA were assessed by real-time RT-PCR. Our results showed in the SZT-mice 1) a loss of mClock and mBmal1 circadian rhythm and 2) an over-expression of melanopsin mRNA. In conclusion, our results indicate that the development of diabetic retinopathy affects the circadian rhythm of two major clock genes involved in the molecular machinery of the retinal clock. The over-expression of melanopsin may induce an alteration in the entrainment process of the circadian timing system and the retinal clock by light.



P122

EFFECTS OF HIGH-FAT DIET INDUCED OBESITY ON PERIPHERAL NERVE REGENERATION IN RATS

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123Objective: The aim of this study was to investigate effects of obesity on sciatic nerve regeneration using electrophysiology, stereology, immunohistochemistry, histopathology.

Materials and Methods: The study was performed using four groups of rats: control(C), obese(O), control damaged(CD) and obese damaged(OD) groups. After perfusion-fixation, the sciatic nerves were removed four different groups processed for electron microscopy. These procedures were completed by embedding the tissues. After than Semi-thin sections (1 µm) were cut by an ultramicrotome and stained with 1% toluidine blue. These sections were analyzed with stereological methods.

Results: Electrophysiology showed that nerve conduction velocity and EMG were not different among experimental groups; the amplitude of compound action potential of C group was significantly higher than O group. Examination of the nerves showed that C and O groups not only had a larger axon diameter but also a thicker myelin sheath. A higher number of myelinated axon was found in both C and O groups in comparison to CD and OD groups. But CD group axon diameter and myelin sheath thickness were significantly higher than OD group. There is significant difference between morphological quantities C, O, CD and OD group. There is no significant difference between functional tests of C, O, CD, OD group. In immunohistochemical staining with antibody GAP-43 CD group was significantly higher than OD group. But no significant difference was detected between the C and O groups. In immunohistochemical staining with antibody TGF-β 3 there is no significant difference between CD and OD group.

Conclusion: Our results suggest that obesity have negative impact on peripheral nerve regeneration after damage.



P123

NEURAL- MORPHOLOGICAL APPROACH FOR THE SEGMENTATION OF MICROSCOPIC COLOR IMAGES: PROVIDE HELP TO THE DIAGNOSIS OF CANCER

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This work fits into the context of medical imaging; it is to process microscopic color images in order to provide aid in the diagnosis of brain cancer. Our goal is the development and implementation of a chain of image analysis, capable of detecting a possible presence of pathological cells in a cell microscopy image. The role of this analysis is to identify nucleus and cytoplasm of brain cells in the microscopic image to be processed. We calculate the surface ratio of nucleus to the cytoplasm of each cell, and classify them into two categories (healthy cell or pathological cell). The identification of the constituents of the image pre-processed is done by operation of the image segmentation; this method is based on mathematical morphology and neural networks. It is the color watershed controlled by a Multi layers Perceptron. Neural networks are involved in this method of image segmentation, to overcome the problem of variability of images to be processed, i.e. they contribute to the robustness of the proposed implementation.



P124

LOSS OF ANALGESIC EFFECTS OF BACLOFEN AND GALANINE IN NEUROPATHIC RATS THROUGH INTERACTION OF GABAB AND GAL1 SIGNALING PATHWAYS

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In dorsal spinal horn, nociceptive transmission is controlled by excitatory and inhibitory modulations. Our general objective is to study desinhibition processes that may disrupt this balance and cause pain sensitization. Beside classical neurotransmitters, such as GABA, neuropeptides may also contribute to inhibitory modulations. Among these, galanin is an inhibitory peptide released from primary afferents and from local GABAergic interneurons. GABA and Galanin metabotropic receptors, GABAB and Gal1 respectively, are both G protein coupled receptors that initiate similar intracellular events and share the same intracellular targets. In the present study, we investigated whether co-activation of these two inhibitory systems may cooperate in limiting neuropathic pain sensitization. Intrathecal injection of either Baclofen or Galanin, GABAB and Gal1 agonists respectively, reduced mechanical and cold allodynia in neuropathic rats. Surprisingly, co-injection of Baclofen and Galanin together totally abolished these inhibitory effects. Using In situ hybridization studies, we show that both GABAB and Gal1 receptor mRNA co-localise in spinal neurons, suggesting possible direct interaction between these two receptors. Using in vitro patch clamp electrophysiology in spinal cord cultured neurons transfected with GALR1, we demonstrate that baclofen induces the activation of potassium inward rectifying currents. This activation is prevented when baclofen is co-applied with galanin. Finally, Using [35S] GTP-gamma-S binding assay, we show that galanin abolishes the baclofen-induced accumulation of [35S] GTP-gamma-S in superficial laminae of spinal cord. Taken together, these data confirm the above hypothesis of interactions between receptor signalling pathways. Moreover, our study provides direct evidence of peptidergic modulatory roles on classical neurotransmission, and suggests a new mechanism for controlling GABAB activity, through interaction with other metabotropic receptors. Moreover, it demonstrates behavioural implications of such interactions in processes leading to pain sensitization.



P125

A RECOGNITION SITE FOR SOMATOSTATIN-14 ON THE GABAA RECEPTOR COMPLEX IN RAT MESENCEPHALON ?

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The GABAA receptor is a ligand-gated chloride channel and is primarily responsible for fast inhibitory neurotransmission in the central nervous system. One of the unique features of this receptor is that, in addition to the GABA binding site, the receptor has several allosteric modulatory sites. We recently reported, on the presence of modulatory action of somatostatin (SRIF) on the GABAA, in rat cerebral cortex, hippocampus and hypothalamus. To further characterise this interaction, we examined the effect of the addition of the SRIF on the binding of ([35S]TBPS), used as a highly valuable tool for autoradiographic labelling of central GABAA receptor complex, in other brain regions located principally in mesencephalon. Furthermore, we analysed the actions of GABA agonists and antagonists in order to determine the presence or not of distinct pharmacological profiles of SRIF action. The quantification of the labelling obtained in the radioautograms, shows that the SRIF (10^{-8} – 10^{-4} M) produced a dose-dependant inhibition of [35S]TBPS binding. Within the rat mesencephalon, interregional differences could not be detected. In all mesencephalic nuclei and areas investigated, SRIF inhibited specific binding with IC₅₀ values in the micromolar range (1.5 ± 0.21 – $3.1 \pm 0.36 \times 10^{-6}$ M). The inhibitory action of SRIF is enhanced in the presence of GABA 1 mM or muscimol 1mM. However, bicuculline 1mM had no effect on the action of SRIF. This pharmacological profile, is different from that shown for forebrain and diencephalic regions. In conclusion, the present data demonstrated a direct interaction between SRIF and the GABAA receptor complex, in the rat mesencephalon and suggest that this peptide could possess a specific recognition site on the GABAA receptor complex. The mechanism and the physiological relevance of this interaction still remain to be determined.



P126

MRI ANALYSIS OF THE SPINAL CORD BY SNAKES GUIDED BY THE GRADIENT VECTOR FLOW (GVF)

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Problem Statement: In order to provide a semi-automatic aid diagnosis of some lesions and spinal cord injury, the aim of our work is to detect the edge of the human spinal cord or dural sac that surrounds it, from MR images of spinal cord sagittal plane, T2-weighted. After a step of pretreatments, we segment the spinal cord using snakes. Traditional snakes have major problems: - Difficulties to fit them into the concavities. - Difficulties in changing contours away from their current position - Difficulties in changing contours, if they cross the real contour To improve the deformation of the active contour, the external force replaces the traditional snake by a vector field. **Approach:** Before segmentation, we must apply a pretreatment phase, including: - Contrast Adjustment to enhance image quality, - A Gaussian filter to reduce noise, - A dilation followed by erosion to improve the contrast performance. This allows for better image quality and a separation between the two tissue-spinal and dural sac. The segmentation phase is to extract the contour of the area of interest from the preprocessed image, by a calculation of the field Gradient Vector (GVF) of this image. This flow must be standardized then obtain a new form of flow, noted "GVFN", that guided our active contour during its deformation to the desired contour of the area of interest. During segmentation, we speak twice manually: once to select points on the dural sac and eliminate unwanted structures, a second to initialize the active contour. **Results:** The tests were performed on MR images showing the possibility of snakes guided by GVF to automatically manage the topology change of the curve still evolving. These tests show the good convergence of GVF snakes and guided by their strong progress towards the concavities. **Conclusions/Recommendations:** Snakes guided by GVF dependent initialization. It would be interesting to automate this segmentation process, eliminating two-step manual intervention.



P127

CORTICAL EXCITABILITY OF AMYOTROPHIC LATERAL SCLEROSIS: TRANSCRANIAL MAGNETIC STIMULATION STUDY

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Objective: Assessment of upper motor neuron (UMN) involvement is essential for the diagnosis of amyotrophic lateral sclerosis (ALS). In a number of amyotrophic lateral sclerosis (ALS) cases, mirror movements (MM) suggest an involvement of transcallosal fibre tracts in conjunction with UMN involvement. The aim of the present work is: to assess the cortical excitability and transcallosal inhibition in ALS patients to understand more about its pathophysiological background, and their implications for the diagnosis and treatment of ALS. **Methods:** Seventeen patients with definite ALS and 17 control healthy volunteers will include in the study. Clinical examination and TMS investigation included measurement of resting and active motor threshold (rTM, and Amt), motor evoked potential (MEP), input-output curve, contralateral silent period and Transcallosal inhibition (CSP and TI) were measured for each participant, **Results:** ALS patients had no significant differences for either rMT or aMT in comparison to control group for both hemispheres. Despite this there was a significant negative correlation between ALSSS and RMT, and AMT meaning that increased severity was associated with the higher thresholds. There were significant lower motor evoked potential amplitudes for ALS patients in comparison to the control group ($P= 0.035$ for right and 0.050 for lt hemispheres). A significant decrease in the slope of I/O relationship of MEP amplitude to TMS intensity was reported in patients group in comparison to control group. ALS patients had a significant prolongation of CSP for right and left hemispheres in comparison to the control group ($P= 0.015$, and 0.04 respectively), as well as a significant increased duration of TI ($P= 0.002$ for right and 0.019 for lt hemispheres). **Conclusion:** The assessment of cortical motor excitatory and inhibitory changes of ALS confirm the presence of hereditability of the cortex.



P128

AMELIORATIVE EFFECT OF DEXMEDETOMIDINE AND ITS COMBINATION WITH TRAMADOL OR AMITRIPTYLINE IN RAT MODEL OF NEUROPATHIC PAIN

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Background: Interactions between sympathetic and somatic nervous system play an essential role in the pathophysiologic mechanisms of neuropathic pain. The aim of the present study was to investigate the possible antinociceptive effect of dexmedetomidine, an A₂-adrenoceptor agonist, and its combination with front-line treatment of neuropathic pain i.e. amitriptyline or tramadol in chronic constriction injury (CCI) model of sciatic nerve in rats. Methods: The effect of intraperitoneal (i.p.) dexmedetomidine (5µg/kg), tramadol (5 mg/kg) and amitriptyline (30 mg/kg) on mechanical allodynia (measured by electrical von Frey apparatus) and hyperalgesia (measured by Randall and Selitto test) was studied after CCI. The sham-operated rats and un-operated hind paw (right paw) press normally on the floor reproduced by a weighted pain score of 0. Behavioral and mechanical tests, confirmed the development of neuropathic pain after CCI. Dexmedetomidine, amitriptyline, tramadol, amitriptyline + dexmedetomidine and tramadol + dexmedetomidine combination did not produce any sedation/motor impairment ($p > 0.05$). The combination of these drugs is more effective in increasing the pain threshold after peripheral nerve injury, when compared with the administration of either of amitriptyline or tramadol alone at several time points.



P129

FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (fNIRS) DURING VESTIBULO-OCULAR AND POSTURAL CHALLENGES

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Introduction. Functional near-infrared spectroscopy (fNIRS) is a non-invasive brain imaging method that uses light to record regional changes in cerebral blood flow during functional tasks. fNIRS uses portable and wearable sensors to allow measurements of brain activation during participant movement. **Methods.** A 32-channel, fNIRS device was used to record brain activation during a series of vestibular experiments. Images of brain activity were estimated from statistical regression analysis. **Results.** **Caloric stimulation.** A bilateral fNIRS probe was used to record brain activity from the frontal and temporal regions of 20 healthy persons: (N=10 young; N=10 older). Brain responses were recorded during warm (44°C) and cool (30°C) caloric irrigations. The older group showed increased bilateral activations of the superior temporal gyrus (STG) compared to the younger population. fNIRS recordings showed that the evoked brain changes in the STG matched the onset and duration of nystagmus. **Dynamic Posturography.** fNIRS was recorded during sensory organization testing (SOT) on an Equitest platform in ten young healthy volunteers. Brain areas in STG, frontal cortex (FC) and the supramarginal gyrus (SMG) were activated during the SOT conditions. We found that loss of proprioception showed a dominant left SMG activation while loss of vision showed a dominant right SMG activation. Bilateral STG and SMG activation was observed when both proprioception and visual inputs were removed. **Rotational testing.** A 4-channel wireless fNIRS system was built to allow measurements in STG during earth-vertical axis rotational testing. Bilateral STG areas were recorded from twenty healthy volunteers (N=10 young; N=10 older) during sinusoidal rotation (0.1 Hz, 60 deg/sec) in the dark. Bilateral activation of STG was observed. **Conclusion.** This set of experiments demonstrates the feasibility of using fNIRS imaging for studying cortical activity during vestibulo-ocular and postural challenges.



P130

EFFECTS OF OBESITY INDUCED BY HIGH-FAT DIET ON PERIPHERAL NERVE REGENERATION IN RATS

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ABSTRACT Objective: The aim of this study was to investigate the effects of obesity on sciatic nerve regeneration using electrophysiology, stereology, immunohistochemistry, histopathological analysis and functional tests. Materials and Methods: The study was consisting of four groups of rats: control (Cont), obese (Ob), control damaged (Cont D) and obese damaged (Ob D) groups. After experimental application, by means of perfusion-fixation, the sciatic nerves were removed tissue processes. After than semi-thin sections (1 μ m) were cut by an ultramicrotome and stained with 1% toluidine blue. These sections were analyzed with stereological methods. Before harvesting tissue blocks from the nerve, electrophysiological records were made. Results: Electrophysiology showed that nerve conduction velocity and EMG were not different among experimental groups; the amplitude of compound action potential of Cont group was significantly higher than Ob group. Examination of the nerves showed that Cont and Ob groups not only had a larger axon diameter but also has a thicker myelin sheath. A higher number of myelinated axons were found in both Cont and Ob groups in comparison to Cont D and Ob D groups. But Cont D group axon diameter and myelin sheath thickness were significantly higher than Ob D group. There is significant difference between morphological appearance of Cont, Ob, Cont D and Ob D group. There is no significant difference between functional tests of Cont, Ob, Cont D, Ob D groups. In immunohistochemical staining with antibody GAP-43 CD group was significantly higher than Ob D group. But no significant difference was detected between the Cont and Ob groups. In immunohistochemical staining with antibody TGF-B 3 there is no significant difference between CD and OD group. Conclusion: Present results suggest that obesity have a negative impact on the peripheral nerve regeneration after damage. Acknowledgement: This study was supported by Ondokuz Mayıs University Scientific Project Found (PYO.TIP.1904.10.042).



P131

FUNCTIONAL MAPPING OF THE BLADDER REGULATORY SYSTEM: COMMUNICATION BETWEEN THE LOWER URINARY TRACT AND THE CENTRAL NERVOUS SYSTEM

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The literature on urinary symptoms describes an incidence about 16 % among people over 50 years that increases with age. In this context, it is necessary to understand the physiological and pathological processes involved in the micturition and the urinary continence for the development of new and more specific treatment options. One of the most frequently encountered urological disorders is the overactive bladder symptom complex. According to knowledge on the bladder innervation, several hypotheses have been proposed to explain the origins of the increased activity of the detrusor muscle. Indeed the functions of the lower urinary tract are controlled by complex pathways in the central nervous system as the periaqueductal gray (PAG) or the pontine micturition center (PMC) that act like switching circuits to voluntarily or reflexly shift the activity of various pelvic organs (bladder, urethra, ...) from urine storage to voiding. Therefore incontinence could be related to the deregulation of these efferent or afferent pathways. The juxtacellular recording-labeling technique is a powerful tool achieving single-cell structure/function correlation studies in living animal. This non-invasive single-cell filling procedure allows to keep alive the extracellularly recorded and stimulated neuron and so to reveal the overall picture of the smallest neurons, including interneurons and to investigate the physiological and architectural bases of cell-cell communication. In order to evaluate the effect of the increased pressure in the urinary bladder on the neural activity, the *in vivo* cystometry technique will be performed at the same time. Taking into account that the rodents bladder shows several features similar to those reported in humans, the experiments will be undertaken in rat. In this project, the juxtacellular recording - labeling technique in combination with *in vivo* cystometry in rat will be used to map the neural innervation in the PAG and to understand the sensory perception and the processing during bladder filling. [sb2]



P132

INVOLVEMENT OF SEROTONIN AND DOPAMINE DYSFUNCTION IN THE PATHOPHYSIOLOGY OF CHRONIC HEPATIC ENCEPHALOPATHY: THE RESTORATIVE ROLE OF DEHYDROEPIANDROSTERONE SULFATE

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Chronic and acute liver failure leads to a syndrome called hepatic Encephalopathy (HE) characterized by a neuropsychiatric complication depending upon the duration and degree of hepatic dysfunction. Patients with chronic HE develop a neurological syndrome related to a general impairment of multiple neurotransmitter systems including the dopaminergic and serotonergic ones. In order to assess the responsiveness of these systems occurring in chronic HE, we underwent an immunohistochemical analysis of dopamine and serotonin expression by means of antibodies respectively against tyrosine hydroxylase (TH) and serotonin (5HT) in different brain areas of bile duct ligated rat (BDL). Four weeks after surgery, BDL rats exhibit an overall loss of TH expression in substantia nigra, ventral tegmental area with the subsequent striatal outputs. Serotonin expression showed the same tendency in the dorsal raphe nucleus and its projections to ventricular borders, whereas, Administration of dehydroepiandrosterone sulfate (5mg/kg), for 3 consecutive days before sacrifice, restores such impairments through a recovery of TH and 5HT expressions in all of the studied nuclei and their projections. The present finding reveals in chronic HE, an obvious dysfunction of two neurotransmitter systems; serotonin and dopamine highly involved in numerous important neurological functions and may be one of the possible causes of the neuropsychiatric symptoms of chronic HE and suggest that treatment with DHEAS as a replacement therapy could be beneficial in chronic HE.



P133

IN VIVO BRAIN REPAIR? ELECTRICAL FIELDS ATTRACT NEWBORN BRAIN CELLS

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Neurogenesis is known to occur at the subventricular zone (SVZ), where the highest number of stem/progenitor cells in the adult brain are hosted. Following proliferation in the SVZ, newborn cells mainly migrate rostrally towards the olfactory bulb. Although specific factors which influence neurogenesis have been identified, tools controlling the direction of migration of newborn cells are not available.

We applied electrical fields (EFs) to the rat motor cortex.

Results showed a striking increase in cell proliferation in the SVZ following cortical EFs. We also found a remarkable increase in the number of BrdU-positive cells in the area below the electrodes. Furthermore, double labeling of cortical BrdU-positive cells with NeuN showed that newborn SVZ cells not only migrate to the cortex, but also differentiate into mature neurons.

Finally, based on the fact that the subependymal 5-hydroxytryptamine (5-HT, or serotonin) plexus overlaps with the SVZ neurogenic area and the existing knowledge of the effects on 5-HT on neurogenesis, we proposed that enhanced 5-HT in the SVZ could be responsible for the proliferation boost following cortical EFs.

Intriguingly, we found clearly enhanced density of the serotonergic fibers in the SVZ and a concurrent increase in neuronal activity in the dorsal raphe nucleus (DRN), the brain's main serotonergic nucleus. Our findings reveal a novel approach to influence proliferation and migration of stem/progenitor cells in the adult brain.

We showed that the application of specific electrical fields can direct migration of newborn brain cells from the SVZ to the area of interest. In addition, our results suggest that this process is coordinated by altered serotonergic input to the SVZ. We propose the possibility of cortical brain repair after epidurally applied electrical fields based on the existence of electrotaxis of newborn brain cells.



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CELL CYCLE ABERRATIONS IN CHORDOMA: A ROLE FOR THE P53- AND RB1-PATHWAY.

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Abstract Background: Despite refinement of surgical techniques and adjuvant radiotherapy, the prognosis for patients suffering from a chordoma remains poor. Identification of prognostic factors related to tumor biology might improve this assessment and result in molecular markers for targeted therapy. Limited studies have been performed to unravel the impact of cell cycle markers in chordoma and those performed have shown inconclusive results. In the current study, we aimed at discovering the impact of cyclin dependent kinase 4 (CDK4) expression and its relation to prognosis and other cell cycle markers in chordoma. **Material and methods:** Twenty-five human formalin fixed paraffin-embedded chordoma specimens were examined by immunohistochemistry for the expression of CDK4, protein 53 (p53) and murine double minute 2 (MDM2). The MIB-1 labeling index (MIB1-LI) and mitotic index (MI) were used for the examination of proliferation. We collected detailed demographic and clinical data. **Results:** Overexpression of CDK4, p53 and MDM2 were found in 5 (20%), 7 (28%) and 14 (56%) of the cases, respectively. All three cell cycle markers showed a significant correlation with MIB1-LI. Expression of CDK4 ($p=0.02$) and P53 ($p<0.01$) were both significantly correlated to poor overall survival (OS). Also, histologically observed necrosis ($p<0.05$) and a dedifferentiated tumor subtype ($p<0.01$) were related to adverse patient outcome. **Conclusion:** Our results show that the expression of CDK4 and p53 are linked to cell proliferation capacity and worse outcome in patients with chordoma.



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MEAGLENCEPHALY & WHITE MATTER DISEASE IN INFANCY AND CHILDHOOD

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Canavan disease is a leukodystrophy that is inherited as an autosomal recessive disorder and is due to deficiency of aspartoacylase activity (ASPA). Aim of work is to present the clinical manifestations of Canavan disease, diagnostic work up, molecular diagnosis & prenatal diagnosis. Materials & methods: the study included 22 cases presenting with macrocephaly & brain MRI findings suggestive of leukodystrophy and their ages ranged from 6ms.-10ys. All cases were subjected to clinical history & examination, fundus examination & organic acid profile in urine, magnetic resonance spectroscopy (7 cases), quantitative analysis of N-acetyl aspartic acid (5cases) molecular diagnosis for ASPA gene of Canavan disease (2cases) & prenatal diagnosis (one pregnant mother), arylsulfatase (4) & hexoseaminidase A activity (one case). Results revealed that Canavan disease were (12cases), megalencephalic leukoencephalopathy with subcortical cysts (4 cases), glutaric aciduria type (1 case), Tay sach's disease (1 case). Cases with Canavan disease presented during the first 18 ms. of life with macrocephaly, upper motor neurone signs, defective vision (6 cases) and seizures in 8 cases. History of similar condition was present in 5 families. Molecular diagnosis for Canavan disease were homozygous for c.244dupA(p.met82AsnfsX809) mutation in 2 cases & prenatal diagnosis was done for one of the (pregnant mother) and showed heterozygous for this mutation. Conclusion: neuroimaging (MRI) is a real achievement for the identification of white matter disease. Organic acid profile in urine is helpful for the diagnosis of Canavan disease hence its molecular diagnosis & prenatal diagnosis but, still some cases of leukodystrophy with macrocephaly requires further work up



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EFFECTS OF ANTI - INFLAMMATORY DRUGS ON RABIES ENCEPHALITIS IN MICE

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Rabies is a highly fatal infectious inflammatory disease of the nervous system that has no cure. Several drugs have been tried with little success. To date only five people have recovered from rabies. Although success rate is very poor, the quest for cure continues. Trials were conducted to investigate the effects of anti-inflammatory drugs on the pathogenesis and course of rabies encephalitis in mice. Sixty weaning mice were inoculated with 0.02 ml of 10% brain suspension from street rabies virus isolated from a dog. At the onset of clinical rabies, twenty infected mice were randomly picked and divided into 4 groups of 5 mice each. Group 1 was treated with dexamethasone at 0.2mg/kg in the *vastus lateralis* muscle twenty four hourly; Group 2 with acetaminophen at 33mg/kg twelve hourly; Group 3 with piroxicam at 1mg/kg forty eight hourly, while group 4 was left as untreated control. Complete physical examination was conducted twice a day. Brain materials from dead mice were fixed in 10% formalin for histopathological analysis. Dexamethasone and acetaminophen had ameliorating effect on the clinical signs of encephalitis observed. The treated mice appeared calmer and lived longer than those treated with piroxicam and the untreated control. Better result was obtained from dexamethasone, and then followed by acetaminophen while piroxicam had no effect on the level of clinical signs and survival rates of the mice. Histopathological lesions of the brain smear of dexamethasone and acetaminophen established less inflammatory reaction in the cerebrum and cerebellum of the brains tested. Dexamethasone and Acetaminophen have the ability to reduce the severity of rabies encephalitis and prolong the life of patients suffering from rabies.



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