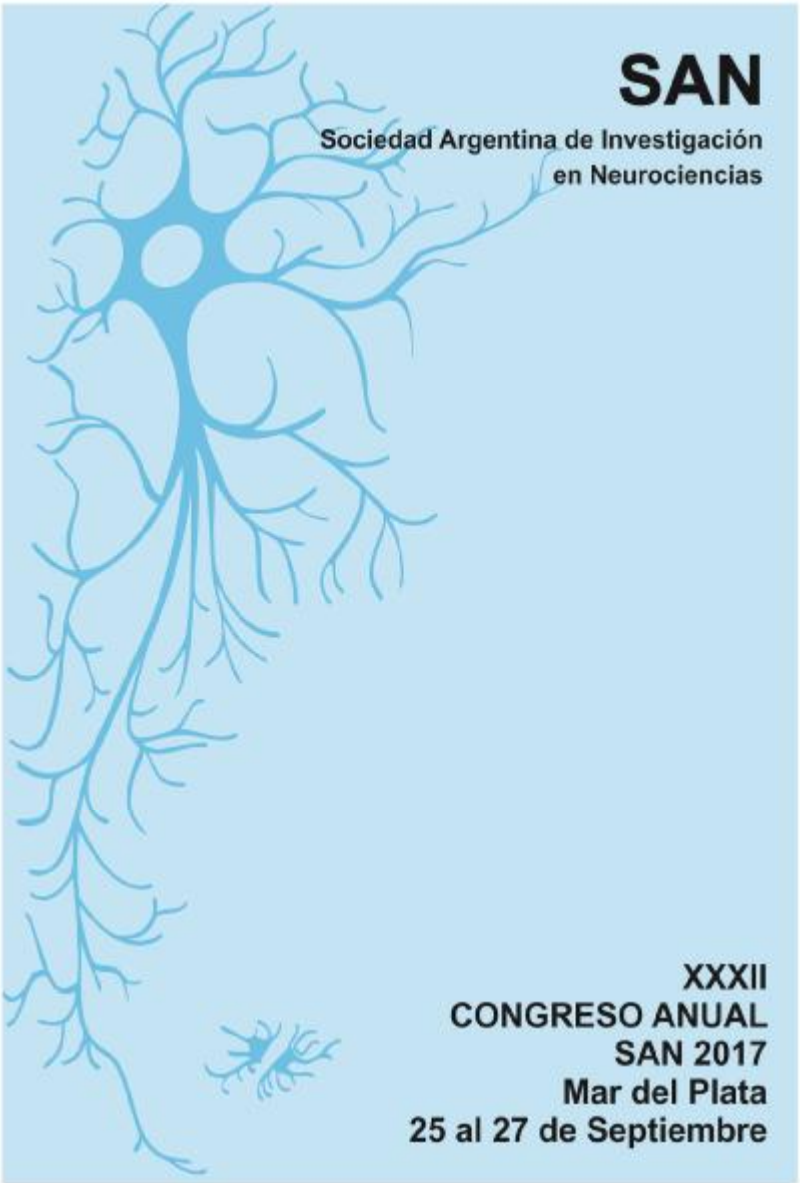

SAN

Sociedad Argentina de Investigación en Neurociencias

XXXII CONGRESO ANUAL SAN 2017

Mar del Plata

25 al 27 de Septiembre

COMMITTEES

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XXXII Congress of the Argentine Society for Research in Neuroscience
Mar del Plata – September 25-28 , 2017

Curso Pre-Congreso

"Análisis Comportamental en Modelos Animales de Desórdenes Psiquiátricos"

Sabado 23/9

15:00h Acreditación

16:30-18:30h ¿Qué es un modelo animal?

19-21h Presentación de tests conductuales

Domingo 24
9-11h Modelos de ansiedad y depresión

11:30-12:30 Discusión de papers (ansiedad y depresión)

12:30-13:30 Lunch

14-16h Comportamientos sociales y modelos de autismo

16:30-18:30 Discusión de papers (autismo)

19-21 Modelos de esquizofrenia

Lunes 25
9-10:30 Discusión de papers (esquizofrenia)

11:00-12:30 Discusión general (orden de tests, estandarizacion y reproducibilidad, etc)

XXXII Congress of the Argentine Society for Research in Neuroscience

DAY 1 / Monday, 25th

09:00 - 15:00 Registration

15:00 - 15:05 Welcome by Organizers

15:05 - 15:55 **SPECIAL LECTURE / ROOM A**
Chair: Damian Refojo, IBIOBA-Max Planck Institute, Buenos Aires, Argentina, and Sebastian Kadener, Hebrew University of Jerusalem, Israel *and Brandeis University Waltham, MA, USA*

Michael Rosbash, Brandeis University, Waltham, USA
"Circadian Rhythms and RNA: Past, Present and Future"

16:00 – 18:30 **Symposium I and Symposium II**

SYMPOSIUM I / ROOM A
"Epigenetic: Interface between the environment and genome"
Chair: Eduardo Cánepa, FCEN, University of Buenos Aires

*"**Epigenetic signature of prenatal stress on adult offspring"***
Marcela Brocco, IIB, San Martín University, Buenos Aires, Argentina

"***Prenatal stress programs sex specific predisposition to Binge Eating through hypothalamic epigenetic adaptations at multiple levels"***
Mariana Schroeder, Max Planck Institute of Psychiatry, Munich, Germany

*"**DNA methylation dynamics and phenotypic plasticity in mouse models"***
Juan Young, University of Miami, USA

"Early life adversities and the epigenetic programming of gene expression"
Eduardo Cánepa, University of Buenos Aires, Argentina

SYMPOSIUM II / ROOM B

"Exocytosis and endocytosis in neuroendocrine cells"
Chair: Fernando Marengo, University of Buenos Aires, Argentina

"The actin binding protein cortactin regulates actin polymerization and exocytosis in neuroendocrine chromaffin cells"
Ana María Cárdenas, Valparaiso University, Chile

"Rab3A regulates the stability of exocytotic fusion pores in human sperm"
Claudia Tomes, Cuyo University, Argentina

"Immediately Releasable Pool (IRP) Exocytosis, Endocytosis and Vesicle Replenishment in Mouse Chromaffin Cells"
Fernando Marengo, University of Buenos Aires, Argentina

18:30 – 18:55 Coffee break

19:00 – 20:00 **EDUARDO DE ROBERTIS LECTURE / ROOM A**
Chair: Agustín Anastasia, Instituto de Investigación Médica Mercedes y Martín Ferreyra, Córdoba, Argentina

*"**Criticality in brain (and biological) function"***
Dante Chialvo, UNSAM University, Argentina

20:00 Welcome Reception / **ROOM C**

DAY 2 / Tuesday, 26th

08:30 – 11:00 **Symposium III and Symposium IV**

SYMPOSIUM III / ROOM A
"Decentralizing the central dogma: new perspectives of RNA function in neurobiology"
Chair: Damian Refojo, IBioBA-Max Planck Institute, Buenos Aires, Argentina

*"**RNA profiling ofcircadian neurons and behavior"***
Michael Rosbash, Brandeis University, Waltham, USA

"A Multi-step Transcriptional and Chromatin State Cascade Underlies Motor Neuron Programming from Embryonic Stem Cells"
Esteban Mazzoni, New York University, USA

"***Rounding the circle: Unravelling the molecular and physiological functions of circRNAs"***
Sebastián Kadener, Hebrew University of Jerusalem, Israel *and Brandeis University Waltham, MA, USA*

"**Small, Circular and Essential: Control of Neuronal Maturation by microRNAs and circRNAs"**
Damian Refojo, IBIOBA, Buenos Aires, Argentina

SYMPOSIUM IV / ROOM B
FALAN Young Investigator Symposium (FALAN-YI) 2017 – "Preclinical assessment of promising genetic, pharmacological and environmental treatments for alcohol consumption"
Chair: Ricardo Pautassi, INIMEC-CONICET, Córdoba University, Argentina

"**Inhibition of depressant effects of ethanol by mutations and small molecules affecting the glycine receptor"**
Luis Aguayo, University of Concepción, Chile

"**Intracerebral Stem Cell Administration Inhibits Chronic and Binge Alcohol Intake in Rats"**
Fernando Ezquer, del Desarrollo University, Santiago, Chile

"**An update on CRF mechanisms underlying alcohol use disorders and dependence"**
Isabel Quadros, Sao Paulo University, Brasil

"**Environmental Enrichment enhances alcohol intake in female adolescent rats"**
Ricardo Pautassi, INIMEC-CONICET, Córdoba University, Argentina

11:00 – 11:25 Coffee break

11:30 – 13:30 **Short talk by students I and II**

SESSION I / ROOM A
Chair: Abel Carcagno, Leloir Institute, Buenos Aires, Argentina

"An integrated model for motor control of song in canaries" - **Rodrigo Alonso**, Dinamic Systems Lab,, DF, FCEN, UBA.
"Enriched environment preserves visual functions and reduces neuroinflammation of the optic nerve" - **Marcos L. Aranda,** NROE, CEFyBO, UBA/CONICET.
"Blockade of D1/D5 dopaminergic receptors in the VTA promotes the persistence of weak appetitive memories" - **Fernando Castillo Díaz**, Laboratorio de Memoria, IBCN, FMED-UBA.
"The surprising effects of acute downregulation of a GABA receptor in Drosophila sleep behavior" - **Florencia Fernández**, IBioBA-CONICET-MPSP
"Activity regulated cytoskeleton-associated protein is required for consolidation of overlapping object, but not spatial memories in the perirhinal cortex" - **Magdalena Miranda**, INECO
"Neuromodulators in the processing of afferent inputs in the dentate gyrus" - **Mora Ogando**, IBioBA-MPSP-CONICET

SESSION II / ROOM B
Chair: Mariela Chertoff, FCEN, UBA, Buenos Aires, Argentina

"Analysis of NMDAR subunits expression after GluN2A knockdown in mature primary neuronal cultures" - **Maria Florencia Acutain**, IBCN, CABA
"Murine hippocampal encephalopathy derived from hemolytic uremic syndrome (HUS) produced by shiga toxin 2 (STX2) from enterohemorrhagic Escherichia coli (EHEC)" - **Clara V. Berdasco**, IFIBIO, UBA-CONICET
"Tetraspanins as promoters of TrkA receptor tyrosine kinase activation, downstream signaling and biological responses to NGF" - **Facundo N. Ferrero Restelli**, IBCN, UBA-CONICET.
"Perinatal malnutrition deregulates PRC2 catalytic subunits and Kdm6b expression" - **Estefanía A. Fesser**, Neuroepigenética Lab, QB, FCEN, UBA.
"The membrane glycoprotein M6a endocytic/recycling pathway involves clathrin-mediated endocytosis and affects neuronal synapses" - **Micaela D. Garcia**, IIB-UNSAM.

"Neural crest derivatives in the liver during development and in fibrogenesis"
R**omina Sierra**, IIMT CONICET- Austral University.

13:30 Lunch break

15:30 – 16:25 **HÉCTOR MALDONADO LECTURE / ROOM A**
Chair: Arturo Romano, IFIBYNE-FCEN, UBA, Buenos Aires, Argentina
"How are memories formed and stored for years to come?"
Rodrigo Quian Quiroga, Research Chair at the University of Leicester, UK.

16:30 – 19:00 **Poster session I: ODD NUMBERS / ROOMS A, C & D**

19:00 Asamblea Anual SAN

DAY 3 / Wednesday, 27th

08:30 - 11:00 **SYMPOSIUM V / ROOM A**
LOCAL SENIOR RESEARCHERS LECTURES
Chair: Mario Guido, CIBIQIC, FCQ, UNC, Córdoba, Argentina, and Liliana Cancela, IFEC, UCQ, UNC, Córdoba, Argentina

"Biological events associated with stress-induced resistance to the fear memory labilization/reconsolidation process"
Victor Molina, Córdoba University

"Generation of neuronal diversity through temporal and spatial patterning in the developing spinal cord"
Guillermo Lanuza, Leloir Institute, Buenos Aires.

"From the central nervous system to the circadian timing system: new paradigms on the road?"
Estela Maris Muñoz, IHEM, Mendoza

"Circadian rewiring of adult networks in Drosophila"
M. Fernanda Ceriani, Leloir Institute, Buenos Aires.

11:00 – 11:25 Coffee break

11:30 – 13:30 **Young Investigator Symposia I & II**

YOUNG INVESTIGATOR SYMPOSIA I / ROOM A
Chair: Antonia Marin Burgin, IBioBA-Max Plank Institute, Buenos Aires, Argentina

"Changes in NMDAR-GluN2A expression as marker of long term memory consolidation"
Baez, M. Verónica, FMED – UBA, Buenos Aires
"Signatures of conscious processing in the resting-state brain activity dynamics"
Sitt, Jacobo, ICM Research Center, Hôpital Pitié-Salpêtrière, France
"Prior stress promotes the generalization of contextual fear memories: Involvement of the gabaergic signaling whithin the basolateral amygdala complex"
Bender, Christian, IFEC-CONICET-UNC, Córdoba
"Role of microRNAs in the establishment of cognitive and emotive deficits derived from perinatal protein malnutrition"
Berardino, Bruno, FCEN-UBA, Buenos Aires

YOUNG INVESTIGATOR SYMPOSIA II / ROOM B

Chair: Alejandra Pacchioni, FCBF, UNR, Rosario, Argentina

"A Local Network Activated by Experience Accelerates the Integration of New Dentate Granule Cells"
Giacomini, Damiana, Leloir Institute, Buenos Aires
"The dentate gyrus role on spatial working memory"
Piatti, Verónica, IIBBA, Buenos Aires
"A novel therapeutic target for neurodegeneration and vascular damage in Retinopathies"
Barcelona, Pablo, FCQ, UNC, Cordoba
"Role of insulin like-peptides in neural control of stress response"
Veuthey, Tania, INIBIBB-DBByF-UNS. Bahia Blanca

13:30 Lunch break

15:30 – 17:55 **Poster session II: EVEN NUMBERS / ROOMS A, C & D**

18:00 – 18:30 **SAN AWARD: Best Doctoral Thesis in Neuroscience 2017**
ROOM A
Chair: Lorena Rela, IFIBIO, FMED, UBA, Buenos Aires, Argentina

"Spatio-temporal map of output connectivity of adult-born dentate granule cells"
Silvio G. Temprana, present address: University of California Berkeley, USA

18:30 – 19:30 **RANWEL CAPUTTO LECTURE / ROOM A**
Chair: María Fernanda Ceriani, Leloir Institute, Buenos Aires, Argentina

"Time in the Brain. Biological Rhythms Clocks in the Lab, to Infinity and Beyond"
Diego Golombek, UNQ, Quilmes, Argentina

19:30 – 19:45 **SAN AWARD to best talks by students & Closing remarks**

21:00 Party in "Espigón de Pescadores".

LECTURE ABSTRACTS

Monday, 25th - 15:05 - 15:55 SPECIAL LECTURE / ROOM A

Circadian Rhythms and RNA: Past, Present and Future

Michael Rosbash
BrandeisUniversity, Waltham, MA, USA

There is a long history of circadian rhythm research, but the modern era began with the now famous Konopka and Benzer 1971 publication on Drosophila. It began the molecular genetics revolution that founded modern behavioral genetics, in mammals as well as flies. I will discuss past history, the present research landscape, describe some important unanswered questions and try to anticipate some future directions.

Monday, 25th - 19:00 – 20:00 EDUARDO DE ROBERTIS LECTURE / ROOM A

Criticality in brain (and biological) function

Dante R Chialvo
Center for Complex Systems & Brain Sciences (CEMSC3), CONICET & Universidad Nacional de San Martın, Buenos Aires, Argentina

It is increasingly accepted that the working brain stays at an intermediate "critical" regime, in between the extremes of highly synchronized states and weakly correlated dynamics. In the last decade, evidence of such criticality has been collected at very different scales, from molecules to single cells, from cortex cultures to full brain neuro-imaging. This viewpoint, introduced by us in the 90's, proposes that some of the most fundamental properties of the functioning brain are only possible because it is spontaneously posed at the border of such (critical) instability. I will first describe briefly the main argument, illustrated with the most significant results, and then explore the implications of this view for the functioning brain.

Tuesday, 26th - 15:30 – 16:25 HÉCTOR MALDONADO LECTURE / ROOM A

How are memories formed and stored for years to come?

Rodrigo Quian Quiroga
Centre for Systems Neuroscience, University of Leicester, United Kingdom

Intracranial recordings in patients suffering from intractable epilepsy allow studying the firing of multiple single neurons in awake and behaving human subjects. These recordings are typically done in the hippocampus and surrounding cortex, an area known to be critical for memory functions. Using the unique opportunity to record directly from such neurons in the human brain, about 10 years ago we found what has been named 'Concept Cells' or 'Jennifer Aniston Neurons' – neurons that represent specific concepts, responding to particular persons or objects, such as Jennifer Aniston, Luke Skywalker or the Sydney Opera House. In this talk will show more recent work on how these neurons are involved in forming and storing declarative, and particularly episodic memories - the memories we have of our life experiences.

Wednesday 27th - 18:30 – 19:30 **RANWEL CAPUTTO LECTURE / ROOM A**

Time in the Brain. Biological Rhythms Clocks in the Lab, to Infinity and Beyond

Diego A. Golombek

Universidad Nacional de Quilmes / CONICET, Buenos Aires, Argentina.

Biological timing encompasses several orders of magnitude, ranging from the microsecond to the year. Among these frequencies, circadian (i.e., about 24 h) rhythms and interval timing (i.e., in the second-to-minute range) have been thoroughly studied in several organisms. In mammals, circadian rhythms are generated in the main biological clock located in the hypothalamic suprachiasmatic nuclei (SCN) which are entrained by environmental signals such as the light-dark cycle through a dedicated retinohypothalamic tract. Most, if not all, physiological and behavioral variables exhibit such circadian variations, which resonate throughout the body thanks to peripheral oscillators. Here we will focus on the signal transduction mechanisms responsible for mammalian entrainment, specifically involving the cGMP/nitric oxide pathway. In addition, as an example of circadian control, we have demonstrated diurnal changes in immune parameters which, in turn, feedback into the SCN in order to fine-tune the biological clock. Experimental models of circadian desynchronization result in severe metabolic disruption, which might represent a window into human situations which compromise entrainment, such as chronic jet lag or shift work. Indeed, in recent years, the importance of an adequate internal (i.e., among organs) and external (i.e., between the body and the environmental) synchronization has been accepted. Diverse diseases involve a varying degree of circadian disruption which, when adequately targeted, might improve the outcome and quality of life of human patients.

SYMPOSIUM ABSTRACTS

Monday 25th - 16:00 – 18:30 SYMPOSIUM I / ROOM A
"Epigenetic: Interface between the environment and genome"
Chair: Eduardo Cánepa, FCEN, University of Buenos Aires

Epigenetic signature of prenatal stress on adult offspring

Marcela A. Brocco[1] Melisa C. Monteleone[1], María Eugenia Pallarés[2], Marta C. Antonelli[2]

[1]. Instituto de Investigaciones Biotecnológicas - Instituto Tecnológico de Chascomús (IIB-INTECH).Universidad Nacional de San Martín - Consejo Nacional de Investigaciones Científicas y Técnicas(UNSAM-CONICET)

[2]. Instituto de Biología Celular y Neurociencias "Prof. Eduardo De Robertis", Facultad de Medicina, Universidad de Buenos Aires.

Prenatal stress (PS) strongly impacts on offspring, affecting gene expression and adult behavior. We studied the epigenetic signature (gene expression, microRNA levels, methylation status) in the hippocampus of adult offspring of pregnant rats subjected to PS. Our previous work showed that chronic stress alters the mRNA levels of GPM6A, a neuronal glycoprotein involved in filopodium extension. Now, we observed that PS also affects gpm6a expression. PS significantly modified the microRNA-133b levels, as well. Moreover, microRNA-133b was validated as a gpm6a regulator. In addition, PS significantly altered the bdnf, mef2a, suv39h1 and tet1 mRNA levels. Together with a reduced total 5-hydroxymetylcytosine content, our findings suggest that part of the long-lasting PS effects are linked to changes in plasticity genes and in the chromatin methylation pathway. Notably, PS altered the methylation pattern within two CpG islands in the gpm6a gene. PS-induced molecular changes alter neural connectivity, increasing the risk for neuropsychiatric disorders. Because of their antidepressant-like effects, histone deacetylase inhibitors (HDACi) are being broadly studied. We treated primary neuron cultures with the HDACi apicidin. It increased GPM6A expression and induced filopodium extension. In summary, PS affected the epigenetic machinery resulting in long-term effects. We propose gpm6a as a novel target for epigenetic regulation and for pharmacological manipulation to revert PS effects.

Prenatal stress programs sex specific predisposition to Binge Eating through hypothalamic epigenetic adaptations at multiple levels

Mariana Schroeder, Mira Jakovcevski, Tamar Polacheck, Maya Lebow, Yonat Drori, Shifra Ben-Dor and Alon Chen

Max Planck Institute of Psychiatry, Munich, Germany

Binge eating (BE) is a common aberrant form of eating behavior, characterized by overconsumption of food in a brief period of time. Recurrent episodes of BE constitute the BE disorder, which like all eating disorders mostly affects females and is frequently associated with early-life adversities. In the present study, we show that prenatal stress (PNS) in the form of corticotropin releasing factor (CRF) overexpression in late gestation predisposes female offspring to BE-like behavior that coincides with hypomethylation of hypothalamic miR-1a locus and downstream

dysregulation of the melanocortin system through Pax7/Pax3. Moreover, exposing the offspring to a diet balanced in methyl donors during adolescence can prevent the dysregulation and predisposition from being triggered. We demonstrate that gestational programming, per se will not lead to BE-like behavior, but pre-existing alterations due to stress-related prenatal programming are revealed only when challenged during adolescence. We provide experimental evidence for long-term epigenetic hypothalamic abnormalities stemming from PNS in predisposing specifically female offspring to BE disorder as well as a potential non-invasive prevention strategy.

DNA methylation dynamics and phenotypic plasticity in mouse models

Juan Young
University of Miami, USA

DNA methylation is a stable epigenetic modification with a critical role in transcriptional regulation. Experience-dependent gain or loss of DNA methylation reshapes the genomic landscape of brain cells, potentially participating in the dynamic regulation of neural circuits. We will discuss the possible roles of DNA methylation in experience-dependent modulation of phenotypic plasticity in mice. Current evidence focusing on the effects of environmental manipulation (administration of drugs of abuse; environmental enrichment) on the brain epigenome and phenotypic manifestations in mice will be presented. We will also discuss whether epigenetic processes may be involved in the passage of induced traits between generations. Overall, current findings suggest that environmental exposures of sufficient biological impact are associated with long-lasting epigenetic changes. These epigenetic changes are a likely mechanistic platform linking the effects of developmental exposure to behavioral and neurobiological phenotypes.

Early life adversities and the epigenetic programming of gene expression

Eduardo T. Cánepa
Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires and CONICET

The quality of brain architecture is established early in life through a series of dynamic interactions in which environmental conditions and personal experiences have a significant impact on the establishment of genetic programming. Current work suggests that epigenetic mechanisms of gene regulation could explain how early life experiences can leave indelible chemical marks on the brain and influence both physical and mental health later in life even when the initial trigger is long gone. When it comes to the effects of adverse environmental stimuli on individual health there are two main and seemingly contradicting views. The “cumulative stress” hypothesis sustain that the stress exposure during a lifetime are accumulative and predispose individuals to be more vulnerable to aversive challenges later in life. The mismatch hypothesis, on the other hand, states that aversive experiences early in life trigger adaptive processes, thereby rendering an individual to be better adapted to aversive challenges later in life. A third and integrative hypothesis considers that specific genes or genetic variants may predispose an individual to be more

susceptible to environmental influences. Finally, as an interface mechanism between genetic and environment several features of epigenetic should be considered when discussing health inequalities: epigenetic traits are established early in development and their effects on health persist throughout the life course; epigenetic are highly responsive to environmental changes which are affected by social institutions; there are evidences that epigenetic traits can be transgenerationally inherited.

Monday 25th - 16:00 – 18:30 SYMPOSIUM II / ROOM B

"Exocytosis and endocytosis in neuroendocrine cells"

Chair: Fernando Marengo, University of Buenos Aires, Argentina

The actin binding protein cortactin regulates actin polymerization and exocytosis in neuroendocrine chromaffin cells

Arlek M. González-Jamett, María José Guerra, Ximena Baez-Matus, Jacqueline Vásquez-Navarrete, **Ana M. Cárdenas**

Valparaiso University, Chile

Cortactin is an actin-binding protein that promotes actin polymerization in synergy with the nucleation promoting factor N-WASP. In the present work we examined the role of cortactin in the Ca2+-induced formation of actin filaments and exocytosis. With this aim we expressed in bovine chromaffin cells different cortactin domains or mutants enable to interact with proline-rich domain (PRD)-containing proteins, like including N-WASP, or to be phosphorylated by Ca2+-dependent kinases, such as ERK1/2 or and Src. Our results show that the activation of nicotinic receptors in chromaffin cells promotes cortactin translocation to the cell cortex, where it colocalizes with actin filaments. We further found that, in association with PRD-containing proteins, cortactin contributes to the Ca2+-induced actin filament formation and to regulate fusion pore dynamics and number of exocytotic events induced by activation of nicotinic receptors. However, whereas the actions of cortactin on fusion pore dynamics depend on the availability of monomeric actin and cortactin phosphorylation by ERK1/2 and Src kinases, this actin binding protein regulates the extent of exocytosis by a mechanism independent of actin polymerization, and that is determined by its phosphorylation by ERK1/2. Together our findings point out a role for cortactin as a critical modulator of actin filament formation and exocytosis in neuroendocrine cells.

This work has been supported by the grants FONDECYT 1160495 and P09-022- F from ICM-ECONOMIA, Chile.

Rab3A regulates the stability of exocytotic fusion pores in human sperm.

Claudia Nora Tomes

Instituto de Histología y Embriología de Mendoza (IHEM) "Dr. Mario H. Burgos" CONICET. Universidad Nacional De Cuyo. Facultad de Ciencias Médicas, Argentina

Secretory cells undergo regulated exocytosis in response to physiological signals. At the final stage of exocytotis, a fusion pore opens between the plasma and a secretory vesicle membranes; typically, when the pore dilates the vesicle releases its cargo. My lab uses the exocytosis of the acrosomal vesicle of human sperm (the acrosome reaction or AR) as model system. Each sperm contains a single, very large and

electron dense granule whose contents are secreted by regulated exocytosis at fertilization. The acrosomal membrane fuses at multiple points with the plasma membrane that overlies the anterior part of the head. Joining of pores originates hybrid plasma membrane-outer acrosomal membrane vesicles. The AR is completed when vesicles and acrosomal contents are shed. The exocytosis of the acrosome depends on members of the standard fusion machinery, including small GTPases and SNAREs. Geranylgeranylated and active Rab3A elicits the AR per se. Its carboxy-terminus domain is necessary and sufficient to promote exocytosis whereas its amino-terminus prevents calcium-triggered secretion. because it stabilizes open fusion pores. Sperm SNAREs engage in α-SNAP/NSF-sensitive complexes at a post-fusion stage. In other words, vesiculation is not spontaneous; rather, post-fusion regulation of the pores determines their expansion and the success of the AR.

Immediately Releasable Pool (IRP) Exocytosis, Endocytosis and Vesicle Replenishment in Mouse Chromaffin Cells

Fernando D. Marengo

Instituto de Fisiología, Biología Molecular y Neurociencias, (CONICET). Departamento de Fisiología y Biología Molecular y Celular. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina

IRP is a pool of vesicles selectively released by brief stimuli. Consequently it might be responsible of chromaffin cell secretion at basal action potential frequency. We previously determined that IRP exocytosis is mainly dependent on a tight coupling between its vesicles and P/Q Ca 2+ channels via the synprint site of the channel. Using membrane capacitance measurements, we recently analyzed the process of exocytosis recovery after the application of an action potential like stimulus (AP ls). The exocytosis triggered by AP ls (ETAP) represents a fraction of IRP (11±2 fF), and recovered with a time constant of 0.730.11 s, what is fast enough to maintain synchronous exocytosis at 0.2-0.5 Hz stimulation. We noted that this recovery process is partially dependent on the transference of vesicles from upstream pools. However, since we regularly observed a fast endocytosis (τ=0.71±0.21 s) after ETAP, we studied the possibility that this process might be also involved in ETAP recovery. When we inhibited fast endocytosis with dynasore, nitrendipine, an anti-dynamin monoclonal antibody, or the dynamin inhibitory peptide GST-Dyn 829-842 , ETAP recovery was delayed respect to the control condition. The application of the same antibody also provoked the progressive inhibition of synchronous exocytosis during low frequency AP ls stimulation. Therefore, we conclude that a fast dynamin-dependent endocytosis is involved in rapid ETAP recovery and in the maintenance of exocytosis at basal APls frequencies.

Tuesday, 26th - 08:30 – 11:00 SYMPOSIUM III / ROOM A
"Decentralizing the central dogma: new perspectives of RNA function in neurobiology"
Chair: Damian Refojo, IBIOBA-Max Planck Institute, Buenos Aires, Argentina

RNA profiling of circadian neurons and behavior
Michael Rosbash
BrandeisUniversity, Waltham, MA, USA

The Drosophila circadian clock functions within 75 pairs of central brain neurons. They are arranged in 7-8 subgroups, each of which is in a specific location with a set of defined anatomic features. We are expanding our understanding of several of these subgroups, including their contributions to behavior, their regulation of sleep and their circuitry. To this end, we have used neuronal purification and deep sequencing "around the clock" to analyze and profile RNA from several of these circadian subgroups as well as from specific non-circadian neurons. The profiling and subsequent characterization has identified molecules that are expressed in discrete neuron subgroups and contribute to specific behavioral modalities.

A Multi-step Transcriptional and Chromatin State Cascade Underlies Motor Neuron Programming from Embryonic Stem Cells
Esteban Mazzoni
New York University, New York, USA

Direct cell programming via overexpression of transcription factors (TFs) aims to control cell fate with the degree of precision needed for clinical applications. However, the regulatory steps involved in successful terminal cell fate programming remain obscure. We have investigated the underlying mechanisms by looking at gene expression, chromatin states, and TF binding during the uniquely efficient Ngn2, Isl1, and Lhx3 motor neuron programming pathway. Our analysis reveals a highly dynamic process in which Ngn2 and the Isl1/Lhx3 pair initially engage distinct regulatory regions. Subsequently, Isl1/Lhx3 binding shifts from one set of targets to another, controlling regulatory region activity and gene expression as cell differentiation progresses. Binding of Isl1/Lhx3 to later motor neuron enhancers depends on the Ebf and Onecut TFs, which are induced by Ngn2 during the programming process. Thus, motor neuron programming is the product of two initially independent transcriptional modules that converge with a feedforward transcriptional logic.

Rounding the circle: Unravelling the molecular and physiological functions of circRNAs
Sebastian Kadener
Hebrew University of Jerusalem (Jerusalem, Israel) and Brandeis University Waltham, MA, USA

Circular RNAs (circRNAs) are a very abundant type of newly described RNA species. Two of them work as miRNA sponges and one buffers the activity of a RNA binding protein, but no function has been assigned for the other thousands of circRNAs expressed across the animal kingdom. Recently, work from our lab has uncovered the mechanism by which these molecules are produced. Moreover, we identified the splicing factor muscleblind as the first modulator of circRNAs production. Here we will present new data regarding the molecular and physiological functions of circRNAs. First, and by combining state of the art methodologies, we demonstrate that a subset of circRNAs produce proteins in neural tissue. Interestingly, we found that circRNAs are translated by membrane-bound ribosomes and that this translation is regulated by FOXO in the fly brain. Second, by generating and testing a collection of 75 fly strains in which specific circRNAs are downregulated we demonstrated their functionality in vivo. We observed that downregulation of eight circRNAs resulted in total/ partial developmental lethality and that downregulation of other four circRNAs resulted in distinct defects in locomotor activity, circadian rhythms and sleep patterns. Moreover, for two of those circRNAs we have investigated the molecular mechanism mediating these defects. Together, our results constitute the first proof of functionality of circRNAs at the organismal level and provide a methodological approach to tackle this issue comprehensively.

Small, Circular and Essential: Control of Neuronal Maturation by microRNAs and circRNAs

Damian Refojo

IBioBA-Max Planck Institute of Buenos Aires, Buenos Aires, Argentina

MicroRNAs (miRNAs) are conserved noncoding RNAs that function as posttranscriptional regulators of gene expression. The current toolkit to investigate the role of miRNAs in vivo is very limited. We developed a transgenic miRNA sponge mouse line that allows the conditional inactivation of the miR-9 family (the most abundant miRNA in the brain) in a spatio-temporal-controlled manner. Using this novel approach, we found that miR-9 controls dendritic growth and synaptic transmission in vivo mostly by repressing the transcriptional repressor REST. Recently studies also indicate that a new class of non-coding RNA, the circular RNAs (circRNAs) might also exert fundamental roles in neuronal development and function. Recent profiling studies suggest that circRNAs are enriched in the brain, increase with neuronal maturation and are abundant in synapses. A first description about the role of the most abundant circRNAs in neuronal development and function will be discussed.

Tuesday, 26th - 08:30 – 11:00 SYMPOSIUM IV / ROOM B

FALAN Young Investigator Symposium (FALAN-YI) 2017 – "Preclinical assessment of promising genetic, pharmacological and environmental treatments for alcohol consumption"

Chair: Ricardo Pautassi, INIMEC-CONICET, Córdoba University, Argentina

Inhibition of depressant effects of ethanol by mutations and small molecules affecting the glycine receptor

Aguayo LG, Muñoz, B. San Martin, L. Guzman, L.
University of Concepcion, Concepcion, Chile

Alcohol abuse is a worldwide problem that causes major social, medical and economic burdens. Therefore, the search for novel, mechanistically oriented therapies is of utmost importance. Basic residues in the intracellular loop of the glycine receptor (GlyR) 1 subunit (316-320 and 385/386) are important for the receptor´s sensitivity to low concentrations of ethanol (5-50 mM). The pharmacological effects of the mutations are specific for ethanol, since the sensitivity to neurosteroids, isoflurane, propofol and Zn2+ are unchanged. Therefore, we generated and studied a Knock In (KI) mouse for 1 GlyRs with mutations in residues 385/386 of the receptor. The KI mice had normal behavior and most importantly did not display a hyperexcitable phenotype demonstrating that the mutation is primarily silent. The study of spinal and brainstem neurons with electrophysiological techniques showed that native GlyRs were less affected by ethanol- and G--mediated modulations. The data also showed that a tonic 1GlyR-mediated current in accumbal neurons, that modulates neuronal excitability, was exclusively sensitive to ethanol only in WT mice. Behavioral studies demonstrated that the KI mice have higher binge drinking and conditioned place preference indicating that GlyRs in the nAc may have a protective role against abuse. Interestingly, the mice exhibited a reduced loss of righting reflex (LORR) time when compared with WT. Results from the DID protocol showed that the KI mice went into binge drinking from day 1 of exposure, drinking three times more than the WT mice. In conclusion, we identified important amino acids that participate in the modulation of GlyR by ethanol. The study opens a novel opportunity for pharmacotherapy development to treat alcohol use disorders.
Supported by Fondecyt DPI 20140008 grant

Intracerebral Stem Cell Administration Inhibits Chronic and Binge Alcohol Intake in Rats

Fernando Ezquer[1] ,María Elena Quintanilla[2], Paola Morales[2] , Marcelo Ezquer[1] Mario Herrera-Marschitz[2] and Yedy Israel[2]
[1]Centro de Medicina Regenerativa, Facultad de Medicina Clínica Alemana-Universidad del Desarrollo, Santiago, Chile
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Alcohol use disorders are accompanied by hippocampal neuronal damage, cognitive deficits and binge-drinking relapse. Neuroinflammation appears to be partly responsible for these dysfunctions, perpetuating chronic alcohol drinking. Studies in

rodents show that chronic ethanol intake, involving the action of lipopolysaccharide and likely salsolinol, leads to neuroinflammation and production of oxidative stress, which act synergistically.In these animals, the administration of N-acetyl cysteine, a strong antioxidant, inhibits chronic ethanol intake by 60-70%, indicating that the reduction in reactive oxygen species (ROS) and inflammatory molecules in the brain has a direct impact on alcohol intake. However, the inhibitory effect of N-acetyl cysteine on alcohol intake required daily administration and disappeared 96-hours after discontinuing its administration. Mesenchymal stem cells (MSCs) of allogeneic origin have emerged as a promising tool for the treatment of a variety of neurodegenerative diseases since these cells can secrete a broad range of neuroprotective factors but also anti-inflammatory cytokines and ROS scavengers. Using an animal model of high alcohol-intake, we demonstrated that the single intra cerebro ventricular administration of MSCs obtained from bone marrow or adipose tissue of alcohol-naïve rats markedly inhibits chronic alcohol intake. Furthermore, MSC administration resulted in an 80-85% reduction of alcohol binge-drinking upon ethanol re-access compared to untreated rats. A marked inhibition of re-access intake (60%) continued 40 days after the single MSC administration (four cycles of alcohol deprivation and re-access), suggesting a marked remodelling or inhibition of the brain reward systems. The inhibitory effect of MSCs on alcohol intake was already significant 24 hours after its administration. Thus, it is likely that these early effects are due to the release of soluble factors by the MSCs.This study constitutes the first proof-of-principle demonstration that the intracerebral administration of MSCs inhibits chronic ethanol intake and virtually reverses the ethanol relapse-like phenotype observed following alcohol deprivation. We are presently evaluating if the intracerebral administration of human-derived MSCs into alcoholic rats is able to replicate the therapeutic effect.

Supported by Fondecyt # 1170146; # 1130012, #1150589, #1150850, Conicyt ACT1411 and Millennium Initiative #P09-015-F.

An update on CRF mechanisms underlying alcohol use disorders and dependence

Isabel Marian Hartmann Quadros, Giovana Camila Macedo, Liz Paola Domingues, Cristiane Aparecida Favoretto.

Department of Psychobiology, Escola Paulista de Medicina, Universidade Federal de São Paulo. São Paulo, SP, Brazil

Alcohol is the most commonly used and abused substance worldwide. The emergence of alcohol use disorders, and alcohol dependence in particular, is accompanied by functional changes in brain reward and stress systems, which contribute to escalated alcohol drinking and seeking. Corticotropin Releasing Factor (CRF) systems, including the closely related peptides Urocortins, have been critically implied in the transition towards problematic alcohol drinking and alcohol dependence. After repeated and chronic exposure to alcohol, rats present hyperactive extra-hypothalamic CRF activity, as indicated by increases in CRF immunoreactivity and/or increases in mRNA for CRF and its receptors in amygdala nuclei and the BNST. Consistently, increased alcohol seeking and intake can be attenuated after the administration of antagonists to CRF type 1 receptors (CRFR1),

particularly in animals with extensive history of alcohol exposure or escalated drinking. While blocking CRFR1 attenuates alcohol drinking, this effect can also be achieved with the activation of CRFR2 signaling, suggesting opposite roles for CRFR1 and CRFR2 in the modulation of excessive alcohol intake. However, manipulation of CRF receptor signaling in different brain regions may reveal differential effects and interactions between CRFR1 and CRFR2. Pharmacological studies start to unveil a role for both CRF receptors within brain reward pathways, as well as CRF binding protein, as critical modulators of escalated alcohol drinking. Moreover, CRF/Urocortin signaling is also recruited during other alcohol-related effects, including alcohol-induced behavioral sensitization, alcohol-escalated aggression and alcohol withdrawal-related anxiety. While effects of alcohol on the HPA axis, the amygdala and other stress-related structures have been more widely characterized, promising contributions of CRF/Urocortin signaling in brain reward pathways and other structures are starting to emerge and will be discussed.

Environmental Enrichment enhances alcohol intake in female adolescent rats

Ricardo Pautassi, Luciana Berardo, María Carolina Fabio
Instituto de Investigaciones Médicas M. y M. Ferreyra (INIMEC-CONICET-UNC), Córdoba, Argentina

There is considerable interest in the use of enriched environments (EE) to prevent development of alcohol (i.e., the drug also known as ethanol) and other drug disorders. Exposure to EE, which in rodents involve larger-than-usual home cages with interactive objects, including tunnels, toys and running wheels that provide opportunity for voluntary physical activity, reduces alcohol drinking, alcohol-induced behavioral sensitization (Rueda et al., 2012) and the rewarding effects of this drug (de Carvalho et al., 2010) and cocaine (Solinas et al., 2009. There are, however, conflicting results, with a few, yet intriguing, studies (e.g., Fernandez-Teruel et al., 2002) indicating greater ethanol intake after prolonged EE exposure. In this work, we assessed ethanol intake in adolescent rats, males and females, exposed to maternal separation during infancy (postnatal days 1-21) and environmental enrichment (EE) during adolescence (postnatal days 21-41). Ethanol intake was tested in 12, two-bottle daily sessions, spread across 30 days. We found a significant, two fold increase (i.e., approximately 6.0 vs 3.0 g/kg/24h) in ethanol intake in males – but not in females -- that had been exposed to EE than in control counterparts, an effect that was not modified by maternal separation. In other experiments we assessed several effects of EE that could explain its promoting effect upon ethanol intake. Ethanol-induced sleep time, sedation and aversion were unaffected by EE, which also did not modify anxiety response patterns. EE, nevertheless, resulted in greater novelty seeking and risk taking behaviors, which were evaluated in a modified version of the concentric square field test. These results put a cautionary note to the use of enriched environments as a means to prevent alcohol initiation, at least during adolescence, a developmental stage characterized by high levels of sensation seeking and novelty response. It is possible that exposure to EE further exacerbates this age-typical behaviors, thus increasing the risk for alcohol initiation and escalation. Future studies should take into account this potential side-effect of EE.

Wednesday, 27th - 08:30 - 11:00 SYMPOSIUM V / ROOM A
LOCAL SENIOR RESEARCHERS LECTURES
Chair: Mario Guido, CIBIQIC, FCQ, UNC, Córdoba, Argentina, and Liliana Cancela, IFEC, UCQ, UNC, Córdoba, Argentina

Biological events associated with stress-induced resistance to the fear memory labilization/reconsolidation process

Victor A. Molina
Instituto de Farmacología Experimental (IFEC)-CONICET. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba

It is well known that consolidated fear memories can enter into a labile state after reactivation followed by a restabilization process defined as reconsolidation. Reactivation-induced destabilization renders memories sensitive to pharmacological interference within a limited time window. Our findings revealed that prior stress resulted into a memory trace that was insensitive to pharmacological interference. Moreover, we observed an enhanced expression of both Zif-268 and the subunit GluN2B-two molecular markers of the labilization/reconsolidation process-following reactivation.in the Basolateral Amygdala Complex (BLA) in control animals. However, no elevation was evidenced in stressed animals.D-cycloserine (DCS), a partial agonist of NMDA sites, administered prior to reactivation restored the vulnerability to the drug interfering effect and the elevation of Zif-268 in the BLA of stressed animals.

We also explored the role of the GABAergic signaling within the BLA on stress-induced resistance. The intra-BLA infusion of Midazolam (MDZ) prior to stress prevented such resistance. In addition, the blockade of GABA-A receptors in BLA prevented the drug interfering effect, similar to that observed with stress exposure. Overall, evidence suggests that the GABAergic signaling within BLA, at the moment of memory encoding, is determinant for the induction of fear memory resistance to the onset of the labilization/reconsolidation process.

Generation of neuronal diversity through temporal and spatial patterning in the developing spinal cord

Guillermo Lanuza
Developmental Neurobiology Lab. Leloir Institute, IIBBA-CONICET. Buenos Aires, Argentina

Considerable progress has been made in understanding the mechanisms that control the production of specialized neuronal types. However, how differentiation timing contributes to neuronal diversity in the developing spinal cord is still a pending question. We have found that the CerebroSpinal Fluid-contacting Neurons (CSF-cNs), an enigmatic cell type of the central canal, arise from unique unrecognized late

neurogenic events in the mouse spinal cord. The genetic program that sustains neuronal differentiation at the gliogenic phase of development are unknown. In this work, we identified that the transcription factors Ascl1, Gata3 and Gata2 sequentially control the specification of CSF-cNs. Through expression analysis and mouse genetics, we discover that Ascl1 is restricted to progenitors that give rise to CSF-cNs. By temporally dissecting Ascl1 activity in vivo, we found that this proneural protein confers neurogenic potential to late progenitors by suppressing ependymal fate, and initiates CSF-cN differentiation. Furthermore, we discover that, downstream of Ascl1, the acquisition of the precise CSF-cN identity depends on the postmitotic action of Gata3 and Gata2. In summary, we demonstrate that Ascl1-Gata3/2 are essential components of the temporally restricted transcriptional program that controls spinal cord late-born neuron specification.

From the central nervous system to the circadian timing system: new paradigms on the road?

Estela M. Muñoz

IHEM-UNCuyo-CONICET–Mendoza, Argentina.

Now it is known that every cell possesses the molecular machinery to generate its own circadian oscillations. In multicellular organisms, however, a circadian timing system synchronizes each cell to temporal cues according to its need, which modulates overall physiology and behavior. The circadian system is a multisynaptic circuit that transduces photic information into chemical signals, and the pineal gland is one of its key components. How the whole circadian system is developed, and what allows this system to be plastic and adaptive, along with its precision, are questions that are still not fully answered. It has therefore been of special interest for us to study the cellular, molecular and genetic mechanisms behind the ontogeny and plasticity of circadian clocks. We have been using the highly rhythmic pineal gland from conventional and genetically modified rodents, as a biological model. Furthermore, we have been comparing pineal ontogeny to the development of the central nervous system (CNS). Differential mechanisms that involve common players such as transcription factors, have emerged from these comparative studies. The participation of constantly ‘activated’ microglial cells on pineal ontogeny and homeostasis has also been characterized, as compared with a more complex spectrum of microglia phenotypes in the brain. Recently published data and future avenues will be presented in this talk. It is expected that a better knowledge of normal development of the circadian system will facilitate our understanding of associated pathologies, including developmental disorders and neurodegenerative diseases.

Circadian rewiring of adult networks in Drosophila

M. Fernanda Ceriani

Laboratorio de Genética del Comportamiento. Instituto Leloir. IIB-BA CONICET, Buenos Aires, Argentina

Oscillations between day and night are dominant, at times neglected, evolutionary driving forces. To cope with such challenges, biochemical timers that run with periods similar to the earth's rotation(¨circadian clocks¨) have evolved. The fruit fly Drosophila melanogaster has been instrumental in understanding how these timekeeping systems work at the molecular level, and to demonstrate that multiple layers of interconnected cellular mechanisms are recruited by the clock to ensure its function. Clock neurons in the brain sustain a cell autonomous clock but rely on the communication among each other for entrainment (i.e., a response to a change in the environmental conditions) and phase adjustments. Aside from neuropeptides and classical neurotransmitters that are differentially released throughout the day, circadian remodeling of the neuronal terminals of clock neurons could contribute to the reconfiguration of the circadian network, necessary to adjust to changes in photoperiod. Such circadian structural plasticity would provide a mechanism by which a neuron can exert sequential control of different target circuits along the day.

Wednesday, 27th - 11:30 – 13:30 YOUNG INVESTIGATOR SYMPOSIA I/ ROOM A

Chair: Antonia Marin Burgin, IBioBA-Max Plank Institute, Buenos Aires, Argentina

Changes in NMDAR-GluN2A expression as marker of long term memory consolidation.

María Verónica Baez

Instituto de Biología Celular y Neurociencia (IBCN)-CONICET

Facultad de Medicina – UBA

NMDA receptors (NMDAR) play a critical role in synaptic plasticity, memory encoding and storage. These receptors are heterotetramers composed by two obligatory GluN1 subunits and two regulatory subunits: GluN2 (A-D) or GluN3 (A-B), being GluN2A and GluN2B the major regulatory subunits in central areas related to cognitive functions (see Shipton and Paulsen, 2014). It was already shown that there is an increase of GluN1 and GluN2A 70’ after 5’ exploration leading to habituation to an open field, in rat hippocampus of young adults Wistar rats (Cercato et al, 2017). We hypothesize that this NMDAR subunits increase could be related to memory tracing; hence, we investigated if those changes would take place following other learning paradigms like an object recognition (OR) or an inhibitory avoidance (IA) task. In this work we showed that 70’ after OR training there was a significant increase in hippocampal GluN1 and GluN2A NMDAR subunits levels. As OR task depends on prefrontal cortex (CPF), we investigated if there was a change in NMDAR subunits at this

structure, however we found that GluN1, GluN2A and GluN2B subunits remained similar to controls, 70' after training. Then we decided to investigate if similar changes occurred after IA training. As IA memory is related to amygdala, we decided to analyze also this structure. Western blot analysis showed that there is an increase in GluN1 and GluN2A subunits 70' after IA training in both hippocampal and amygdala protein extracts. Although, these results did not demonstrate that NMDAR subunits changes are associated to memory consolidation. For this reason, we used 4 months hemyzigous McGill-R-Thy1-APP rats (Leon et al, 2010) where IA LTM is impaired. In those animals, we showed that NMDAR subunits remained similar to controls after IA training, at least, at the analyzed times. These results strongly suggest that changes in hippocampal NMDAR subunits could be a mark for LTM consolidation.

Signatures of conscious processing in the resting-state brain activity dynamics.

Jacobo D. Sitt

ICM Research Center, Hôpital Pitié-Salpêtrière, France

At rest, the brain is traversed by spontaneous functional connectivity patterns. Two hypotheses have been proposed for their origins: (1) they reflect a continuous stream of ongoing cognitive processes and/or (2) they are mere random fluctuations shaped by a fixed anatomical connectivity matrix. In this presentation, I'll show that both sources contribute to the shaping of resting-state networks, yet with distinct contributions during conscious and unconscious conditions. I'll present a series of studies that uses fMRI and dynamical functional connectivity to contrast conscious versus conscious conditions in two different experimental models (anesthesia and brain-injury). In both experimental models, unconscious conditions are characterized by a dominant functional connectivity patterns that inherits the structure of anatomical connectivity. These patterns exhibit inferior small-world properties, and they are also characterized by the disappearance of negative correlations between brain-regions. Conversely, also in both studies, wakefulness is characterized by the sequential exploration of a richer repertoire of functional configurations, often dissimilar to anatomical structure, and comprising positive and negative correlations among brain regions. These results reconcile theories of consciousness with observations of long-range correlation in the unconscious conditions and show that rich functional dynamics might constitute a signature of consciousness, with potential clinical implications for the detection of awareness in anaesthesia and brain-lesioned patients.

Prior Stress Promotes The Generalization Of Contextual Fear Memories: Involvement Of The Gabaergic Signaling Within The Basolateral Amygdala

Complex

Christian Luis Bender

Instituto de Farmacología Experimental de Córdoba. IFEC-CONICET-UNC

Fear generalization occurs when a response previously acquired with a threatening stimulus is transferred to a similar one. However, it could be maladaptive when stimuli that do not represent a real threat are appraised as dangerous, which is a hallmark of several anxiety disorders. Stress exposure is a major risk factor for the occurrence of anxiety disorders and it is well established that influences different phases of fear memory, but its impact on the generalization of contextual fear memories has been less studied. Here, we characterized the impact of acute restraint stress prior to contextual fear conditioning on the generalization of this fear memory and the role of the GABAergic signaling within the basolateral amygdala complex (BLA) on the stress modulatory effects. We found that a single stress exposure promoted the generalization of this memory trace to a different context that was well discriminated in unstressed conditioned animals. Moreover, this effect was dependent on the associative properties and on the order of presentation of the testing chambers (i.e., conditioning vs generalization chamber). Furthermore, we observed that increasing GABA-A signaling by intra-BLA midazolam administration prior to the stressful session exposure prevented the generalization of fear memory, whereas intra-BLA administration of the GABA-A antagonist (Bicuculline) prior to fear conditioning induced the generalization of fear memory in unstressed rats. We conclude that stress exposure prior to contextual fear conditioning promotes the generalization of fear memory and that GABAergic transmission within the BLA has a critical role in this phenomenon.

Role of microRNAs in the establishment of cognitive and emotive deficits derived from perinatal protein malnutrition

Bruno G. Berardino

Laboratorio de Neuroepigenética, Departamento de Química Biológica (QB), Facultad de Ciencias Exactas y Naturales (FCEyN), Universidad de Buenos Aires (UBA)

Early life stress -such as maternal malnutrition- during the critical perinatal period modifies cellular differentiation and neurogenesis programs promoting lifetime social and cognitive disturbances. However, the role of microRNAs in the CNS linking malnutrition with behavioral deficiencies has not been described. First, we found that miRNA biogenesis pathway was affected in low-protein maternally malnourished mice (LP) compared to their normal-protein fed counterparts (NP). Additionally, we found an increase in anxiety-like behavior and impaired memory. Both emotional and cognitive phenotypes in LP mice could be reversed by an enriched environment post

weaning. A global high-throughput sequencing analysis of miRNAs in the hypothalamus suggested three miRNAs (miR-187-3p, miR-132-3p and miR-369-3p) that could be part of the molecular basis of the behavioral phenotype. The expression of miR- 132-3p was shown to be negatively correlated with BDNF expression. Axon guidance pathway was enriched among the pathways to be potentially regulated by the target mRNAs predicted to interact with the altered miRNAs. Consistently, perinatal malnutrition and EE affected myelination and oligodendrocyte morphology. Alterations in the emotional and cognitive behavior of LP mice could have molecular bases in the deregulation of miRNAs that affect axonal targeting, potentially through BDNF. On the other hand, the phenotypic reversal may be due, in part, to the increased efficiency of myelination in face of environmental enrichment. These results suggest that miRNAs could play a role in neuroplasticity, allowing adaptive responses to adverse environments.

Wednesday, 27th - 11:30 – 13:30 YOUNG INVESTIGATOR SYMPOSIA II /ROOM B
Chair: Alejandra Pacchioni, FCBF, UNR, Rosario, Argentina

A Local Network Activated by Experience Accelerates the Integration of New Dentate Granule Cells

Damiana P. Giacomini*, Diego D. Alvarez*, Sung M. Yang, Mariela F. Trinchero, Silvio Temprana, Karina Büttner and Alejandro F. Schinder
Laboratorio de Plasticidad Neuronal, Instituto Leloir, Buenos Aires, Argentina

The addition of adult-born dentate granule cells (GCs) in the dentate gyrus is a unique form of network plasticity. GCs develop and integrate into the local networks in a process that lasts several weeks. It has been shown that the level of local networks activity has a positive impact on the maturation speed of adult-born GCs. Here we show that developing GCs in the adult mouse hippocampus display a critical period whereby they are prone to activity modulation long before they acquire cortical excitatory inputs. A brief exposure to an enriched environment (EE) of immature GCs undergoing this critical period for two days, accelerated their functional integration. Furthermore, direct in vivo depolarization of young GCs during the critical period using synthetic DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) was sufficient to also accelerate dendritic growth. In addition, activation of mature GCs by means of the hM3Dq receptor was used to monitor the influence of local circuits on developing GCs. Indeed, in vivo chemogenetic activation of a limited population of mature GCs accelerated the integration of developing GCs. Slice recordings showed that mature GCs recruit GABAergic feedback mediated by parvalbumin interneurons (PV-INs) that depolarizes developing GCs.Accordingly,chemogenetic stimulation of PV-INs accelerated GC integration, while inactivation of PV-INs prevented the effects of EE.In agreement with recent

works we propose that PV-INs are responsible of controlling neuronal maturation. Our results suggest that during EE exposure, mature GCs activate PV-INs, which, in turn, “prime” young GCs promoting their functional recruitment through a disynaptic feedback loop.

The dentate gyrus role on spatial working memory

Verónica del Carmen Piatti

Instituto de Investigaciones Bioquímicas de Buenos Aires (IIBBA) – CONICET

The dentate gyrus (DG) has been shown to be critically involved in spatial discrimination and spatial working memory (sWM). The first role has been shown to be dependent on the integrity of the dorsal DG and the neuronal process of pattern separation but little is known about the mechanisms by which the DG supports sWM. Working memory is the ability to transiently store and process information that is relevant for completing goal-directed actions. We first hypothesized that DG´s role in sWM is a consequence of its ability to separate similar inputs to avoid generalization in this transient memory traces before reaching the goal. If this was the case animals with dorsal DG lesion should be impaired in sWM performance. We addressed this hypothesis with selective colchicine lesions of the dorsal, ventral or the entire DG of different Long-Evans rats that were previously trained in asWM task. Contrary to our hypothesis we found that both regions support sWM in equal manner than controls animals. These results suggest a novel DG’s network computation to contribute to sWM. Therefore, we implanted controls and entire DG-lesioned trained rats with an electrode array and recorded the neuronal activity of the DG and its target area, CA3 region, while the animals performed the same task. We found a distinctive firing pattern in the DG from the one previously described in the dorsal DG. Neurons recorded in the entire dentate granule cell layer fired associated to the reward of the sWM task instead of firing in response to a particular location, named place field, only recorded in the dorsal layer. In addition, we observed that sharp-wave ripples, hallmark of hippocampal mnemonic processing, were increased in CA3 of controls rats but not in CA3 of DG lesioned rats during the reward timing of the task. Therefore the entire DG may be able to generate the transient memory traces in CA3 to reach the goal during working memory performance.

A novel therapeutic target for neurodegeneration and vascular damage in Retinopathies

Pablo F. Barcelona

Department of Clinical Biochemistry, School of Chemical Sciences, National University of Cordoba. Haya de la Torre y Medina Allende, Ciudad Universitaria (5000) Córdoba Argentina

Propose: The p75NTR is a neurotrophin receptor, which promotes neuronal pruning and death. In the healthy adult retina, p75NTR and proNGF are expressed at very low levels, but they are up regulated in many neovascular and neurodegenerative diseases. Here, we studied the mechanism of action of p75NTR and its ligand in the modulation of vascular and neurodegenerative events on Retinopathies. Methods: Drug-like pharmacological antagonists of p75NTR or biological antagonists of proNGF (anti-proNGF mAb), were administered after disease onset of retinopathy animal models. Drug delivery was performed using various rout of administration. At optimized endpoints we quantify retinal structure by FD-OCT, p75NTR signals by measured TNFα, receptor and ligand kinetics expression by IF, in situ hibridization and biochemical analyses. Neuronal survival was analyzed by TUNEL assay and by counting of BRN3 labeled cells in whole retina. Finally, vascular permeability were quantified by Evans Blue extravasation. Results: p75NTR was up-regulated in Muller glial cells, and it was responsible for promoting production of neurotoxic cytokines such as TNFα and α2M which kill RGCs. In vasculature p75NTR also was up-regulated. The kinetics of p75NTR expression correlated with the disease progression. Pharmacological inhibition of p75NTR or proNGF normalized the levels of neurotoxic cytokines, prevented neuronal fiber loss and RGC death and reduced vascular permeability and decreased retinal avascular area and neovascularization. Conclusion: In retinopathies, the p75NTR mechanisms showed a paracrine regulation on glia and vasculature, impacting on health RGC. Using p75NTR or proNGF antagonists, it was possible to ameliorate the neuronal as well as the vascular components. These studies validate p75NTR as a druggable therapeutic target for retinopathies and potentially for other diseases of the nervous system.

Neuronal control of the systemic stress response in C. elegans

Veuthey Tania[1] , Giunti S.[1], Blanco G.[1], Alkema M. [2], De Rosa M.J.[1], Rayes D.[1]
[1]*INIBIBB-CONICET, DBByF-UNS, Argentina.* [2] *UMASS-USA*

Homeostasis is the ability of cells and organisms to maintain an internal equilibrium state. It is known that environmental factors disrupt homeostasis. In response to environmental challenges, multicellular organisms trigger conserved and tightly regulated molecular mechanisms to minimize cellular damages, known as “stress response”. Neural coordination of systemic stress response is key to handle unfavorable conditions. The signals that coordinate sensorial stress perception with the response in non-neural cells are still unknown. We proposed to study neural modulation of stress response in C. elegans under different environmental challenges such as heat, oxidative stress or food deprivation. Our studies reveal that neural tyramine release, the invertebrate counterpart for epinephrine, leads to suppression of cellular response to these aggressions. Intestinal expression of the adrenergic-like

receptor TYRA-3 is essential for this inhibition. By analyzing null mutants of insulin receptor DAF-2, we found that this neural regulation of stress response entirely depends on the highly conserved insulin/insulin-like growth factor signaling. We now aim to elucidate the role of the insulin like-peptides (ILPs) in this stress coordination. Our results show that, similar to worms deficient in tyraminergic signaling, ins-3 and ins-7 null mutants are also resistant to thermal and oxidative stress. Strikingly, we found that both ILPs are expressed in the tyraminergic neuron RIM, and co-express with intestinal TYRA- 3. Moreover, INS-3 is down-regulated upon oxidative and thermal stress. Genetic analysis confirms that both ILPs play a key role in neural control of stress response. Our results suggest that environmental stressors, independently of their nature, leads to a common neuronal signaling to coordinate systemic stress response in C. elegans. As most of the pathways involved are conserved throughout the animal kingdom, our findings can be universally significant.

SAN AWARD

Best Doctoral Thesis in Neuroscience 2017

Wednesday, 27th - 18:00 – 18:30 Best Doctoral Thesis SAN AWARD / ROOM A
Chair: Lorena Rela, IFIBIO, FMED, UBA, Buenos Aires, Argentina

Spatio-temporal map of output connectivity of adult-born dentate granule cells

Silvio G. Temprana
Laboratorio de Plasticidad Neuronal, Instituto Leloir, Buenos Aires, Argentina

The hippocampus is one of the few structures in the mammalian brain where new neurons are added throughout adult life. Adult born neurons integrate into the granule cell layer of the dentate gyrus, providing the circuit with a striking kind of plasticity: the addition of new functional units for information processing. The computational role of these new-born granule cells (nGCs) and their impact on behaviour still remain unknown. Once they are fully mature, nGCs are functionally indistinguishable from granule cells (GCs) born during development, regarding the kind of inputs they receive and how they are activated in response to them. It has been shown that during their maturation they undergo a critical period of enhanced synaptic plasticity and high excitability which may confer the circuit with a temporal window of unique processing capabilities. In order to unveil the circuital relevance of nGCs it is necessary to establish the nature of the postsynaptic networks they recruit. In this work we combine optogenetics, acute slice electrophysiology, and in vivo chemogenetics to activate nGCs at different stages of maturation and study the recruitment of local circuits. We show that young nGCs can efficiently drive distal targets but poorly activate proximal interneurons responsible for feedback inhibition. As nGCs transition towards maturity, they reliably recruit GABAergic feedback loops that restrict spiking of neighbor GCs, a mechanism that would promote sparse coding.

SHORT TALKS BY STUDENTS ABSTRACTS

Analysis of NMDAR subunits expression after GluN2A knockdown in mature primary neuronal cultures

Maria Florencia Acutain, Cecilia Vazquez, Diana Alicia Jerusalinsky, Maria Veronica Baez.

Instituto de Biologia Celular y Neurociencias "Prof. E. De Robertis" (IBCN, CONICET-UBA), Buenos Aires, Argentina.

For several years, NMDA receptors (NMDAR) have been investigated through different approaches because of their role in synaptic plasticity, learning processes and memory. NMDAR are composed by two GluN1 obligatory subunits and two regulatory subunits: GluN2 (A-D) or GluN3 (A-B). In hippocampus and other memory related brain structures GluN2A and GluN2B are the most expressed regulatory subunits, with different expression patterns. While GluN2B is expressed in immature synapses, GluN2A is characteristic of mature and stable synapses. In order to understand the role of GluN2A during memory acquisition and plasticity induction we built two AAV-eGFP vectors: one of them codifying a shRNA anti GluN2A (AAV-sh2A), and the other carrying a shRNA scramble as control (AAV-shSc). In this work we analyzed the specifity of GluN2A knockdown in primary neuronal cultures infected with AAV-sh2A or AAV-shSc. We observed a decrease in GluN2A mRNA by qPCR only in primary cultures infected with AAVsh2A, without changes in GluN1 or GluN2B expression. Interestingly in those cultures, GluN2A decreased expression was accompanied by a significant diminution on GluN1 protein level. On the other hand, GluN2B levels were similar to control cultures infected with the AAV-shSc. These results suggest that GluN2A decrease does not change NMDAR subunit expression at transcription level. However GluN2A decayed levels could activate some postranscriptional regulatory mechanisms that change GluN1 protein levels.

An Integrated Model for Motor Control of Song in Canaries

Rodrigo G. Alonso, Ana Amador, Gabriel B. Mindlin
Departamento de Física, FCEyN, Universidad de Buenos Aires, e IFIBA-CONICET, Argentina

Birdsong is a learned motor behavior that emerges from the interaction between a nervous system with a peripheral vocal device.
The neural substrate that controls song production is known as the song system and consists of an interconnected structure of neural nuclei that is bilaterally organized, with anatomically indistinguishable structures in each hemisphere. These nuclei ultimately project to the periphery, (i.e. expiratory and inspiratory muscles and syringeal muscles) and therefore oversee the generation of complex motor gestures necessary for phonation.
The vocal organ, or syrinx, is a bipartite structure that contains two pairs of phonatory membranes (labia) that can be controlled independently to produce complex sounds. Then, to vocalize, a bird must coordinate these motor gestures that regulates the tension of the labia, the airflow, and the gating patterns.
In this work, we present a computational model that puts together the neuronal substrate with the biomechanics into an integrated model for birdsong production: First, we propose a computational model whose variables are the average activities of different neural nuclei of the song system of oscine birds. As an output of this model, two variables represent the air sac pressure and the tension of the labia during canary song production. Then, we show that these time dependent gestures can drive a biomechanical model of the vocal organ into synthesizing realistic canary like songs.

Enriched Environment Preserves Visual Functions And Reduces Neuroinflammation Of The Optic Nerve

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The therapeutic potential of environmental enrichment during neuroinflammation was scarcely examined. Optic neuritis (ON) is an inflammatory, demyelinating, and neurodegenerative condition of the optic nerve, which might induce blindness. We examined the effect of enriched environment (EE) on visual pathway damage provoked by experimental ON induced by bacterial lipopolysaccharide (LPS) injection into the optic nerve from Wistar rats. After LPS or vehicle injection, animals were housed in EE or remained in standard environment (SE) for 21 days. EE housing prevented the decrease in pupil light reflex (PLR), visual evoked potentials, anterograde transport, phosphorylated neurofilament immunoreactivity, microglial reactivity, astrocytosis, myelination, axon and retinal ganglion cell number induced by LPS injection. EE prevented the increase in oxidative damage, nitric oxide synthase-2, cyclooxygenase-2, interleukin-1β and TNFα mRNA levels induced by experimental ON. In addition, EE housing increased optic nerve brain-derived neurotrophic factor levels. When EE housing started at 4 (but not 7) days post-injection of LPS, a preservation of the PLR was observed at 21 days post-LPS, which was blocked by the daily administration of ANA-12 from day 4 to day 7 post-LPS. Moreover, EE housing from day 4 to day 7 post-LPS significantly preserved the PLR at 21 days post-injection. These data suggest that EE preserved visual functions and reduced neuroinflammation of the optic nerve.

Murine Hippocampal Encephalopathy Derived from Hemolytic Uremic Syndrome (HUS) Produced by Shiga Toxin 2 (STX2) from Enterohemorrhagic *Escherichia coli* (EHEC)

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Stx2 from EHEC causes hemorrhagic colitis, HUS and neurological dysfunctions. In the hippocampus, Stx2 produces cognitive deficits in patients. EHEC not only secretes Stx2, but it also releases LPS. The aim of this study was to determine whether a sublethal dose of Stx2 or Stx2 with LPS altered the hippocampal neurovascular unit. Male NIH mice (n=4) were injected iv with either: control (C); 800ηg of LPS (L); 1ηg of Stx2 (S) or 1ηg of Stx2 with 800ηg of LPS (S+L). Fixed brains were subjected to immunofluorescence with lectins to determine the microvasculature profile, anti-GFAP and anti-NeuN to identify reactive astrocytes and neuronal damage respectively. Primary microglial cultures were incubated with either DMEM or 100ηg of Stx2 following immunofluorescence to identify Stx2 and microglial cells (anti-IBA1). The deepest hippocampal deterioration was observed after 2 days of S+L. S and S+L treatments resulted to increase fragmented immunopositive lectin particles (22 ±0.81 C; 29 ±0.8 L; 33 ±1.22 S; 40 ±1.57 S+L), expression levels of GFAP (0.19 ±0.02 C; 0.36 ±0.04 L; 0.52 ±0.02 S; 0.60 ±0.02 S+L) and decreased the thickness of pyramidal layer (59 ±1.3 C; 48 ±1.44 L; 42 ±1.15 S; 36 ±1.5 S+L) all in comparison to C group, $p<0.05$. Stx2 was found inside of activated microglia. Stx2 damaged the microvasculature, affected the astrocytic state and caused neurodegeneration. Also, LPS and activated microglia trigger an inflammatory reaction that may contribute to the observed damage.

Blockade of D1/D5 dopaminergic receptors in the VTA promotes the persistence of weak appetitive memories

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Ventral tegmental area (VTA) dopaminergic neurons innervate the hippocampus and DA neurotransmission has been shown to modulate synaptic plasticity and memory. Dopaminergic inputs to the dorsal hippocampus are involved in the persistence of cocaine-associated memory 12 h after a single dose of cocaine. In this study we use a conditioned place preference (CPP) paradigm in rats using cocaine as a positive reward to analyze which are the structures involved in the persistence of this memory from the first exposure to the drug. Behavioral experiments were carried out with dopaminergic receptor agonists (SKF 38393) and antagonists (SCH 23390) infusions into the VTA, nucleus accumbens (NAcc) or medial prefrontal cortex (mPFC). We found that the blockade of the D1/D5 dopamine receptors in the VTA promotes the durability of a weak memory when it is infused at 12 h or immediately after conditioning. We also found that the neural activity in the NAcc is necessary for the formation of the memory from the beginning. In addition, mPFC may not be involved in this type of appetitive memory. Lastly, we wanted to test whether the VTA is involved in the maintenance of other types of appetitive memories. To do that we developed a food-CPP protocol in which animals were conditioned with food instead of drug. Same results as with cocaine were obtained showing that the memory persistence of appetitive tasks is due to the activation of neural circuits involving VTA.

The surprising effects of acute downregulation of a GABA receptor in Drosophila sleep behavior

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Sleep is a complex and vital behavior regulated by both, circadian and homeostatic mechanisms. The so called sleep homeostat is responsible for sensing the sleep debt that is accumulated during wake. The neural circuits involved in sleep homeostasis are not well described yet, but it has been suggested that GABAergic inputs to the large lateral ventral neurons (lLNvs) of the adult brain of Drosophila melanogaster may have the role of informing those arousal neurons about the sleep homeostat status.
Starting from this point, our aim was to analyze the mechanisms of GABAergic inhibition on those neurons, their influence on sleep behavior and their role on the sleep homeostat. For this, we quantified sleep behavior by inferring it from locomotor activity. In addition, we studied the circadian neuropeptide PDF (pigment dispersing factor) levels in the axonal projections of the lLNvs in order to evidence the effect over neuronal outputs under those circumstances.
Our findings indicate that downregulation of the GABAA receptor Rdl in the LNvs affects sleep behavior in the way it was previously reported. Moreover, we have now confirmed its previously suggested role on the sleep homeostat. However, we have surprisingly found that sleep can be differentially affected by the downregulation of Rdl in the LNvs when the genetic manipulation is performed in a constitutive or an acute way, opening unexpected possibilities of their mechanism of action.

Tetraspanins as promoters of TrkA receptor tyrosine kinase activation, downstream signaling and biological responses to NGF

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Nerve growth factor (NGF) is a target-derived cue that controls many aspects of sensory neuronal development and plays a key role in pain sensation. The identification of signaling molecules that regulate TrkA activation and mediate NGF-dependent axonal growth and target tissue innervation currently represents a major challenge. Here, we identify an essential role of Tetraspanins (TSPANs) in the control of NGF/TrkA activation. In PC12 cells, TSPANs overexpression accelerated neurite outgrowth and promoted TrkA activation by NGF, while TSPAN knockdown inhibited both TrkA activation and neuronal differentiation in response to this neurotrophin. Furthermore, we show that TSPAN is expressed by developing TrkA-positive dorsal root ganglion (DRG) neurons and that downregulation of TSPAN in these sensory neurons inhibits axonal growth in response to NGF. Additionally, We also provide a mechanism by which TSPNs may be regulating the activity of TrkA. Together, these results provide an insight into TSPAN function and establish a new endogenous mechanism to modulate signaling and biological responses induced by NGF and TrkA in neuronal cells.

Perinatal malnutrition deregulates PRC2 catalytic subunits and Kdm6b expression

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Early life adversities such as perinatal malnutrition can modulate neuronal plasticity through epigenetic mechanisms contributing to neurophysiologic and behavioral alterations. However, factors mediating these effects remain still unknown.
To evaluate these factors we used CF1 dams fed with normal protein (NP, casein 20%) or low protein diet (LP, casein 8%) during pregnancy and lactation, and the offspring were analyzed at P56. Using high-throughput sequencing we evaluated the global gene expression profile in medial prefrontal cortex (mPFC) of NP and LP mice. From the analysis of the RNA-seq, demethylase Kdm6b, methytransferases Ezh1 and Ezh2 (PRC2 subunits) and transcription factor Npas4 turned out to be interesting candidates for this study since methylation/demethylation of H3K27 and Npas4 pathway are involved in neurodevelopment and cognitive abilities. RT-qPCPR analysis showed that these four genes were differentially expressed in primary cultures of mouse embryonic fibroblasts (MEFs). Further, Kdm6b and Ezh1 expression were significantly decreased in the mPFC of LP female mice at P56. Predicted microRNAs that potentially regulate Kdm6b or Ezh1 mRNAs were analysed by stem-loop RT-qPCR. miR-138-5p, miR-20a-5p, miR135a-5p and miR-103-3p were not differentially expressed. These results suggest that perinatal malnutrition could affect epigenetic mechanisms, particularly histone methylation, that mediate the development and the cognitive and social deficits in later life.

The membrane glycoprotein M6a endocytic/recycling pathway involves clathrin-mediated endocytosis and affects neuronal synapses

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SNPs or variations in the expression of the gene encoding the neuronal glycoprotein M6a have been associated with psychiatric disorders such as Alzheimer´s disease, depression and schizophrenia. In cultured neurons, M6a positively contributes to neurite extension, axon guidance, filopodia/spine outgrowth, and synapse formation. The endocytic processes of neuronal membrane proteins are linked to the differentiation, growth, signalling and plasticity of neurons. However, the roles of M6a and the precise mechanisms through which M6a internalizes and recycles back to the neuronal membrane are unknown. Here, by in vitro assay, we showed that if 30-40% of M6a is endocytosed, the number of synapses in hippocampal neurons decreases. When re-establishing the levels of M6a at the cell surface, the number of synapses returned to its normal values. M6a internalization involves clathrin-coated pits, AP2 and the 251YEDI254 motif located within the C-tail of M6a. Upon endocytosis, M6a is sorted to EEA 1- and Rab5-positive endosomes and, then sorted back to the cell surface via Rab11- or to degradation via Rab7 and, finally LAMP-1-positive endosomes. Our results demonstrated that the levels of M6a at the cell surface modified the formation/maintenance of synapses, without altering the protein levels of synaptophysin or NMDA-R1. This novel mechanism might be relevant during neuronal development, pruning and/or many of the mental disorders in which the number of synapses is affected.

Activity regulated cytoskeleton-associated protein is required for consolidation of overlapping object, but not spatial memories in the Perirhinal cortex

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Successful memory involves not only remembering information over time but also keeping memories distinct and less confusable. The ability to separate the components of memories into distinct memory representations relies on pattern separation, a computational process by which differences are amplified. Pattern separation has been investigated in the dentate gyrus of the hippocampus and shown to occur in a spatial domain (DG), but little is known about this process in other brain regions like the perirhinal cortex (Prh) that process a different type of information (ie. non-spatial object memories). In this work, we used a PRH-dependent task and manipulated the load of pattern separation during information encoding. We showed in male rats that consolidation of pattern-separated object memories (and not spatial memories) depends on the expression of the gene Arc is required in the PRH for separable storage of overlapping, but not distinct, object representations, and also the neurotrophin BDNF is required for this pattern separation process, which is identical to its role in the DG., and that interaction between Arc and the neurotrophin BDNF is necessary for successful pattern separation. We provide novel evidence regarding the proteins involved in pattern separation outside the DG and suggest that, despite the anatomical differences, similar mechanisms underlie pattern separation in the DG and Prh that are engaged depending exclusively on the similarity of the stimuli.

Neuromodulators in the processing of afferent inputs in the dentate gyrus

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Neurogenesis in the adulthood continuously provides the dentate gyrus (DG) of the hippocampus with pools of granule cells (GC) which integrate into the preexisting network.

The maturation process of this newborn neurons is well characterized and is similar to the maturation of GC during development. It has been shown that newly born GC are necessary for many types of memory but how these neurons contribute to the hippocampal function is under intense investigation.

As inputs arrive to DG, they activate both excitatory and inhibitory neurons, and the excitation to inhibition (E/I) balance results in a pattern of population activity. Immature 4 week old GC have specific processing features, as they exhibit a higher E/I balance compared to mature GC. Thus, even though this population of neurons represents only 3-6 % of the total GC, their contribution to processing could be important due to their higher activity, their higher spiking rate and their higher plasticity. Neuromodulatory circuits projecting to the DG could modulate E/I balance in GC, providing a new level of plasticity for information processing of afferent stimulation.

Neural crest derivatives in the liver during development and in fibrogenesis

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Introduction: We aimed to analyze the phenotype of neural crest derived cells (NCDCs) in the healthy and fibrotic liver, since this issue remains largely unknown. Methodology: We based our study on genetic lineage tracing analyses of NCDCs by using double transgenic mouse lines (embryonic stages: PLP1creERT2-Rosa26YFP and SOX10creERT2-Rosa26YFP; adult: Wnt1cre-Rosa26Tom and GLASTcreERT2-Rosa26Tom). Fibrosis models: intraperitoneal chronic injection of thioacetamide (TAA; 4 and 8 weeks; 3 doses/week) and bile duct ligation (2 weeks). Results: During embryonic stages, only when tamoxifen (Tx) was applied at E12.5, but not at E15.5, some YFP+ cells were also cytokeratin 18+ and alpha-fetoprotein+ but desmin-. In the adult, some Tomato+ cells showed properties of hepatocyte-like cells (HLCs; in GLASTcreERT2-Rosa26Tom this feature was only seen when Tx was applied at P2 but not at P60). In fibrotic livers, the incidence of glia and Tomato+ HLCs was largely increased. Finally, in adult WNT1cre-Rosa26Tom mice which were treated with TAA for 1 week and then injected with the oligonucleotide IMT504 the incidence of HLCs Tomato+ was further increased. Conclusions: NCDCs would be a source of HLCs (NCD-HLCs) during development. In fibrogenesis, numbers of glia and NCD-HLCs were largely increased, with eventual contribution of progenitor cells from the bone marrow. These two mechanisms would influence the worsening of this pathology and occurrence of regenerative events, respectively.

POSTER ABSTRACTS

P1.-Incredible Mind!

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Neuroscience researchers visited 2 elementary schools in Rosario to raise 3rd and 2nd grade students' consciousness about the important role of the brain in our daily life through games and fun activities. Each grade worked in its classroom coordinated by at least 3 members of the team and their teachers. Incredible Mind! consisted in short interventions using visual aid that were alternated with games and fun activities. For instance, after presenting the neuron´s shapes and parts, the students did one or more puzzles with neuron´s parts on a color cardboard. Then, to explain how neurons communicate they were asked to make neuronal circuits with their puzzles on a big poster. After that, and to talk about brain areas and their functions, they were asked to prepare a "brain hat". To do that they needed to paint, cut and glue the brain lobes. Both brain lobes, left and right, with their divisions were draw in a piece of paper. Then, they were asked to put on the "brain hat" and point out the different brain areas while one of the team members described their functions. Finally, they learned about types of memories, perspective and the five senses through fun games. The whole activity was a big success because 3rd and 2nd grades were really engaged and have lots of fun. At the end, the students, their teachers and the school received small presents to remind them about Brain Awareness Week.

P2.-Brain Week in Luján

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This activity was held at the National University of Luján (UNLu), in the context of the Brain Awareness Week sponsored by the Dana Alliance for Brain Initiatives. The activity was carried out under the supervision of teachers, researchers and students. The aim of the event was to disseminate current topics on neuroscience in order to bring a more comprehensive vision, generate a formative space for undergraduate students involved in the organization and guide the event to the Community in general. The event consisted in a series of talks carried out by researchers from different disciplines working in neuroscience. The topics covered the general physiology of the brain, where and how memory is formed and the importance of neuroscience in the process of constructing pedagogical concepts and how all this information is currently used in high performance sport. The talks were open, interactive and for a general audience. Also, a neuroscience fair was held by undergraduate students from UNLu, in which didactic and educational activities were performed about how the brain and nervous system work. As a future perspective we think about continuing the activity every year, spreading the importance of neurosciences, and trying to renew and update the information to be disclose taking into account the scientific innovations in the area and related topics, so that it can be accessible to a diverse audience and not just to specialists in the area.

*Contributed equally to this work

P3.-ConurBAW: the third time, is the charm?

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The Brain Awareness Week at the National University of Quilmes (UNQ) was carried out on April 5st. It was the third BAW event held on the south of the metropolitan area of Buenos Aires. The core of the event was a "Neuro-Fair" with stands prepared by neuroscience research laboratories and scientific popularization groups, covering topics such as sensorial perception, biological rhythms, development of the nervous system, animal laboratory models, and brain anatomy, among others. The stands allowed participants to chat with presenters and engage in games and interactive experiences. The graphical displays and activities were specifically designed for a high-school level audience, aimed to both inform as well as to promote scientific formation.
Also during the day, special talks were held by the BAW organizing team from La Plata (Buenos Aires, Argentina) on electrophysiology, and by Bruno Bianchi about auditory and visual illusions. In the afternoon popularization lectures were presented by the recognized neuroscientists Juliana Leone, Ramiro Vergara, Mariana Feld, Julia Hermida, Cecilia Calero and Pablo Gonzales.We estimate that the event reached an audience of over 2,000 people, outnumbering the attendance of the 2016 event. We hope we will be able to work towards an even greater and longer lasting event for next year, offering more activities to reach a bigger and more diverse audience.The event was supported by SAN, the UNQ Department of Science and Technology, and SPU.

P4.-Analysis of NMDAR subunits expression after GluN2A knockdown in mature primary neuronal cultures

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For several years, NMDA receptors (NMDAR) have been investigated through different approaches because of their role in synaptic plasticity, learning processes and memory. NMDAR are composed by two GluN1 obligatory subunits and two regulatory subunits: GluN2 (A-D) or GluN3 (A-B). In hippocampus and other memory related brain structures GluN2A and GluN2B are the most expressed regulatory subunits, with different expression patterns. While GluN2B is expressed in immature synapses, GluN2A is characteristic of mature and stable synapses. In order to understand the role of GluN2A during memory acquisition and plasticity induction we built two AAV-eGFP vectors: one of them codifying a shRNA anti GluN2A (AAV-sh2A), and the other carrying a shRNA scramble as control (AAV-shSc). In this work we analyzed the specifity of GluN2A knockdown in primary neuronal cultures infected with AAV-sh2A or AAV-shSc. We observed a decrease in GluN2A mRNA by qPCR only in primary cultures infected with AAVsh2A, without changes in GluN1 or GluN2B expression. Interestingly in those cultures, GluN2A decreased expression was accompanied by a significant diminution on GluN1 protein level. On the other hand, GluN2B levels were similar to control cultures infected with the AAV-shSc. These results suggest that GluN2A decrease does not change NMDAR subunit expression at transcription level. However GluN2A decayed levels could activate some postranscriptional regulatory mechanisms that change GluN1 protein levels.

P5.-Cellular pathway through which Gpm6a functions in filopodium formation is dysregulated in the hippocampus of chronically stressed rats

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Chronic stress exposure modifies expression level of neuronal membrane glycoprotein M6a (Gpm6a) in a variety of animal models. Gpm6a functions in the processes of neuronal remodeling and plasticity. Recently, we have shown that in the formation of neuronal filopodia, Gpm6a acts through the actin regulator Coro1a and Rac1/Pak pathway. Lots of evidence exists for impairment of neuroplasticity after chronic stress exposure but intracellular mechanisms underlying these alterations are poorly understood. Previously, we have shown that in the hippocampus of chronically stressed rats, the exposure to restraint stress, apart from Gpm6a mRNA levels, decreases also Coro1a and Pak1 mRNA levels. To expand our analysis, we have performed qPCR and quantified mRNA levels of Rac1, Cdc42, Pak2, and Pak3. In addition, expression levels of miR-133b, miR-124a, and miR-9-5p, the epigenetic mechanisms described to regulate Gpm6a mRNA levels, have been analyzed. Decreased levels of these miRs in the hippocampus of stressed rats along with decreased levels of analyzed mRNAs suggest their mode of action through the common repressor and not directly through the decay or translational repression of Gpm6a mRNA. Moreover, we show that BDNF upregulates miR-133b, miR-124a, and miR-9-5p in primary hippocampal neurons, in agreement with reported findings that these miRs act downstream of BDNF and that BDNF expression is decreased in the hippocampus of stressed animals.

P6.-Effects of phytoestrogens on the expression of genes involved in serotonin, glutamate and GABA pathways in RNDA cells

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Phytoestrogens are plant-derived xenoestrogens that bind to estrogen receptor-β (ER-β) and are widely known due their potential use as therapeutic agents to overcome menopausal brain complications, which often reduce life quality in women. To elucidate their effect on neurotransmitters pathways we used RNDA cells, a cell line model consisting on serotonergic cells derived from embryonic day-13 rat raphe nuclei stably transduced with the human ER-β gene. RNDA cells were grown in proliferative conditions (37°C) until confluence and were then shifted to differentiation conditions (39°C). Different flasks were treated with the following ER-β ligands: Genistein (10 μM), Daidzein (10 μM), Equol (10 μM) and the soy isolate Novasoy (0.5 μg/ml). Estradiol (10 nM) was used as a positive control. RNA was purified from treated RNDA cells using TRIzol, retrotranscribed to cDNA and expression levels of several genes involved in the serotonergic, glutamatergic and GABAergic pathways cells were evaluated. Our results showed that phytoestrogens and estradiol increase the gene expression of glutamate decarboxylase 1, an enzyme involved in GABA synthesis, and slightly decrease the gene expression of tryptophan hydroxylase, a key enzyme in serotonin synthesis. The expression of genes related to glutamate synthesis and metabolism remained unchanged. These results indicate that phytoestrogens could promote a switch from the serotonin-producing phenotype of RNDA cells towards a GABAergic phenotype.

P7.-α1,2-AP2 EXPRESSION IN THE DEVELOPING BRAIN OF SPONTANEOUSLY HYPERTENSIVE RAT

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Offsprings of spontaneously hypertensive rats (SHR) suffer chronic hypoxia during gestation, they have low body weight at birth and impaired neurological development. Clathrin-mediated endocytosis is a mechanism involved in neuronal signaling, integrity and homeostasis. We aimed to assess changes in the expression of a member of the endocytic pathway, the adaptor protein AP2, in the developing brain of SHR. AP2 subunits (α1 and α2) expression were evaluated by western blot in cerebellum (CB), motor cortex (MC) and hippocampus (HIP) from P5 to P30 in SHR and WKY rat pups. Proteins levels were analyzed in postnuclear (PN), membrane (MB) and cytosol (CYT) subcellular fractions. Our results show that α2-AP2 expression increased gradually from P5 to P30 in PN and MB fractions of CB, MC and HIP in both groups of rats. On the contrary, α1-AP2 did not present significant changes during development. In the CYT of CB and MC, the expression of α1-AP2 increased gradually in both strains and α2-AP2 remained stable; interestingly, in the HIP α2 subunit increased with postnatal age. These results indicate that for both rat strains, the subcellular distribution of α2-AP2 is region specific and the pattern of the protein expression is equivalent in all brain areas studied, throughout postnatal development. We conclude that the delay in the neurological development observed in SHR might not be related to alterations in the neurotransmission mechanism, endocytosis-dependent.

P8.-Expression and function of KCNQ channels in Ciliary Body

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The ciliary epithelium (CE) consists of two layers of secretory cells which are responsible for aqueous humor formation. One strategy in the treatment of glaucoma is to reduce the inflow of aqueous humour, which relays on Cl- movement trough the epithelia. The rate of anion secretion depends on pumps, transporters, Na+ channels and still-unknown K+ channels, which aid the outflow of Cl- by increasing its driving force. KCNQ channels (Kv7) are voltage-gated K+ channels with 5 members in mammals (KCNQ1-5). Among some of their functions they participate in cell volume regulation and epithelial transport. We study the role of KCNQ channels in this process using KO mice for each channel. Whole-eye RT-PCR analysis showed expression of KCNQ3, 4 and 5. Total homogenates of CE exhibited immunoreactive bands for KCNQ4. Using KO controlled immunohistochemistry we found specific labeling for KCNQ4 on the membrane of the pigmented cells (PC) of the CE, while KCNQ3 and 5 were not present. KCNQ4 was confined to the basolateral as well as the apical membrane of PCs, co-localizing with Connexin-43. Preliminary patch-clamp studies of non-pigmented cells lacking KCNQ4 expression, showed no changes in potassium currents. We conclude that KCNQ4 is expressed in the pigmented cells of the CE. This channel could contribute to the Cl- movement from the ciliary body stroma to the aqueous humor, being responsible for the K+ current.

9.-The neddylation pathway regulates cytoskeletal dynamics in early neuronal stages

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Neuronal development is controlled by signaling cascades tightly controlled a myriad of post-translational modifications. The role of ubiquitin has been well stablished but the function of the family of ubiquitin-like proteins remains poorly understood. Nedd8 is the UBL with the highest homology to Ub and we recently demonstrate that is highly abundant in the brain and is critical for synapse formation and maintenance. Blocking Nedd8 conjugation with genetic and pharmacological tools reduced axonal and dendritic growth both in cell culture systems and in utero electroporation approaches. These effects were partially reverted by Cytochalasin D, and low doses of Taxol. These results suggest that cytoskeleton dynamics is involved in the effects of Nedd8 on axodendritic growth.

To identify the structural details underlying the effects of Nedd8 we employed superresolution and fluorescent microscopy. Neddylation blockade with the pharmacological inhibitor MLN4924 strongly reduced microtubular polymerization, induce ectopic lamellipodia formation and increase the growth cone size in early neurons. Finally in biochemical screenings we identified several neddylated targets related to the cytoskeleton structure and function. The potential effects of neddylation on some of these specific targets will be discussed.

10.-Medial ganglionic eminence restricted transcription factor expression and their relevance in cortical interneuron fate

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The human cerebral cortex is composed by two types of neurons: pyramidal projection neurons and interneurons. They use glutamate and GABA as their main neurotransmitter and are excitatory and inhibitory respectively. Parvalbumin and Somatostatin interneurons comprise 70% of the total cortical interneuron population. They are born from a transient embryonic region named medial ganglionic eminence, and have their peak of birth at different stages of development. Specification of both Parvalbumin and Somatostatin subtypes of interneurons is accomplished by the sequential expression of several known transcription factors. However, the molecular requirements for the specification of one type of interneuron from the other are currently unknown. The aim of our work is to identify the molecular pathway imposed by transcription factors or molecules that are involved in this process. Using Cre-lox technology, in situ hybridization, real time PCR, immunofluorescence and birthdating approaches we are in the way to elucidate the relevance of transcription factors with restricted expression in the medial ganglionic eminence in driving interneuron progenitors to a specific fate.

P11.-MURINE HIPPOCAMPAL ENCEPHALOPATHY DERIVED FROM HEMOLYTIC UREMIC SYNDROME (HUS) PRODUCED BY SHIGA TOXIN 2 (STX2) FROM ENTEROHEMORRHAGIC ESCHERICHIA COLI (EHEC)

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Stx2 from EHEC causes hemorrhagic colitis, HUS and neurological dysfunctions. In the hippocampus, Stx2 produces cognitive deficits in patients. EHEC not only secretes Stx2, but it also releases LPS. The aim of this study was to determine whether a sublethal dose of Stx2 or Stx2 with LPS altered the hippocampal neurovascular unit. Male NIH mice (n=4) were injected iv with either: control (C); 800ηg of LPS (L); 1ηg of Stx2 (S) or 1ηg of Stx2 with 800ηg of LPS (S+L). Fixed brains were subjected to immunofluorescence with lectins to determine the microvasculature profile, anti-GFAP and anti-NeuN to identify reactive astrocytes and neuronal damage respectively. Primary microglial cultures were incubated with either DMEM or 100ηg of Stx2 following immunofluorescence to identify Stx2 and microglial cells (anti-IBA1). The deepest hippocampal deterioration was observed after 2 days of S+L. S and S+L treatments resulted to increase fragmented immunopositive lectin particles (22 ±0.81 C; 29 ±0.8 L; 33 ±1.22 S; 40 ±1.57 S+L), expression levels of GFAP (0.19 ±0.02 C; 0.36 ±0.04 L; 0.52 ±0.02 S; 0.60 ±0.02 S+L) and decreased the thickness of pyramidal layer (59 ±1.3 C; 48 ±1.44 L; 42 ±1.15 S; 36 ±1.5 S+L) all in comparison to C group, $p<0.05$. Stx2 was found inside of activated microglia. Stx2 damaged the microvasculature, affected the astrocytic state and caused neurodegeneration. Also, LPS and activated microglia trigger an inflammatory reaction that may contribute to the observed damage.

P12.-GDNF/GFRα1 complex abrogates self-renewing activity of cortical neural precursors inducing their differentiation

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The balance between factors leading to proliferation and differentiation of cortical neural precursors (CNPs) determines the correct cortical development. In this work, we show that GDNF and its receptor GFRα1 are expressed in the neocortex during the period of cortical neurogenesis. We show that GDNF/GFRα1 complex inhibits selfrenewal capacity of mouse cortical neural precursor cells induced by FGF2, promoting neuronal differentiation. While GDNF leads to decreased proliferation of cultured cortical precursor cells, ablation of GFRα1 in glutamatergic cortical precursors enhances its proliferation. We show that GDNF treatment of CNPs promoted morphological differentiation even in the presence of the self-renewal-promoting factor, FGF2. Analysis of GFRα1 deficient mice shows an increase in the number of cycling cells during cortical development and a reduction in dendrite development of cortical GFRα1-expressing neurons. Together, these results indicate that GDNF/GFRα1 signaling plays an essential role in regulating the proliferative condition and the differentiation of cortical progenitors.

P13.-Role of CB1R in hippocampal dendritic arborization

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Endocannabinoid system (eCBs) regulates neurogenic processes (neuronal proliferation, specification and maturation). Cannabinoid receptor Type 1 (CB1R) is expressed in the progenitor cells of the subventricular zone and dentate gyrus (DG) in adult brain. In addition, intermediate progenitor cells are also targeted by eCBs. eCBs is involved in physiological processes such as memory, learning, motor coordination, anxiety and mood. CB1R deficient mice (CB1 - / -) is a genetic model of depression since it deregulates the serotoninergic system, producing mood alterations. The aim of this work was to evaluate the effect of genetic ablation of CB1R in hippocampal neuronal morphology in vitro and in vivo. Neuronal morphology was studied by MAP2 immnostaining in hippocampal area CA1 from CB1 - / - and their respective wild type (CB1 + / +) at postnatal day 0, and in primary cultures of hippocampal neurons of postnatal day 0, after 7 days of culture. In vitro observation shows that CB1-/- present a higher number of primary dendrites than CB1+/+, with a shorter length. In vivo the number of nucleus per area in pyramidal layer is lower in CB1 -/- mice as well as the relative area of dendritic profiles in the corresponding stratum radiatum. This result is in accord with the in vitro result. Conclusion: CB1R is implicated in the development of dendritic arborization of hippocampal neurons.

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P14.-Expression and function of the transcription factor Isl1 in the mammalian hypothalamus

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The hypothalamus is a brain region that regulates several basic homeostatic processes including reproduction, metabolism, energy balance, circadian rhythms, the response to stress and several behaviours. Its high anatomical complexity and location in the ventral forebrain has made it a difficult region to study, but the recent availability of gene expression atlases of the hypothalamus has helped the study of the generation of the different neuronal types in this structure. One transcription factor expressed during hypothalamic development is Islet-1 (Isl1), a member of the LIM-homeodomain family that regulates cell fate specification in multiple tissues. In the hypothalamus, Isl1 has a role in regulating gene expression of some neuronal populations of the arcuate nucleus, but its role in other areas has not been described. With this aim, we are creating a map of Isl1 expression at several timepoints in the developing mouse hypothalamus. In addition, with the purpose of elucidating the function that Isl1 exerts in the generation of hypothalamic neuronal diversity, we are employing a conditional knockout model which allows for the inactivation of the Isl1 gene at specific timepoints during embryonic development. Our research will shed light on the genetics of neuronal differentiation within the mammalian hypothalamus.

P15.-Analysis of cochlear outer hair cell degeneration in a mouse model of DFNA2 deafness

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DFNA2, a slowly progressive deafness, is characterized by sensorineural loss that starts affecting high frequencies and progresses across all frequencies. Mutations in KCNQ4 channel, the voltage-activated K+ channel expressed in outer hair cells (OHCs), are the main responsible factors for deafness, leading to cell death by unknown mechanisms. To analyze the role of KCNQ4 channel we used a mouse model that lacks its expression (KO mouse). Our aim is to determine OHCs degeneration over time analyzing cell death in different cochlear segments. We dissected cochleas from wild type (WT) and KO mice and analyzed by immunofluorescence the presence of OHCs in whole mount preparations. Our results indicated that at 4 weeks-old, the number of OHCs along the whole cochlear length decreased ~24% in KO compared to WT mice. The degenerative process progressed reaching 40% of cell loss at 8 weeks-old. OHCs loss was different depending on the cochlear turns: basal, middle and apical. We determined maximum degeneration of OHCs in the basal turn. In KO mice, at 8 weeks-old the number of OHCs in the basal fragment decreased 40% while it was ~25% in the other two fragments. Additionally, our preliminary analysis suggested that OHC loss was higher in the middle row than in the outer and inner rows. We concluded that cell death progresses at a rate of ~5% cell loss/week, starting at the basal turn, suggesting a higher expression or functionality of KNCQ4 channel in OHCs from the basal fragment.

P16.-ANALYSIS OF THE EXPRESSION PATTERNS OF ZEBRAFISH NICOTINIC ACETYLCHOLINE RECEPTOR SUBUNITS AT THE EFFERENT-LATERAL LINE SYNAPSE

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The alpha9 alpha10 (a9a10) nicotinic acetylcholine receptor mediates transmission at the synapse between efferent fibers and outer hair cells of the cochlea, controlling the activity of auditory afferent fibers. Fishes and amphibians have a superficial mechanosensory system, the lateral line (LL), which detects hydromechanical variations around their body. It comprises clusters of hair cells, called neuromasts, which share structural, functional and molecular similarities with hair cells of the cochlea. As in the cochlea, LL efferent innervation is mediated by acetylcholine and its stimulation leads to inhibition of afferent transmission. However the molecular actors at the LL efferent synapse remain unknown. The Genome Reference GRCz10 describes for Danio rerio (zebrafish) two CHRNA9, located in chromosomes 1 (a9-1) and 14 (a9-14), and two CHRNA10, located in chromosomes 15 (a10-15) and 21 (a10-21). To decipher the molecular identity at the LL efferent synapse we are studying the spatiotemporal expression pattern of alternative zebrafish a9 and a10 RNAs, performing RT-PCR and wholemount in situ hybridization. Our results show that all a9 and a10 subunits are expressed from early developmental stages up to 7 days post fertilization (dpf), and in adult tissues. Moreover, a9-1 and a10-15 expression is localized to neuromasts in 5 dpf embryos. We aim to extend the analysis to a9-14 and a10-21 subunits, performing wholemount in situ hybridization at different developmental stages.

P17.-Biochemical evidence for altered protein levels of plasticity-related genes in inducible TDP-43- **Δ**NLS transgenic mice

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Mislocalization and aggregation of the nuclear protein TDP-43 are hallmark features of the neurodegenerative diseases amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). We have shown in mice that inducible overexpression of a cytoplasmically-localized form of TDP-43 (TDP-43-ΔNLS) in forebrain neurons recapitulates several features of TDP-43 proteinopathies. Here, we focus on plasticity-related genes (PRGs) which are key for normal cognition, a function affected in both human disease and our mouse model. Using gene expression data from microarray studies in TDP-43-ΔNLS brain tissue as a springboard, we identified decreased mRNA levels of Zif268, c-fos and Arc, PRGs critically involved in cognitive function and neural plasticity. These changes were corroborated by immunofluorescence analysis of TDP-43-ΔNLS cortical and hippocampal tissue. Here, we complement this data using immunoblot analysis and investigate in TDP-43 mice the protein levels of BDNF, a neurotrophin with key functions in plasticity. We found that Zif268 protein levels are dramatically decreased in TDP-43-ΔNLS brain, while exposure to a behavioural challenge such as an open field does not elicit proper PRG induction in these mice. Remarkably, BDNF protein levels are increased in TDP-43-ΔNLS brain, suggesting a compensatory mechanism involving this neurotrophin. These results indicate that abnormal PRG protein levels may underlie the behavioural abnormalities in TDP-43 related pathologies.

P18.-Lrig2 promotes the development of hippocampal dendritic arbors and spines

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Dendrite size and morphology are key determinants of the functional properties of neurons, and many neurodevelopmental and psychiatric disorders are due primarily to structural abnormalities of dendrites and their connections. Dendritic development results from the interaction between extracellular signals, intrinsic modulators and electrical activity. Compared with the many identified factors that promote general dendritic growth and branching, little is known about the cell-type specific modulators that allow neurons to sculpt distinctive dendrite patterns. Here, we show that leucine-rich repeats and immunoglobulin-like domains-2 (Lrig2) is expressed in developing hippocampal pyramidal (CA1-CA3) neurons. Sholl analysis reveals that overexpression of lrig2 increases hippocampal dendrite complexity by promoting dendrite growth and branching. Gain and loss of function assays also reveals that Lrig2 affects dendritic spine density and the assembly of the presynaptic machinery to the synapses. Further behavioral and morphological analysis in Lrig2 mutant mice will be required to more fully characterize the effects of Lrig2 in hippocampal development and function.

P19.-Protein acetylation and synaptic composition during Inhibitory Avoidance Long-Term memory consolidation in mouse hippocampus.

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Protein acetylation affects synaptic plasticity and memory, but its effects on synapse composition “in vivo” during long term memory consolidation have not been addressed. Here we show that there is a correlation between the synaptic protein acetylation level and the synaptic protein composition at hippocampus during memory consolidation. We also show that altering the acetylation levels by administration of a Lysine deacetylase inhibitor specific for KDAC6 (mainly cytoplasmic) immediately after training facilitates retention at testing. These results suggest that the post translation modification, lysine acetylation, has a role regulating the synaptic changes that occur during memory consolidation.

P20.-Inmunological and behavioral modulation of Diazepam in a chronic model of Experimental autoimmune encephalomyelitis

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Experimental autoimmune encephalomyelitis (EAE) is an inflammatory demyelinating disease that mimics many of the clinical and pathological features of multiple sclerosis. The aim of the present study was to analyze the effects of diazepam on clinical signs and its neurobehavioral consequences in a monophasic model of the disease in mice. Female mice were immunized with MOG35-55 peptide or adjuvant alone and pertussis toxin. At first symptom, animals were injected with diazepam or saline alone every 48 hs. After recovery of clinical signs, animals went through a behavioral test battery in order to identify motor skills, anxiety, and cognitive deficits. mRNA expression of inflammatory and anti-inflammatory cytokines and BDNF were measured in hippocampus and spinal cord using Real-Time PCR. We found that 2 mg/kg diazepam reversed motor signs of the disease without affecting locomotor activity or anxiety. These results correlated with no differences of inflammatory cytokines at the spinal cord. However, EAE animals showed cognitive deficits in the T-maze test. Diazepam did not improve this symptom but EAE animals treated with this drug displayed a significant attenuation of inflammatory cytokines at hippoccampus. Future experiments are needed in order to understand the mechanisms by cognitive deficits persist in EAE animals.

P21.-Short-term selection for high and low ethanol intake yields differential baseline and ethanol-induced Fos immunoreactivity in the adolescent Wistar rat brain

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Adolescence is associated with the initiation and escalation of ethanol intake and is characterized by increased and reduced sensitivity to ethanol's appetitive and aversive effects, when compared to adulthood. It is unclear if this this differential sensitivity to ethanol's motivational effects has a casual role in the exacerbated ethanol intake pattern exhibited by adolescents. We performed, in Wistar rats, a short-term selective breeding program, as a function of low- or high-ethanol intake during adolescence. This work measured, in adolescent Wistar rats derived from parents that were selected for high (STDRHI) or low (STDRLO) ethanol consumption, baseline (0.0 g/kg) and ethanol-induced (1.25 or 2.5 g/kg ethanol) Fos immunoreactivity (ir) in central, basolateral and medial amygdaloid nucleus (Bla, Cem and Me, respectively); nucleus accumbens core (AcbC) and ventral tegmental area (VTA). Baseline (i.e., after 0.0 g/kg ethanol) neural activity was significantly greater in STDRHI than in STDRLO rats. STDRLO, but not STDRHI, rats exhibit ethanol-induced Fos-ir in Cem, yet the inverse pattern was found in Me. Moreover, STRDHI rats exhibited an ethanol-induced Fos-ir depression in AcbC. These results are consistent with the possibility of STDRHI rats exhibiting and anxiety-prone phenotype as well as an altered pattern of response to ethanol's pharmacological effects.

P22.-Tetraspanins as promoters of TrkA receptor tyrosine kinase activation, downstream signaling and biological responses to NGF

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Nerve growth factor (NGF) is a target-derived cue that controls many aspects of sensory neuronal development and plays a key role in pain sensation. The identification of signaling molecules that regulate TrkA activation and mediate NGF-dependent axonal growth and target tissue innervation currently represents a major challenge. Here, we identify an essential role of Tetraspanins (TSPANs) in the control of NGF/TrkA activation. In PC12 cells, TSPANs overexpression accelerated neurite outgrowth and promoted TrkA activation by NGF, while TSPAN knockdown inhibited both TrkA activation and neuronal differentiation in response to this neurotrophin. Furthermore, we show that TSPAN is expressed by developing TrkA-positive dorsal root ganglion (DRG) neurons and that downregulation of TSPAN in these sensory neurons inhibits axonal growth in response to NGF. Additionally, We also provide a mechanism by which TSPNs may be regulating the activity of TrkA. Together, these results provide an insight into TSPAN function and establish a new endogenous mechanism to modulate signaling and biological responses induced by NGF and TrkA in neuronal cells.

P23.-The membrane glycoprotein M6a endocytic/recycling pathway involves clathrin-mediated endocytosis and affects neuronal synapses

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SNPs or variations in the expression of the gene encoding the neuronal glycoprotein M6a have been associated with psychiatric disorders such as Alzheimer´s disease, depression and schizophrenia. In cultured neurons, M6a positively contributes to neurite extension, axon guidance, filopodia/spine outgrowth, and synapse formation. The endocytic processes of neuronal membrane proteins are linked to the differentiation, growth, signalling and plasticity of neurons. However, the roles of M6a and the precise mechanisms through which M6a internalizes and recycles back to the neuronal membrane are unknown. Here, by in vitro assay, we showed that if 30-40% of M6a is endocytosed, the number of synapses in hippocampal neurons decreases. When re-establishing the levels of M6a at the cell surface, the number of synapses returned to its normal values. M6a internalization involves clathrin-coated pits, AP2 and the 251YEDI254 motif located within the C-tail of M6a. Upon endocytosis, M6a is sorted to EEA 1- and Rab5-positive endosomes and, then sorted back to the cell surface via Rab11- or to degradation via Rab7 and, finally LAMP-1-positive endosomes. Our results demonstrated that the levels of M6a at the cell surface modified the formation/maintenance of synapses, without altering the protein levels of synaptophysin or NMDA-R1. This novel mechanism might be relevant during neuronal development, pruning and/or many of the mental disorders in which the number of synapses is affected.

P24.-Altered gene expression in the hippocampus of young adult female mice by early protein malnutrition

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Early life nutrition plays a key role in central nervous system development. An adequate dietary protein content appears to be critical for the development of neurological functions. To study the impact of perinatal protein restriction, we fed mice with a low protein diet (LP, 8% casein) or a control diet (NP, 20% casein) during pregnancy and lactation. These mice constituted the F0 and were the only ones exposed to the treatment diet, their offspring after weaning (F1) was fed with standard diet. Previous work in this model has shown a detrimental effect on maternal behavior of F0 and F1 LP mice and spatial and working memory deficits in LP offspring. In consequence, we have focused on studying the expression of genes related to memory formation, such as immediate-early genes; and genes relevant for the adaptation to environmental stress, for example the glucocorticoid receptor gene. In this work, we show that in 8-week-old female offspring hippocampus there is a significant decrease in Egr1, Arc, Fos, Nr3c1 and Ppp1r3c mRNA levels, as well as a strong tendency for Bdnf transcript variant 4 and Fosb expression decrease. This set of genes has been shown to be affected in several models where deficits in memory tasks and maternal behavior are observed, suggesting that the altered expression profile that is present in our model might be mediating the behavioral effects observed in previous studies.

P25.-CIRCADIAN CONTROL OF LIPID AND REDOX METABOLISMS IN PROLIFERATIVE GLIOBLASTOMA CANCER CELLS

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Immortalized cell lines contain circadian clocks conducting transcriptional/translational rhythms in gene expression whereas metabolic rhythms can persist without transcription. Circadian rhythm disruption by modern life may cause higher cancer risk; however, little is known about clock functioning in tumor cells. Here we evaluated glycerophospholipid (GPL) and redox metabolisms in cultures of glioblastoma T98G cells under proliferation (P) or partial arrest (A), synchronized with dexamethasone (100 nM) (time 0) and collected at different times. In arrested cultures, mRNAs for clock- (Bmal1, Per1, Rev-erbα) and GPL enzyme genes, and 32P-GPL labeling exhibited circadian rhythmicity; oscillations were also found in the redox state/peroxiredoxin oxidation cycles. In proliferating cells, circadian rhythms of gene expression were lost or their periodicity shortened whereas the metabolic rhythms persist with a similar or longer period to that observed under A. Also, cell viability significantly changed over time after bortezomib (500 nM) treatment. Nevertheless, cell viability and redox state rhythms were altered when Bmal1 expression was knocked down by CRISPR/Cas 9 genomic editing technology. Results support that a metabolic clock operates in proliferative tumor cells regardless the molecular clock; property that may confer tumor susceptibility for a time-dependent chemotherapy.

P26.-Regulation of gene expression by neuronal activity patterns

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Activity-driven transcription is an integral part of the neuronal response to environmental stimulation and it is crucial for different molecular mechanisms underlying synaptic plasticity (LTP/ LTD), learning and memory, behavioral responses and neuronal survival. The way in which gene expression is regulated by neuronal activity patterns has been broadly studied during the last few years and different studies have shown that neuronal activity stimulates the expression of a wide variety of Immediate Early Genes (IEG). Previous approaches studied the induction of IEG by applying different protocols of chemical neuronal deporalization that are quite robust, but highly artificial and far from any physiological condition. In this work, we compared the expression of IEG by using chemical, optogenetics and electrical stimulations on primary neuronal cultures and using brain slices from mice previously injected with AAV-ChR2 virus. Neurons were stimulated with different patterns of activity. Both, experiments performed in slices and in cultured neurons, showed an increase in the expression of particular IEG in response to stimulation at different frequencies or to chemical stimulations. The results indicate that activity patterns can determine the temporal dynamics of activation of IEG.

P27.-Neuronal maturation and synaptic function is affected by glyphosate exposure

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The right functioning of the brain relies on the precise connectivity of neuronal networks. Nowadays there is growing evidence of the high vulnerability of developing nervous system to environmental contaminants. Glyphosate-containing herbicides are the most used agrochemicals around the world, particularly on genetically modified cultures. Our previous studies have demonstrated that glyphosate affects the initial neuronal development in hippocampal neurons. Therefore, in this work, we study the potential effect of the herbicide on the nervous system during maturation through in vivo and in vitro assays. We found that rats exposed to glyphosate during a critical period of synaptogenesis (first three postnatal weeks) showed different signs of neurotoxicity, such as lower body weight, decreased motor activity and memory impairment. To go further, we analyse the effect of glyphosate on synaptic function on 14 DIV-hippocampal cultured neurons. We observed that glyphosate exposure markedly decreased the number of clusters of the pre-synaptic marker, synapsin I. After that, we analyzed whether the herbicide affects the formation and maturation of dendritic spines in 20 DIV pyramidal neurons. Our results evidenced that glyphosate induces a significant decreased in the spines density after 1 week of treatment. In conclusion these findings suggest that subletal doses of glyphosate alter nervous system functionality both in vivo and in vitro impairing synaptic activity.

P28.-Expansion Microscopy Allows for The Detection And Characterization of the Diffraction-limited Actin/Spectrin Membrane-associated Periodic Skeleton of Axons

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Expansion Microscopy was recently developed to decrease the limit of resolution of conventional fluorescence microscopy. Fixed biological specimen are embedded in a polymer network, which is then expanded up to ~4-fold in linear dimension (specimen-gel) and maintains the structure of the specimen and its labeling. In this work, we show the expansion of neuronal cells to identify the Actin/Spectrin membrane-associated periodic axonal cytoskeleton (MPS), previously characterized using super-resolution nanoscopy (STED and STORM). We first show that the adaptation of the technique in cell lines stained for microtubules, obtaining a consistent expansion of 3.5-fold. Hippocampal and sensory neurons in culture were successfully expanded and the MPS was characterized, with a structure indistinguishable from descriptions using superresolution microscopy. This is of interest for future investigations in our laboratory and we show preliminary results assessing MPS structure during axonal degeneration.

P29.-Co-expression of D1R increases GHSR1a constitutive inhibition of CaV2.2 calcium currents

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Voltage-gated calcium channels (Cav) respond to depolarizations of the axon terminal, allowing calcium influx and the following release of neurotransmitters to the synaptic cleft. They are highly regulated points of neurotransmission. G protein coupled receptors (GPCR) signaling pathways are efficient Cav control mechanisms. The ghrelin receptor GHSR (growth hormone secretagogue receptor) is a GPCR that modulates presynaptic Cav (Cav2), constitutively reducing channel density and through agonist-evoked inhibition. Among GPCRs, GHSR has the highest known constitutive activity and the ability to heterodimerize with other GPCRs. It heterodimerizes with dopamine D1 receptor (D1R), another GPCR with agonist-evoked inhibition on Cav2. This interaction modifies their signaling pathways and physiological aspects, as GHSR alters D1R's effects on memory processes. We investigated how GHSR/D1R co-expression modifies Cav2 regulation. Through patch clamp recordings on heterologous expression systems, we found that D1R expression increases Cav2.2 currents, whereas GHSR/D1R co-expression drastically reduces them. Cav2.2 current levels were same as control when D1R co-expressed with GHSR-A204E, a mutant lacking constitutive activity, suggesting current decrease is due to a raise in GHSR's constitutive activity. Co-expression and individual expression of these receptors would have different effects on Cav channels, resulting in a wider range of action of these GPCRs over synapsis regulation.

P30.-Implications of Wnt/Fz signaling pathways on axonal development

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Neuronal morphogenesis is crucial on brain development and requires complex signaling carried out by several molecules, such as Wnts. These ligands bind to receptors of the Frizzled (Fz) family, activating 3 pathways: Wnt/B-catenin, planar cell polarity (PCP) and Calcium. Our research focused on Wnt7b and its participation on neuronal development. Initially, we identified Fz7 as Wnt7b receptor and characterized its temporal and spatial expression in neurons. We found that Fz7 expression increased over time and is located on the cell body, dendrites and spines. According to this, we then evaluate the role of Wnt7b-Fz7 on dendritogenesis and observed that neurons exposed to Wnt7b or those overexpressing Fz7 developed more complex dendritic arbours. That effect was blocked when Fz7 is suppressed. To go further, we examined the intracellular signaling triggered by Wnt7b-Fz7 interaction and found that both CaMKII (Wnt/Ca2+pathway) and JNK (PCP pathway) are involved on its effects over dendritic architecture. Based on these previous results, we decided to evaluate the contribution of Wnt7b-Fz7 during earlier periods, particularly on axonal growth. We analyzed pyramidal neurons at early stages of development and observed that Fz7 is present along neurites and mainly at the growth cones. Furthermore, through Fz7 overexpression in neurons we noted it had an effect on axonal outgrowth. More analyses are yet to be performed in order to fully evaluate Wnt7b-Fz7 role on axon development.

P31.-Early microgliosis in a conditional mouse model of TDP-43 proteinopathies.

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Microglia-driven neuroinflammation can play an important role in the pathophysiology of neurodegenerative disorders. Frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are two neurodegenerative diseases associated to mislocalization and aggregation of TAR DNA-binding protein 43 (TDP-43). We developed transgenic mice conditionally overexpressing human wild-type TDP-43 protein (hTDP-43-WT) in forebrain neurons, a model that recapitulate key features of FTD/ALS. After post-weaning transgene induction during 1 month, these mice display impairment in cognitive and social domains in the absence of motor abnormalities. In order to determine whether there is an inflammatory signature when the early behavioral phenotypes are established, we used immunofluorescence analysis of Iba1 staining to characterize the regional microglial cell activation after short-term (1 month) expression of the transgene. hTDP-43-WT mice showed significantly higher levels of microglial activation in hippocampal CA1 region respect to controls. Somatosensory cortex of hTDP-43-WT mice displayed higher Iba1 staining than controls, while there were no significant differences in motor and prefrontal cortices. In sum, these results expand our understanding of the relationship between early-stage neuroinflammatory processes and behavioral deficits in TDP-43 animal models of FTD/ALS. This in turn will help elucidate the underlying mechanisms of these and other TDP-43 proteinopathies.

P32.-MOLECULAR AND FUNCTIONAL CHARACTERIZATION OF THE NICOTINIC CHOLINERGIC RECEPTOR AT THE EFFERENT SYNAPSE OF ZEBRAFISH LATERAL LINE

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Zebrafish (z) lateral line (LL) is a mechanosensory system that detects water movements and pressure changes. It consists of hair cells innervated by afferent neurons that transmit information to the CNS and by efferent neurons that contact directly to hair cells. LL hair cells share structural, functional and molecular characteristics with those in vertebrate inner ear. Efferent stimulation to the LL and the inner ear leads to similar effects suggesting the existence of similar synaptic mechanisms. It is known that the alpha9 alpha10 (a9 a10) nicotinic receptor (nAChR) mediates efferent transmission in the cochlea, however this information is lacking for zLL. Zebrafish has two a9 genes, located in chromosomes 1 (a9-1) and 14 (a9-14) and two a10 genes in chromosomes 15 (a10-15) and 21 (a10-21). To characterize the nAChRs at the efferent synapse in zLL, we have cloned all za9 and za10 subunits, expressed them in X. laevis oocytes and performed electrophysiological recordings under two-electrode voltage-clamp. Whereas ACh activates za9-1 homomeric nAChRs (EC50=11.71 uM), zα10-15 are only functional when co-expressed with zα9-1 (ACh EC50=437 uM). Moreover, zα9-1 nAChRs are blocked reversibly by strychnine with an IC50 of 0.12 uM. Both za9-1 and za9-1 za10-15 nAChRs exhibit high Ca2+ permeability and large desensitization rates. To study the properties of native nAChR at zLL, we are setting up procedures to perform whole cell patch clamp in zLL hair cells

P33.-Mice presenting a schizophrenia-like phenotype show alterations in maturation of perineuronal nets.

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Although the etiology of schizophrenia is not known, cortical GABAergic interneurons expressing the calcium-binding protein parvalbumin (PVs) have been implicated in its pathophysiology: levels of GAD67 and PV have consistently been found to be decreased in human postmortem brain studies. Furthermore, perineuronal nets (PNNs) have also been shown to be diminished in brain tissue from schizophrenic patients especially in PVs. PNNs – reticular structures of extracellular matrix that surround the soma and proximal dendrites of many neurons in the CNS, including PVs – are reportedly involved in synapse formation and stabilization.

Given that normal wiring of cortical circuits relies on the proper maturation of PVs during the postnatal period, and considering the neurodevelopmental aspect of schizophrenia, we hypothesized that an unsatisfactory formation of PNNs in early adulthood could be related to the onset of the disease. In order to address this, we resorted to an NMDA receptor knockout mouse model of schizophrenia and performed immunofluorescent stainings against PV and PNNs in young and adult mice, focusing in the medial prefrontal cortex. We found no differences in PNNs among asyntomatic pre-adolescent animals, but adult KO mice showed a greater percentage of PVs not enwrapped by PNNs when compared to adult controls. Thus, we conclude that the unsatisfactory maturation of PNNs during adolescence could be pathogenetically relevant for the emergence of the altered state.

P34.-The transcription factor Etv5 in adult neurogenesis

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The subgranular zone (SGZ) of the mammalian hippocampal dentate gyrus (DG) generates new neurons during adulthood. These adult-born neurons become functionally active and contribute to memory formation. The neurotrophin BDNF has been implicated in the regulation of adult hippocampal neurogenesis at different levels.

Based on our previous results indicating that the transcription factors Etv4 and Etv5 mediates the effects of BDNF in hippocampal pyramidal neurons, we analyzed the potential role of these transcription factors in adult-born neuron development. We observed that Etv4 and Etv5 are expressed in the majority of mature neurons from the adult DG. However, Etv5 but not Etv4 are expressed in the immature adult-born granule cells (GCs). Animals deficient in Etv5 (NestinCre:Etv5 f/f) showed an increased in the number of immature adult-born GCs. Moreover, our data indicates that proliferation of these cells is not affected in Etv5 deficient mice. The evidence obtained from our work indicates that Etv5 may play a relevant role in adult-born GC maturation.

P35.-Light-induction of the enzyme Aralkylamine N-acetyltransferase (AANAT) in the chicken inner retina and its potential physiological role

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The neurohormone melatonin is synthesized from serotonin through two steps of which serotonin is converted first to N-acetyl-serotonin (NAS) by the enzyme Aralkylamine N-Acetyltransferase (AANAT). AANAT is present mainly in the pineal gland, retina and other regions while NAS can activate the TrkB receptor to generate neuroprotective effects and neurogenesis. Melatonin synthesis is controlled by light (L) and the circadian clock. In photoreceptor cells, AANAT activity peaks during the dark and at subjective night while activity is significantly decreased by L exposure. By contrast, melatonin synthesis, AANAT expression and activity are high during the subjective day or L phase in chicken retinal ganglion cells (RGCs) (Garbarino et al 2004). Here we investigate the expression of AANAT and of nonvisual opsins in highly enriched RGC cultures obtained from embryos by a discontinuous BSA gradient, and exposure to different L conditions. Cultures expressed melanopsins, Opn3 and Opn5 which may confer intrinsic photosensitivity. In fact, cultures exhibited blue L induction of AANAT immunoreactivity as compared with dark or red L treated cells. In addition, expression of this enzyme was significantly increased by forskolin (10 uM), an adenylate cyclase activator, in the dark. Results suggest that AANAT is a blue L-induced enzyme in RGCs controlled by cAMP. Further studies will investigate the cascade controlling AANAT expression in RGCs and its effects on retinal cells.

P36.-Charged amino acid residues K250, D253, K255, E258 and E259A within the C-terminal cytoplasmic tail of Gpm6a mediate its function in filopodium formation

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Neuronal filopodia underlie many major morphogenetic events ranging from the initiation, extension, guidance and branching of neuronal processes to the formation of synapsis. A conserved cellular function in filopodium formation has been described for a neuronal membrane glycoprotein Gpm6a. It displays structural similarity to tetraspanins with four transmembrane domains, a small extracellular loop (EC1), a short intracellular loop, and a large extracellular loop (EC2), flanked by N- and C-terminal cytoplasmic tails. In our previous study we have showed that Gpm6a lacking C- but not N-terminal cytoplasmic tail fails to induce filopodium formation in hippocampal neurons. Here we used charged-to-alanine scanning mutagenesis to identify functionally critical residues within the C-terminus of Gpm6a. We show that neurons expressing K250A, D253A/K255A or E258A/E259A mutants display decreased filopodium number. Their recognition by a function-blocking monoclonal antibody directed to the EC2 and the accessibility to digestion with the extracellular proteinase K demonstrate surface exposure of these mutant proteins. When D253, K255, E258 and E259 were mutated individually, the effect on filopodium formation was lost suggesting that these residues function in synergy. Subsequent bioinformatic analysis revealed that the residues D253, E258 and E259 form a part of the internalization motifs pointing to the functional significance of the active membrane turnover in filopodial dynamics.

P37.-Brain-derived neurotrophic factor (BDNF) prevents 3-nitropropionic acid-induced death in Huntington's disease neuronal striatal cell model

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Huntington disease (HD) is an autosomal dominant disease caused by mutation of the huntingtin (Htt) gene leading to expanded polyglutamine repeats in mutant Htt (mHtt) that promotes oxidative stress, mitochondrial dysfunction, neurotoxicity, and motor and behavioral changes. Also, impairment in BDNF synthesis is considered determinant in the pathogenesis of HD. We have previously shown that BDNF prevents astrocyte apoptosis induced by 3-nitropropionic acid (3-NP), a toxin that causes mitochondrial dysfunction and oxidative stress as it occurs in HD. Now, we studied BDNF effects on HD neuronal striatal cell model ST14a-Q120 (Q120), which express human mHtt with 120 glutamine repeats and ST14a-Q15 (Q15) which express normal human Htt with 15 glutamine repeats. We detected mHtt aggregates in Q120 cells treated with 3-NP which were undetectable by coincubation with BDNF. Q120 cells were more susceptible to 3-NP-induced cell death than Q15. BDNF had a significant protective effect on 3-NP-induced death of Q120 cells while it was ineffective on Q15 cells. Finally, in agreement with this latest result, we found that ACM from 24h BDNF-treated astrocytes, reduced the decrease in viability induced by 3-NP in Q120 but not in Q15 cells. Altogether data suggest that BDNF protects Q120 cells but not Q15 cells from 3-NP actions, and that astrocytes may contribute to neuroprotection by BDNF. Understanding BDNF protective mechanisms may help find new targets for treating neurodegeneration.

P38.-Regional and temporal assessment of neurodegeneration in inducible TDP-43-WT transgenic mice

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Neurodegenerative diseases such as frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are characterized by neuronal inclusions mainly composed of insoluble Transactive Response DNA-binding Protein 43 (TDP-43). We developed a transgenic mice model with inducible overexpression of human wild-type TDP 43 protein (hTDP-43-WT) in forebrain neurons, which recapitulate several features of TDP-43 proteinopathies. These animals develop time-dependent brain weight loss and dentate gyrus (DG) neurodegeneration. In the present study we analyzed in detail the region-specific neuronal loss, at early (1 month) and late (6 months) time points of transgene (TG) induction. Using immunofluorescence against NeuN (a marker of mature neurons), we measured the total width and NeuN-positive cell count in three cortical regions (motor, somatosensorial and prefrontal) and in two hippocampal structures (CA1 and DG). The results show mild neurodegeneration on prefontal cortex, CA1 and DG with absence of neuronal loss on both motor and somatosensorial cortices after 1 month of TG induction. These results are consistent with the early behavioral phenotype observed in hTDP-43-WT mice, displaying spatial and work memory deficits but normal motor performance. Preliminary results of the late time point in the same structures indicates more extensive neurodegeneration. Ours findings contribute to our understanding of the pathological mechanisms underlying these TDP-43 proteinopathies.

P39.-Removal of Rab11 endosomes affects spines morphology and dendritic arbor development

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The neuronal dendritic arbor development requires a proper spatiotemporal distribution of the elements of the secretory and endocytic pathways, as well as a dynamic and regulated communication between them. Accordingly, our work has focused on characterizing the role of the recycling endosome (RE) during the development of the dendritic arbor in primary embryonic hippocampal neurons. We first determined the endogenous localization of the RE at different times in culture from day 1 to 21. In the first 24 hours the RE shows a juxtanuclear distribution and on the process tips. After 24 hours the RE, changes its localization to a more broad distribution throughout the neurites until the day 14 where it mainly concentrate on the processes tips.
Upon using a shRNA-Rab11 we observed morphological changes of the normal development of dendritic arborization. In addition, we observed a shortening of the main neurite and a concomitant increase in number of dendritic branches. Moreover, suppression of Rab11 resulting a significant change in distribution of two membrane receptors protein (TfR and GluRI). Taken together, our experimental results suggest that the temporal and spatial localization of Rab11 endosomes have a distribution dependent on the stage of neuronal development. This localization could be a possible requirement for the elongation of dendritic processes.

P40.-Lidocaine does not modify GFAP and NF expression in an excitotoxic spinal cord injury model

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Lidocaine has some neuroprotective and anti-neuroinflammatory effects when administered at certain concentrations. After a spinal cord injury (SCI), astrocytes may contribute either to the formation of an inhibitory glial scar or can participate in neural repair. Increased expression of GFAP is one of the hallmarks of their activation while neurofilament (NF) expression is an indicator of neuronal integrity. The goal of the present work was to determine the effect of an intraparenchymal injection of lidocaine on GFAP and NF expression in a rat spinal cord kainic acid (KA) excitotoxic model. Male Sprague-Dawley rats were injected either with 1mM KA (KA1), 0.5% lidocaine (L05), 1 mM KA + 0.5% lidocaine (KA1-L05) or saline (sham) at the C5 segment. Intact rats were used as controls. Rats were euthanized either at 1, 2, 3, 7 or 14 post-injection days and their spinal cord was extracted, segmented and immunohistochemically processed. Besides KA1-L05 protocol has previously shown that neuronal cell counting was not significantly reduced as it occurs with the KA1 group, in this work we showed that lidocaine alone or simultaneously injected with KA significantly avoids the GFAP+ astrocytes increase observed for the KA1 and the sham groups. In addition, KA1-L05 did not reduced NF expression as observed for the KA1 group, along the experiment. These results suggest that lidocaine might be preventing neuronal damage and astrocytes reactivity in the KA-excitotoxic SCI process.

P41.-SUMO-E3 ligase PIAS4 regulates tau stability and promotes its phosphorylation

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Tau is a microtubule-associated protein expressed mainly in neurons which plays a key role in regulating tubulin dynamics, axonal transport and axonal growth. Tau deregulation leads to neurodegenerative diseases known as tauopathies which are characterized by the formation of intracellular deposits of hyperphosphorylated tau. Hsp90 is a major cellular chaperone which assembles large complexes with a variety of co-chaperones like the immunophilin FKBP51. The Hsp90/FKBP51 complex has been described as a potential enhancer of abnormal tau stability, by inhibiting its proteosomal degradation. Our group has recently demonstrated that FKBP51 SUMOylation is necessary in order to form this complex, and that PIAS4 is its specific SUMO E3 ligase. Taking this into consideration we propose to study the role of PIAS4 on tau's function. Our preliminary results suggest that PIAS4 promotes tau and phospho-tau accumulation, increasing tau stability probably by inhibiting it´s degradation by the ubiquitin-proteasome system. PIAS4 effect over tau protein is dependent on PIAS4 E3 ligase activity and FKBP51 SUMOylation.

P42.-α5β1 integrin and Cdc 42 participate in axon growth promoted by urokinase plasminogen activator

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Axon growth requires control of mechanisms that include the activation of kinases, and small GTPases and the subsequent reorganization of the actin cytoskeleton. The complex formed by urokinase plasminogen activator (uPA) and its receptor (uPAR) promotes neural migration and neuritogenesis and is closely related to the phosphorylation of the focal adhesion kinase (FAK). The aim of this work was to investigate the role of α5β1 integrin and the small GTPase Cdc42 in uPA:uPAR mediated-axon growth. For this purpose we employed the chicken optic tectum (OT) at 7 days of development (E7). In order to explore whether α5β1 is necessary for uPA:uPAR-mediated axon growth and signaling, we performed explants cultures and evaluated the axon growth with uPA, echistatin (integrin inhibitor) or with both molecules. The level of FAK phosphorylation was evaluated by Western blot in similar experimental conditions. To evaluate whether Cdc42 activity is necessary for uPA:uPAR-mediated axon growth, we compared the axon growth between control and transfected explants with a plasmid coding for an inactive variant of Cdc42, with or without uPA. The results showed that α5β1 integrin is a necessary participant in the intracellular signaling processes activated by uPA:uPAR complex and Cdc42 GTPase is part of the signaling pathways activated after that uPA binds with its receptor and would be responsible for assembly-disassembly of the actin filaments responsible for axonal growth.

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P43.-The role of the inward rectifier potassium current IKir in the intrinsic pacemaker activity of thalamocortical neurons

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Repetitive burst firing of thalamocortical (TC) neurons has been linked to the expression of the rhythms that characterize slow wave sleep and the pathological spike and wave discharges (SWDs) of absence epilepsy. Oscillatory activity in the thalamocortical system is produced by the interaction between the membrane properties of TC neurons (i.e. intrinsic pacemaker activity that results from the interaction of sub-threshold operating ion conductances), and the synaptic inputs from reticular thalamic nucleus (nRT, recurrent inhibition) and the cerebral cortex (recurrent excitation). By combining electrophysiological techniques and dynamical systems analysis we show that the inward rectifier potassium current IKir promotes repetitive burst firing. The unique biophysical properties of IKir – specifically the existence of a negative slope region of membrane potential in the current/voltage relationship–induce bistability of the membrane potential which, in combination with the hyperpolarization activated cationic current Ih, induces oscillations at physiologically relevant frequencies. The troughs of these IKir-Ih mediated oscillations engage, in turn, the low threshold calcium current IT, resulting in repetitive low threshold spikes and repetitive bursting. We discuss the physiological and pathophysiological implications of this novel mechanism of amplification of the oscillatory activity of TC neurons.

P44.-High plasticity of new granule cells in the aging hippocampus

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The aging brain displays a generalized decline in cognitive capacity and circuit plasticity, including a marked decrease in production of adult-born hippocampal neurons. It is unclear whether development and integration of those new neurons are also affected by age. We have found that adult-born granule cells (GCs) in aging mice are scarce and exhibit slow development, but they display a remarkable potential for structural plasticity. Retrovirally labeled three-week-old GCs in middle-aged mice were small, underdeveloped and disconnected. Voluntary exercise induced substantial dendritic growth and the formation of functional glutamatergic inputs. The effects of aging were also attenuated by knockdown of Lrig1, an endogenous negative modulator of neurotrophin receptor signaling. Moreover the acceleration of neuronal development exerted by running was blocked by overexpression of Lrig1 highlighting neurotrophin signaling as a key player in the mechanism of neuronal plasticity in the aging brain.

P45.-Identification of a subpopulation of proopiomelanocortin neurons with a major role in energy balance and glucose homeostasis

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The hypothalamus is a main regulator of energy balance and glucose homeostasis. In particular, proopiomelanocortin (POMC) neurons in the arcuate nucleus of the hypothalamus sense the energy status of the organism by the integration of peripheral signals. In turn, POMC neurons coordinate energy balance by decreasing food intake and promoting energy expenditure, and facilitate glucose utilization. Some studies demonstrated the existence of two subpopulations of POMC neurons expressing GABA or glutamate. Considering the opposite responses elicited by these neurotransmitters, we hypothesize that both subpopulations have different physiological roles. In order to prove this hypothesis, we first characterized GABAergic-POMC neurons by using obese and diabetic mice bearing a reversible mutation that prevents arcuate POMC expression. Interestingly, specific Pomc re-expression only in GABAergic neurons, significantly decreased body weight and completely restored food intake, metabolic efficiency and glucose intolerance. Surprisingly, these improvements were achieved by rescuing only 25% of total arcuate POMC neurons. Finally, immunohistochemical analysis showed that GABAergic-POMC neurons preferentially project to the dorsolateral hypothalamus (DMH), a nucleus that induces food intake by releasing NPY. Altogether, these results suggest that GABAergic Pomc neurons participate in an arcuate-DMH circuit with a major role in the regulation of energy balance and glucose metabolism.

P46.-Microglia and astrocyte reactivity in a rat spinal cord excitotoxic model

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Different glial responses have been reported in kainic acid (KA)-induced excitotoxic models at the Central Nervous System. Our goal was to evaluate microglia and astrocyte number and morphological changes in an experimental excitotoxic model induced by the intraparenchymal injection of KA in the spinal cord. Male rats were injected either with 1 mM of KA (KA group) or saline (sham group) at the C5 segment and euthanized at days 1, 2, 3 or 7 post-injection (pi). Non-operated rats were used as intact controls. Total number of cells, morphological phenotype (microglia types I-V) and branches length (astrocytes) were evaluated. Immunohistochemistry/fluorescence using anti-IBA-1 and anti-GFAP antibodies were used to identify microglia and astrocytes, respectively. In the KA group, total microglia number significantly increased in comparison to controls along the experiment, and by day 3 pi in comparison to sham group. Types IV and V microglia increased by days 2 and 3 pi while types I and II did it by day 7. Astrocyte number was significantly higher at day 3 pi in sham and KA groups in comparison to controls, and their global branch length was longer in KA group than that of sham rats at days 2 and 3 pi. We found that microglia and astrocytes are morphologically reactive in the spinal cord under the KA-excitotoxicity model. Further molecular studies may define whether the glia is involved in the progression or the resolution of the neurodegenerative process in the present model.

P47.-Circadian modulation of motivational behavior in mice

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The striatal dopaminergic system is particularly important in the regulation of two key behaviors: temporal processing in the seconds-to-minutes range (interval timing) and motivation. In addition, evidence suggests that the dopamine D2 receptor (DRD2) plays a main role in this regulation. We have previously reported that interval timing, as well as striatal dopamine content, is subjected to modulation of the circadian system. In the present work we present evidence of circadian modulation of motivation for food reward in young (4-months old) but not in old-aged (over 1.5 years old) C57BL/6 mice. Motivation was assayed through the progressive ratio (PR) schedule. Young mice under a 12:12 light/dark (LD) cycle exhibited a significant reduction (almost 4-fold) in motivation during the daytime. Indeed, motivation during the nighttime was increased compared to both the daytime and to constant light (LL) conditions. Aged mice, however, did not display any differences in motivation. Moreover, young mice under a normal 12:12 LD cycle exhibited a daily oscillation in the striatal DRD2 content, both at mRNA and protein level, which was coincident with the observed variation in motivation. DRD2 daily oscillation did not persist under LL conditions. Taken together, our results may contribute to improve treatment related to psychiatric disorders or drugs of abuse. This knowledge would also be of great importance when planning behavioral experiments in animal models.

P48.-Photic synchronization of the circadian clock: Role of phosphatase 2A in the NO-cGMP-PKG pathway

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Circadian rhythms are 24-hour oscillations at the physiological and behavioral levels. In mammals, they are generated and synchronized to the light-dark cycle by a master clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus. It has been demonstrated that a light pulse delivered during circadian night activates the ON-cGMP-GC-PKG signaling pathway in the SCN. Little is known about the molecular components downstream PKG activation leading to necessary changes in the activity of circadian core clock genes (i.e: Per1). Previous studies have identified specific PKG activity on G substrate (GS) peptide, which is found in different areas of the brain like cerebellum, retina, and olfactory bulb. It has also been reported that phosphorylated GS inhibits the phosphatase 2A (PP2A) activity, one of the most versatile and important phosphatases of the cell. In this work, we studied the putative role of PP2A in the pathway transmitting photic signals to the SCN. We show that PP2A activity is decreased at SCN homogenates after a light pulse delivered at the circadian night. In behavioral experiments, we found that intracerebroventricular administration of okadaic acid, a specific inhibitor of PP2A, potentiates the light-induced phase shifts of circadian locomotor rhythms, correlating with an increased number of PER1 positive cells in the SCN. These results indicate a possible role of PKG-pGS-PP2A as a positive branch in the photic pathway of the circadian rhythms.

P491.-Photic and thermic synchronization of Caernorhabditis elegans

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Circadian rhythms are driven by endogenous clocks and are synchronized by environmental cues. Although circadian responses of C. elegans have been extensively reported, the mechanism and pathways of synchronization of the nematode are still unknown. Here we present a novel behavioral approach to study entrainment to two of the most studied zeitgeiber: light and temperature, as well as the interaction between them and their possible pathways of actions. We show that the wild-type strain is able to synchronize to both stimuli, with a better performance when assessed under an optimal combination of light and temperature. Significantly lower performances of the mutant strain MT21793 (lite1-gur3 ko) and IK597 (gcy 8, 18 and 23 ko) were found in response to light and temperature, respectively; however, when both zeitgeiber were present and coordinated the mutants were able to entrain. Our results shed light on the C. elegans' response to different zeitgeiber as well as their possible synchronization pathways, the genes involved in this pathway and their relative strength. E are also presenting a mathematical model to approach the population dynamics, with a Kuramoto Model of coupled phases. With this method, we obtained a coupling value for the nematode of each strain and zeitgeiber.

P50.-The surprising effects of acute downregulation of a GABA receptor in Drosophila sleep behavior

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Sleep is a complex and vital behavior regulated by both, circadian and homeostatic mechanisms. The so called sleep homeostat is responsible for sensing the sleep debt that is accumulated during wake. The neural circuits involved in sleep homeostasis are not well described yet, but it has been suggested that GABAergic inputs to the large lateral ventral neurons (lLNvs) of the adult brain of Drosophila melanogaster may have the role of informing those arousal neurons about the sleep homeostat status.
Starting from this point, our aim was to analyze the mechanisms of GABAergic inhibition on those neurons, their influence on sleep behavior and their role on the sleep homeostat. For this, we quantified sleep behavior by inferring it from locomotor activity. In addition, we studied the circadian neuropeptide PDF (pigment dispersing factor) levels in the axonal projections of the lLNvs in order to evidence the effect over neuronal outputs under those circumstances.

Our findings indicate that downregulation of the GABAA receptor Rdl in the LNvs affects sleep behavior in the way it was previously reported. Moreover, we have now confirmed its previously suggested role on the sleep homeostat. However, we have surprisingly found that sleep can be differentially affected by the downregulation of Rdl in the LNvs when the genetic manipulation is performed in a constitutive or an acute way, opening unexpected possibilities of their mechanism of action.

P51.-Cell autonomous and non-autonomous mechanisms underlying axonal terminal remodeling of pacemaker neurons in Drosophila

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A number of years ago we reported that pigment dispersing factor (PDF) neurons, which are essential in the control of rest-activity cycles in Drosophila, undergo circadian remodeling of their axonal projections. We then proposed that such adult-specific remodeling could provide a means of transmitting time-of-day information complementary to differential neurotransmitter release (i.e., PDF). In terms of clock- dependent mechanisms, several neuronal types undergoing circadian remodeling hinted to a differential effect of clock genes; suggesting these genes could be playing additional roles to those ascribed to core clock function. To shed light onto this possibility we altered clock gene levels through RNAi-mediated downregulation and expression of dominant negative forms exclusively in the adult. These experiments confirmed that a cell-autonomous circadian clock is sufficient to drive the remodeling process independently of the clock protein affected. Interestingly, affecting the positive and negative elements of the feedback loop associated to distinctive configurations. Given the extent of the structural changes involved, glia would be expected to play a role to balance changes in neuronal volume and structure. Thus, we explored the contribution of glia to the remodeling of PDF neurons through disruption of their internal clock. Our results reveal the complexity of the mechanisms underlying structural remodeling taking place daily in taking place daily in the adult brain.

P52.-Differential thermoregulatory pattern in the circadian response to LPS-induced septic shock

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Bidirectional interactions between the immune and the circadian systems have been under intensive study under physiological or pathological conditions. Septic shock is a lethal condition caused by a pathogen-induced chain of events. In 1960, Halberg et al, reported a susceptibility rhythm to lipopolysaccharide (LPS) - induced septic shock, which showed that the same dose of LPS which is compatible with survival at the middle of the night (ZT19) can be lethal at the end of the day (ZT11). Also, mice that lack the clock gene Per2 are more resistant to LPS-induced septic shock (Liu, et al. 2006). In this study, we aim to further characterize the circadian response to high doses of LPS in mice. First, we measured skin temperature of animals injected with LPS at both times and we found that there was a higher decrease in mice injected at ZT11 than at ZT19. Moreover, in mice which survived the decrease was smaller. We analyzed neuronal activation by cFos immunoreactivity in the preoptic nucleus (PON) and paraventricular nucleus (PVN) of the hypothalamus, brain regions associated with thermoregulation and neuroendocrine/autonomic control, respectively. We found that both at the medial and the lateral PON, as well as in the PVN, cFos immunoreactivity was significantly higher after LPS administration at ZT11 than at ZT19. Also, we found differences in immune peripheral cellular activation. These results suggest a central thermoregulatory dependency of circadian response to LPS.

P53.-Sleep quality of a sample of the adolescent population in Bariloche, Argentina

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Sleep disorders can be a negative factor both for learning as for the mental and physical development of adolescents. Thus, it is important for Public Health to assess the quality of adolescent sleep. We have conducted a study in the city of Bariloche, aimed at measuring the sleep quality of an adolescent population, as part of the activities of the Semana del Cerebro (March, 2017), the local version of the Brain Awareness Week. We used the Pittsburgh Sleep Quality Index (PSQI), obtained from a questionnaire administered individually to groups of secondary students. Some adults (visitors and teachers) were also given the questionnaire, thus providing a small adult sample. Participants were 523 adolescents (age 15–19) and 204 adults (age 20-69). The results show that sleep quality is consistently worse for women than for men, in all age groups, and is worse for adolescents than for adults. The most important component to explain this is sleep dysfunction (i.e. daytime sleepiness). As there is no significant difference between the number of hours slept, this shows that adolescents should sleep more than adults (on average). In men, there is also a significant difference in sleep latency, which measures how fast the individual gets asleep. The difference between adolescent men and women is mainly due to greater sleep dysfunctions in women. We also found that sleep disturbances ("bad dreams") are more frequently reported by women and have a negative correlation with PSQI.

P54.-A novel treatment for glioblastoma: a chronopharmacological approach of the novel drug 1A and Temozolomide

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Glioblastoma, the primary brain tumor with highest incidence in the adult population, has a 90% mortality rate (five-year), a 14 month average survival time and had no therapeutical improvements in the last 30 years. Research for novel drugs and treatment strategies becomes critical. It was reported that the efficacy of several drugs is modulated by the circadian system leading us to hypothesize that a chronopharmacological approach (i.e., to study the effect of the drug as a function of the circadian time) would improve the efficacy of glioma treatment. We studied the effects of 1A (a Rac1 inhibitor), a novel candidate drug to glioblastoma treatments and Temozolomide (current treatment of choice) when applied at different circadian times to LN229 glioma cells.

Because two of the main roles of Rac1 are related to cell proliferation and migration, we studied the effects of 1A and TMZ over these processes when applied at different circadian times. We found that the effectivity of 1A is rhythmic and depends on the administration time showing a minimum of 15% inhibition of proliferation when applied 28 hs after a serum shock and a maximum of 60% inhibition when applied at 43 hs. A similar result was obtained for TMZ, the current drug of choice. Migration assays were performed at 28 hs and 43 hs with no significant effects at 28hs and over 50% inhibition of migration observed at 43 hs. Our results suggest that effects of this drugs are modulated by the circadian system.

P55.-Preliminary Data On Brain Representation Of Emotional Prosody (EP) In Patients With Mesial Temporal Epilepsy (MTLE) Resistant To Medication: Insights On Plasticity

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Lateralized epileptic seizures let us disentangle functional hemispheric differences. EP, a key social skill, depends mainly on a right temporofrontal circuit, and it is often affected in MTLE. We aim to reveal EP brain representation in right and left MTLE compared to controls (CTRL). 24 CTRL, 8 right-sided MTLE and 4 left-sided MTLE patients did an EP event related fMRI task by classifying utterances with different emotional tones. We acquired 165 volumes with a 2´ RT on a 3T Siemens Trio scanner. We applied random effects analysis with SPM12, computing a BOLD contrast image for each subject. Patient groups were compared to CTRL by t-tests. We compared EP (joy, fear and anger) Vs. baseline (neutral & silence). All groups activated the posterior superior temporal gyrus (STG) bilaterally; and also the bilateral precentral gyrus, right (R) frontal operculum, pallidum and cerebellum, and left (L) hippocampus. Right MTLE patients activated L pars triangularis and precentral gyrus, and R medial cingulate compared to CTRL. Instead, left MTLE patients activated R parahippocampal gyrus compared to CTRL. Our preliminary data replicates previous findings on EP representation in the STG and its associated components (frontal operculum, R pallidum, cerebellum, and hippocampus). Additionally, it suggests EP cerebral reorganization in right MTLE, as they recruited contralateral nodes (L pars triangularis); and in left MTLE, as they recruited right nodes (R parahippocampal gyrus).

P56.-Exploratory activity, habituation and object recognition memory in *Drosophila*

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Spontaneous recognition of novel objects is commonly used to examine exploratory behavior and recognition memory in vertebrates. In this assay, animals are exposed to two identical objects (where objects became familiar for the animal). Next, animals are tested with one of those familiar objects and a novel object. The natural tendency to explore novelty makes evident the memory of the familiar object. This behavioral paradigm does not require the use of unpleasant stimuli (e.g. electric shock) and make use of the natural tendency of animals to explore; seeking for food and other needs essential for survival. However, the neurophysiological mechanisms of these behaviors are largely unknown. Motivation is the driving force that prompts individuals to perform specific behaviors. Motivational states are essential determinants for innate and learned behaviors.
In this study we characterized in fruit flies the behavioral performance for exploratory activity, the subsequent habituation in distinct contexts and motivational states and finally novel object recognition memory. Our investigation showed that fruit flies have some behavioral properties similar to vertebrate, including the initial exploratory activity, the subsequent decay of such activity and habituation memory to the context. We expect that this behavioral assay in fruit flies contribute to determine genetic and neuronal components involved in motivation and its effects on learning and memory.

P57.-A combination of novel and familiar information is required to trigger Novel Object Recognition Memory Reconsolidation

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Memory reconsolidation is a process by which new information can be integrated into a previously consolidated memory. Following reactivation, the memory trace is destabilized and requires a new wave of de novo protein-synthesis to re-stabilize. NF-kappa B is a transcription factor that, when active, is involved in regulating memory-related gene expression. Several studies in different memory tasks show the requirement for a mismatch between the training and the re-exposure sessions in order to trigger the reconsolidation process. However, this had not yet been established in Novel Object Recognition (NOR) hippocampus-dependent reconsolidation. Here, we use sulfasalazine, a specific inhibitor of the NF-kappa B pathway, as a reconsolidation-blockade treatment, to study whether different re-exposure session protocols are effective in triggering memory reconsolidation. Trained animals exposed to a combination of novel and familiar objects underwent memory reconsolidation, while those exposed eiter only to familiar objects or only to novel objects, did not. These results show the requirement for novel as well as familiar information during the re-exposure session in order to trigger NOR memory reconsolidation.

P58.-Subjective Rather Than Absolute Reward Value Determines Long-Term Memory Formation In Honey Bees

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The honey bee is a classical model for studying the neural bases of associative learning. The establishment of a protocol in which bees learn the association between an odor and a reward while they provide access for neural recordings has been critical to elucidate many of the neural pathways involved in olfactory learning. The training protocol is based on the proboscis extension response which at the beginning of training is elicited by touching the antennae with sucrose solution. During conditioning an odor is presented few seconds before the sucrose solution. After few paired trials, the bees extend the proboscis toward the odor anticipating the reward. Several works have shown that increasing sucrose concentration, reward volume, or the number trials, have a positive impact on learning and memory. Here we studied if the effectiveness of reward to elicit memory formation does depend on the absolute value of the reward or if it is affected by its subjective value, which can be manipulated based on the animal's expectations. We found that positive and negative changes in the sucrose concentration of the reward used during the training, do have positive and negative consequences on long-term memory formation. In addition, we found that bees form short and long-term reward expectations that modulate how training induces long - term memory. The results are consistent with previous studies that analyzed the effect that different rewards have in memory in free flying bees.

P59.-Switching strategies to solve spatial navigation tasks requires striatal cholinergic interneurons

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Basal ganglia are classically related to motor function, including command of voluntary movements and motor skill learning. They are also involved in cognitive processes as decision making and balance between goal-directed and habitual behaviors. The striatum is the mayor input nuclei of basal ganglia and is strongly modulated by interneurons, in particular by cholinergic interneurons (SCIN). SCIN encode salient environmental events and contribute to context-dependent action selection. For that reason, SCIN are perceived as crucial elements for flexible switching of behaviors under changing environmental conditions. We have previously shown that SCIN ablation leads to exacerbated spontaneous emission of repetitive behaviors, including social interaction. Here we ask if perseverative behavior induced by SCIN ablation relates to an inability to switch from strategies while solving spatial navigation tasks. We selectively ablate SCIN using a Cre/loxP transgenic system combined with intrastriatal diphtheria toxin administration. Mice were repeatedly exposed to Barnes and cross mazes. We did not find differences in learning curves between groups. In both tests, control mice change their task-resolution strategy across days. However, lesioned mice fail to adapt their solving strategy. This result suggests that SCIN are necessary to switch between solving-problem strategies to optimize cost benefit ratios.

P60.-Dopamine responses to reward and reward-related cues are altered in a mouse that overexpresses dopamine D2 receptors in the striatum

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Dopamine (DA) hypothesis has been the leading pathoetiologic theory of schizophrenia (SZ) for many decades. Striatal DA hyperfunction has been consistently linked to psychosis. However, more recent studies show a generalized DA deficit including cortical areas and extrastriatal regions not previously considered to be hypodopaminergic in SZ such as the ventral striatum, with increase presynaptic DA activity restricted to the associative striatum. DA neurons compute reward prediction errors proposed to serve as the basic process underlying associative learning in classical and instrumental conditioning procedures. Patients show deficits in reinforcement learning including reward anticipation, reversal learning, probabilistic learning and reward representation. Such deficits, part of the cognitive and negative symptoms, do not improve with antipsychotic medication and their severity determines patient´s prognosis. To understand DA dysregulation in SZ, we use fast-scan cyclic votammetry to monitor DA release in the nucleus accumbens of a mouse model for cognitive and negative symptoms of SZ that presents a 15% increase in striatal D2 receptor levels as has been observed in patients with SZ. We hypothesize that striatal D2R overexpression induces changes in DA release that are responsible for the behavioral deficits observed in the mice. We show DA release to be altered and to correlate to altered behavior in order to explain the observed SZ-like phenotype.

P61.-Acute stress facilitates the generalization of contextual fear memory

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The generalization of fear is an adaptive function that allows an organism to respond quickly to new stimuli/contexts that resemble a previously acquired fear experience. However, it may be maladaptive when stimuli/contexts that do not represent a real threat are inappropriately treated as dangerous, as it occurs in patients with anxiety disorders. Exposure to stress is a major risk factor in this type of disorders and it is a modulator of fear learning; however, its impact on the generalization of contextual fear memory has been barely studied. To test the generalization of fear in a context (cxt-B) which is different to the original conditioning context (cxt-A) we used a 2 x 2 design, with stress and conditioning as factors. The restraint stress session (1 hr) was performed one day before the fear conditioning (2 shocks 1mA/3s, after 3 minutes of exploration of the conditioning box). The tests were performed at 24 and 48 h after conditioning in the cxt-B and cxt-A, respectively. The index of fear used was the percentage of freezing time. Conditioned animals that were previously stressed showed an increase of fear behavior in the cxt-B compared to non-stressed animals, which presented similar levels of freezing to those observed in the non-conditioned groups. In conclusion, a stress session prior to the contextual fear learning promoted the generalization of fear memory and it could be prevented by previous exposure to the conditioned context.

P62.-Pattern of ictal intracerebral EEG at the start of alteration of consciousness (AOC)

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Objective= AOC during seizures is one of the most striking features in patients with focal epilepsy and the subjacent mechanisms are incompletely known. Methodology= 9 patients (45 seizures) with drug resistant epilepsy were included. We analysed the patterns and localization of seizure onset and propagation, beginning and degree of AOC. Results= In mesial temporal epilepsy, the seizures with AOC were longer, the most commonly pattern of seizure-onset was sharp activity at ≤ 13Hz and the AOC occurred with the propagation of activity to contralateral hippocampus. In frontal seizures, the AOC occurred when is compromised more adjacent contacts in frontal lateral cortex. Meanwhile in insular seizures the AOC occurred when both part of insula were compromised. The hippocampi were never involved. Most common patterns at AOC were sharp activity high-amplitude at 10Hz, low-voltage fast activity and rhythmic slow waves at 4-5Hz. Conclusion= In our work, the AOC were mostly with of after the propagation of the seizure-onset activity. In mesial temporal seizures, the most of the AOC seizures were with contralateral hippocampus compromised. Meanwhile in frontal and insular seizures the AOC occurred when the area of discharged is enlarged without hippocampus compromised. Future works that apply different techniques for signal analysis are necessary to characterize functional connectivity between spatially distributed regions and pathophysiological mechanisms during AOC.

P63.-Tolerance and sensitization induced by ethanol in preweanling rats: effects of the administration of a sequestering agent of acetaldehyde

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Preweanling rats consistently display a locomotor stimulating effect in response to medium-to-high ethanol doses, and we have recently reported that chronic ethanol exposure during the second postnatal week results in tolerance or sensitization to this effect of the drug. The locomotor stimulating effect of ethanol and sensitization of this effect has not been frequently reported in adult rats. One possible explanation to this ontogenetic difference in the sensitivity to ethanol is the difference in central and peripheral ethanol metabolism observed at each age. Our goal was to explore the effect of the administration of d-penicillamine (dp), a sequestering agent of acetaldehyde, over the stimulating effect of ethanol after acute or chronic exposure to the drug in two-week-old rats. Firstly, we administrated rats (PD 12) with 2.5 g/kg ethanol, 25 min after being treated with saline or dp (50 or 75 mg/kg). Both dp doses reduced the acute stimulating effect of ethanol. Then we evaluated whether dp administration at training reduced tolerance and sensitization. Our results revealed that dp did not block these ethanol effects. These data suggests that acetaldehyde metabolism is involved in the acute locomotor response of ethanol, but not in the development of tolerance and sensitization in infant rats.

P64.-Blockade of D1/D5 dopaminergic receptors in the VTA promotes the persistence of weak appetitive memories

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Ventral tegmental area (VTA) dopaminergic neurons innervate the hippocampus and DA neurotransmission has been shown to modulate synaptic plasticity and memory. Dopaminergic inputs to the dorsal hippocampus are involved in the persistence of cocaine-associated memory 12 h after a single dose of cocaine. In this study we use a conditioned place preference (CPP) paradigm in rats using cocaine as a positive reward to analyze which are the structures involved in the persistence of this memory from the first exposure to the drug. Behavioral experiments were carried out with dopaminergic receptor agonists (SKF 38393) and antagonists (SCH 23390) infusions into the VTA, nucleus accumbens (NAcc) or medial prefrontal cortex (mPFC). We found that the blockade of the D1/D5 dopamine receptors in the VTA promotes the durability of a weak memory when it is infused at 12 h or immediately after conditioning. We also found that the neural activity in the NAcc is necessary for the formation of the memory from the beginning. In addition, mPFC may not be involved in this type of appetitive memory. Lastly, we wanted to test whether the VTA is involved in the maintenance of other types of appetitive memories. To do that we developed a food-CPP protocol in which animals were conditioned with food instead of drug. Same results as with cocaine were obtained showing that the memory persistence of appetitive tasks is due to the activation of neural circuits involving VTA.

P65.-Impact of NMDAR ablation in dorsomedial striatum on behavior

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Goal directed behavior and habit formation depend on corticostriatal circuit operation. It is assumed that alterations in these circuits are related to neuropsychiatric conditions like obsessive compulsive disorder, attention deficit and hyperactivity disorder and Tourette syndrome. In a previous study we found a decrease in prefrontostriatal connectivity in mice with neonatal dopamine (DA) depletion that emerge in parallel with deficits in exploration of novel environments, social behavior and exploitation of nutritional resources and shelter. Here we specifically study whether a decrease in prefrontostriatal connectivity in adult mice could be related to some behavioral features observed in DA depleted mice. Since blockade of NMDA receptor (NMDAR) decreases the response of striatal neurons to cortical inputs, to mimic a prefrontostriatal disconnection we have ablated the NMDAR in dorsomedial striatum by injecting a GAD-Cre virus in loxP-flanked NR1 adult mice. Preliminar results show that NMDAR ablation produces a decrease in exploration in a task dependent manner. This reduction seems not to be due to a general decrease in locomotion because in some settings we did not observed differences. Mice with NMDAR ablation also showed deficits in nesting and marble burying behavior but not in social exploration. In summary, NMDAR ablation in dorsomedial striatum produced deficits in exploration but does not fully reproduce the behavioral phenotype of DA depleted mice.

P66.-Influence of the fear memory labilization/reconsolidation process on the hippocampal structural plasticity.

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Under certain conditions, the reactivation of a consolidated fear memory induces a labile state followed by a stabilization process (reconsolidation). During destabilization, the memory trace is vulnerable to interfering agents such as propranolol (PROP). We evaluated whether the reactivation of a fear memory impact on the dendritic spines remodeling in CA1 dorsal Hipocampus (DH) associated with contextual fear memory. Stressed and control animals were fear conditioned and 24hs post conditioning or post retrieval, were sacrificed. Additionally, animals were Basolateral Amygdala complex (BLA) cannulated and PROP administered after fear reactivation. One day later the animals were sacrificed. Independently from the reactivation session, conditioned animals -but not stressed- exhibited a higher number of dendritic spines in comparison to non-conditioned animals. Prior stress exposure prevented such increase; even the behavioral freezing response was similar. Likewise, the intra-BLA PROP administration prevented the increase in the number of dendritic spines in comparison to SAL administration.
Fear conditioning induced structural remodeling in DH is not affected by memory reactivation. However, stress-induced resistance to memory reconsolidation or the blockade of this process prevented the structural plasticity suggesting that destabilization/reconsolidation following reactivation is a critical step to induce spines remodeling after reactivation in fear conditioned animals.

P67.-Insight into the amphibian brain: the amphibian medial pallium as a model of an ancestral hippocampus?

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We are interested in the evolution of neural mechanisms that rule spatial learning. Our group is looking for learning patterns potentially present in a common ancestor to several vertebrates using as model the terrestrial toad, Rhinella arenarum. It is known that mammalian hippocampus is a critical brain structure involved in spatial learning and amphibians have a homologous area to this hippocampal formation, the medial pallium. The analysis of how involved this structure is in spatial orientation tasks will help us to infer potential ancestral spatial abilities and its neural basis. We conducted medial pallium lesion studies with toads daily trained in a plus maze for the acquisition of two basic spatial orientation strategies: a visual cue guided response and a turn response to reach a goal. In addition, spatial learning and memory related morphological changes in the argyrophilic nucleolar organizer region (AgNOR) of medial pallium neurons were quantitatively evaluated by means of AgNOR neurohistochemical stain in other set of experiments. Altogether, our results suggest that medial pallium is involved in basic spatial orientation strategies in amphibians, supporting thus the idea that hippocampus and medial pallium are partially functional equivalents. Furthermore, these results telling us that this ability is evolutionary conserved.

P68.-Differential role of retrosplenial cortex in object recognition memory

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Several studies had demonstrated that the retrosplenial cortex (RSC) is strongly implicated on navigation and contextual memory. Furthermore, lesions in animal models show that RSC shares functional similarities with the hippocampus (Hp), suggesting that RSC has a supporting role to the hippocampal function. In this study we contrasted the role of RSC and Hp on recognition memory, particularly on the "what" and "where" components of this memory, using three variants of the object recognition task: two of them focused on objects themselves (the non-spatial Y-shaped maze object recognition, Y-OR, and the spontaneous object recognition, SOR, which includes spatial cues) and the third focused on the position of the objects in the context (object location, OL). Our behavioral and molecular results demonstrate functional differences between RSC and Hp on recognition memory. When we tested the "what" component of memory (Y-OR and SOR) the inactivation of RSC, but not Hp, impaired memory formation and expression. Moreover, there was an increase in RSC, but not hippocampal, c-Fos level one hour after the animals were exposed to Y-OR sample phase. In contrast, the inactivation of both structures decreased memory index on OL task, indicating the requirement of RSC and Hp for the "where" component of recognition memory. Our current findings suggest a novel role of the RSC in recognition memory, processing not only the "where", but also the "what" component of this memory.

P69.-A massive experiment on choice blindness in political decisions

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We implemented a Choice Blindness Paradigm containing political statements in Argentina, Brazil and the USA to reveal the existence of categorical ranges of introspective reports, identified by confidence and agreement levels, separating easy from very hard to manipulate decisions. CBP was implemented in both live and web-based forms. Importantly, and contrary to what was observed in Sweden, we did not observe changes in voting intentions. Also, confidence levels in the manipulated replies where significantly lower than in non-manipulated cases even in undetected manipulations. We name this phenomenon unconscious detection of self-deception. Results in argentina have also shown that females are more difficult to manipulate than men. This difference was not significant in our Brazilian sample. Additionally, participants closer to the conservative axis were easier to decieve compared to their progressive counterparts. This result was consisten through all three countries.

P70.-Contribution of ERK/MAPK activation to the formation of a two trial long term memory in the crab Neohelice granulata

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Long term memory (LTM) model of the crab Neohelice granulata has been extensively studied from different points of view (e.g. behavioural, pharmacological, molecular and electophysiological). For context-specific LTM to be successfully expressed in a 24h-postraining testing session, the training protocol typically used consists of 15 trials with a 3-min intertrial interval. We study a long-term memory induced by two-trial training with an intertrial interval of 45 min. This type of training represents an attractive model for studying individual trials and intertrial interval contribution to the activation of putative molecular pathways involved in memory formation during training. It has been proposed that in two-trial training protocols the first trial induces a specific molecular context mediated by the activation of the ERK/MAPK pathway, which enables the formation of a long term memory only after a 45 min intertrial interval training. Here, we present preliminary results regarding context-specificity of this type of memory as well as synaptic ERK/MAPK pathway's activation dynamics and dependence.

P71.-Understanding memory loss: Development of a retrieval-induced forgetting paradigm in rodents

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In the last two decades there´s been a growing human literature on a phenomenon called retrieval-induced forgetting (RIF). RIF has pointed to inhibitory control processes that resolve retrieval competition as a cause of adaptive forgetting. Using spontaneous recognition memory in rats, we have developed a rodent paradigm for RIF. We were able to show that forgetting of an item associated with a particular context happens under conditions that cause competition between memory traces for two items that share a particular retrieval cue. Under these conditions, forgetting is long lasting and independent of the selected retrieval cue. We used local pharmacological inactivation to show that this kind of forgetting requires the activity of the medial prefrontal cortex (mPFC). With pharmacological inactivation, we showed that the Ventral Tegmental Area (VTA) is necessary for the forgetting to occur and that the infusion of a D1/5 agonist in the mPFC is sufficient to rescue the expression of the RIF phenomenon impelled by the inactivation of the VTA. These results are consistent with the idea that the RIF occurs via a top-down inhibitory control mechanism exerted by the mPFC on structures linked by hypothesized memory traces. With the latter results, we bring new evidence supporting the role of dopamine in the resolution of interference via mPFC inhibitory control.

P72.-The spectral signatures of serotonergic and dissociative psychedelics in the human brain

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Recent findings in psychedelic research have highlighted the need for a deeper understanding of how these drugs affect brain activity. Several psychedelic drugs have proven to be useful for the study of consciousness (Schartner et al, 2017), and for a wide range of psychiatric therapies (Vollenweider and Kometer, 2010). Yet, their applications are hard to exploit since the neural mechanisms behind their actions are still on debate. It has well been established that subjective psychedelic-like effects can be produced by two kinds of substances with partially overlapping molecular actions: serotonergic psychedelics (SP) and dissociative drugs in sub-anesthetic doses (DP). No study has quantitatively compared their effects on brain activity. The present work analyzed magnetoencephalography recordings after the administration of two SP (LSD and psilocybin) and one DP (ketamine). For quantifying the similarities and divergences, machine learning algorithms were implemented. Classifiers were trained using power spectrum and connectivity values obtained for one drug, and tested on another drug dataset. It was found that, in some spectral bands, the generalization capacity of the classifiers extended only to SP. However, in other frequency bands, DP can be used to efficiently decode the effects of SP, and vice versa. Results might then support the hypothesis that the similarities and differences in the molecular underpinning of both drugs are also expressed at a system's level.

P73.-Single Neuron Recordings In The Human Medial Temporal Lobe

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Surgical treatment is indicated for some patients with pharmacologically intractable epilepsy. In these cases, depth electrodes were implanted to localize the epileptic focus to be surgically removed. This offers an exceptional opportunity to record directly the single neuron (SN) activity in the human brain while patients perform different types of cognitive tasks. The aim of this work is to assess the response of SN in the medial temporal lobe to visual stimuli. The electrical activity of multiple SN and local field potentials (LFP) from the hippocampus and amygdala of 5 patients (males, 19-49 y/o) during the presentation of pictures through a laptop monitor (persons, landmarks, objects and animals) was recorded. Then, 3 different pics, text and audio were presented corresponding to the concept whose picture triggers a response in previous session. The recorded activity from depth electrodes were processed using "spike sorting" algorithms. The activity of dozens SNs were identify, many of which selectively responded to specific concepts. It were recorded 33 SNs (22 hippocampus and 11 amygdala) that responded in an invariant way to 44 concepts (famous characters, landmarks, animals, family and medical members). The implantation of depth electrodes in epileptic patients allows us to observe SN responses to different concepts in brain areas related with memory, which provides unique information on the neural mechanisms involved in the formation and coding of memories.

P74.-Early Cognitive Impairment associated with a parkinsonian animal model: synaptic plasticity and initial approaches with IGF-1 gene therapy

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Parkinson´s disease (PD) is a neurodegenerative disorder with a progressive dopaminergic (DA) neuronal loss and a variety of non-motor symptoms such as cognitive dysfunctions Growth factors as IGF-1 could be neuroprotective in PD models by improve changes in neuronal activity. 1) To determine the early cognitive decline and the correlation of hippocampal changes in 6OHDA model 2) to carry out therapeutic approaches with IGF-1 to understand plasticity processes associated with cognitive decline. Male Wistar rats were CPu bilaterally injected with 6OHDA or vehicle (SHAM). Independent groups were tested after 7, 14, 20 and 28 days for Y-maze and locomotor activity. Another set of rats were divided into 6 groups according the adenoviral therapy in hippocampus: SHAM, 6OHDA, SHAM-RAd-DS-Red, SHAM-RAd-IGF-1, 6OHDA-RAd-DS-Red and 6OHDA-RAd-IGF-1. At 20 days post lesion, were tested for behavioral tasks. Then rats were perfused, the brains fixed and IHQ performed for TH and IGF-1R and hippocampal synaptic plasticity. At 20 post-lesion, memory deficits, changes in dendritic spines were observed in 6OHDA rats compared to SHAM rats. This behavioral cognitive decline was partially modified with IGF-1 overexpression in 6OHDA-RAd-IGF-1 rats. 6-OHDA was sufficient to cause memory impairments. Knowledge of this neurodegenerative progression could result in potential therapeutic strategies as IGF-1 gene therapy which motivates us to further studies under this experimental model

P75.-Memory updating in crabs: adding opposite information during reconsolidation

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Reconsolidation theory postulates that, once reactivated, a stable memory becomes labile and goes through a process of stabilization, enabling memories to be modified or updated depending on new information acquired during retrieval and allowing animals to adapt their behavior to a changing world. Although memory updating has been studied in diverse species and several memory paradigms, it is not yet clear what would happen if during reconsolidation animals receive information that contradicts the prediction generated by a previous experience. A recent work performed in rats, has shown that contextual fear memory is weakened if animals receive a positive stimulus during retrieval in a previously learned aversive context. In this study we trained crabs in either aversive or appetitive paradigms and, once memories were consolidated, animals were re-exposed to the training context and received a training session with opposite valence to the previous one. We demonstrated that, despite the strength of protocol, the original memory is not occluded by the new one and the memory associated with the new stimulus can be revealed, together with the original trace. Considering previous results showing that two parallel memories are built when crabs receive two training paradigms with opposite valence at the same time, we wonder if under these conditions animals are forming two memories or, on the contrary, new information is added to the original trace.

P76.-STRESS EFFECTS ON STUDENTS LONG TERM MEMORY

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Long-term memory (LTM) formation requires protein synthesis. We have demonstrated in rodents that a weak learning task (spatial object recognition-SOR) which only induces short-term memory (STM) can be stabilized into LTM if an event of acute stress is experienced 1 hour after. It was postulated that stress provides the necessary proteins, which could be captured at tagged sites induced by the weak learning task, process referred as behavioral tagging. However it was observed that if stress occurs 1 hour before learning is not able to promote a LTM and results suggest an effect of stress on the tag. Surprisingly, when the rats are exposed to a stress 1 hour after strong SOR the promoting effect does not occur and we postulated that could be due to competition for resources necessary for memory consolidation. In the present work we want to assess if an acute stress could induce similar effects in humans. We made activities using a modification of the Rey-Osterrieth's complex figure task to test graphic memory in students and analyze the effects of exams on the promotion of LTM and its temporal course. The behavioral results are similar to those found in rodents: when students have a programmed exam before learning they do not show LTM promotion, while students who have an exam 60 min after learning show positive or negative effects on figure retention depending of the learning strength.

P77.-Effect of stevia sweeteners consumption on the expression of **Δ**-FosB in nucleus accumbens and striatum in adolescent rats

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Stevia sweeteners (steviosides) are natural non-caloric sweeteners 100–300 times sweeter than sucrose which are obtained from the leaves of Stevia rebaudiana Bertoni (family Asteraceae) and contain a complex mixture of sweet diterpene glycosides. Little is known about the effect that NNS could cause on the reward system and their potential addictive properties. On the other hand, sugar has been demonstrated to activate the mesolimbic reward pathway the same way drugs as nicotine, alcohol, and other recreational drugs do, for instance, increasing the expression of the transcription factor Δ-FosB, a transcription factor member of the Fos family, which plays a role in the addiction process. Thus, the aim of this study is to evaluate the effect of stevia sweeteners on relevant areas of the mesolimbic reward system. Adolescent rats had continuous access to 0.2% stevia extract solution for 20 days (from postnatal day 30-50) using a two-bottle free choice test, at the end of the treatment were sacrifice and serial coronal sections (40 µm) of the nucleus accumbens and striatum (from bregma +2.16) were obtain and immunohistochemistry to Δ-FosB was performed. Images were obtained using a digital camera. Quantification of the Δ-FosB positive nuclei was performed. Results compared with a control group with only access to water show not just preference for stevia extract solution but also an increment in chow consumption, besides a tendency in overexpression of Δ-FosB in nucleus accumben

P78.-Words, hands or looks? Understanding teaching strategies in children with cochlear implants

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Some aspects of human communication rely on an implicit communication protocol. Previous studies (Csibra & Gergely, 2009) demonstrated that learning in children changes when demonstrations are accompanied by ostensive behavior. Ostensive cues (OC), which are signaled by a broad set of non-verbal behavior, act as prosodic markers providing emphasis to relevant items of the discourse. At the lab, Calero et al observed that preschool children can not only detect, recognize and react to OC, but furthermore, they are capable of generating them when teaching. Also, there are other non-verbal behaviors that are not ostensive but nonetheless have clear pedagogical importance. The clearest examples are gestures. Children spontaneously produce gestures early in life and it has been shown that encouraging them to use gestures brings out implicit knowledge and leads to learning. However, we wonder whether non-verbal language will have the same impact on all populations. Previous studies have shown that deaf children use their gaze more and develop more gestures as iconic symbols to communicate, even without being exposed to sign language. With that in mind, we performed an study in collaboration with Oral Model Institution, a school of children with cochlear implants. We are trying to understand if they are able to receive and emit the same OC in pedagogical events described in children with expected development, or, as an alternative, they develop other strategies with the same goal.

P79.-Analysis of the complexity of electrophysiological recordings acquired during three different meditation traditions

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A wealth of experimental studies suggests that different meditation practices can modify global brain activity parameters such as connectivity and the power of spectral oscillations (Cahn and Polich, 2006). These studies, in combination with the phenomenomenological experience of meditation, suggest that meditation is capable of inducing a distinct brain state that can be characterized by idiosincratic modes of information processing. Recently, Carhart-Harris and colleagues (Carhart-Harris et al., 2014) proposed that global brain states can be characterized as a continuum parametrized by the level of entropy/complexity of brain activity. For instance, it has been shown that states of reduced awareness correlate with reduced levels of complexity (Schartner et al., 2015), whereas serotonergic psychodelics increase complexity (Schartner et al., 2017).
In this work, we attempt to place the brain states induced by three different meditation traditions (Vipassana, Himalayan Yoga and Isha Shoony) in the aforementioned continuum of brain states. By analyzing high-density EEG data acquired from 67 expert meditators and 32 controls, we explored a wide array of complexity metrics including temporal correlations, information integration, algorithmic complexity and sampling entropy. Our results indicate that meditation can increase the complexity of brain activity, resulting in a “scrambling” effect that could underlie some of its reported physical and psychological health benefits.

P80.-Electrophysiological correlates of encoding faces in different emotional contexts

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It has been well established that emotion enhances memory; however, it is still unclear if experiencing a non-emotional event in positive or negative emotional contexts affected recognition. The aim of the present study was to investigate the effects of encoding faces with neutral expressions under different emotional contexts (positive, negative or non-emotional) on the subsequent memory effect (SME). Event related potentials, heart rate (HR) and skin conductance response (SCR) were also examined. Twenty-eight adults participated in a betting-game task in which they could win (positive context) or lose (negative context) money. The participants also completed a non-betting task (non-emotional context). Afterward, the participants completed an old/new recognition task for the faces. The recognition was superior for the faces encoded under positive emotional contexts than for those encoded in the non-emotional ones. The SCR amplitude was equivalent for both of the emotional contexts and greater than for the non-emotional contexts. Electrophysiological findings showed that the N170 and P300 components at occipital sites and the frontal slow wave manifested SME that were modulated by positive contexts; neither negative nor non-emotional contexts influenced these effects. The behavioral and neurophysiological data demonstrated that positive contexts are stronger predictors of episodic memory than negative or non-emotional contexts.

P81.-Role of dorso-medial telencephalic adult-born neurons on Active Avoidance learning in a teleost fish model

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Teleosts exhibit adult neurogenesis throughout their brain, making them an excellent model to study the way in which network remodeling by adult neurogenesis shapes brain function. Cognitive ability was assessed by Active Avoidance (AA) paradigm in adult rainbow trout (Oncorhynchus mykiss). Learning performance correlated with neuronal activity in dorso-medial (Dm) telencephalic region. To investigate the relationship between Dm neuronal addition and cognitive performance we attempted to behaviorally modulate adult neurogenesis. For this purpose, adult trouts were injected intraperitoneally with bromodeoxyuridine (BrdU), and then housed either in an Enriched Environment (EE) or in Social Restriction (SR) for 4 weeks. In order to avoid treatment-related stress on learning tasks, individuals from both groups were transferred to a common barren tank for 2 more weeks, until sacrifice. On week 6, AA learning, short and long-term memory performance were assessed (STM & LTM: 1h and 24h post-training, respectively). Fish reared in EE showed a better learning, STM and LTM performance, in terms of latency and % of avoidance, in contrast to SR fish. Proliferation, cell survival and neuronal activity analysis are currently being assessed.

P82.-Actin cytoskeleton: the backbone of memory trace?

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Long-term memory has been associated with morphological changes in the brain, in strict correlation with changes in synaptic efficacy. Such plasticity is proposed to rely on dendritic spines as a sort of neuronal canvas on which these changes can take place. Given its key role on spine morphology, actin cytoskeleton dynamics and its major regulating factors (such as ADF/Cofilin) become an attractive target to study processes underlying dendritic plasticity.

Using a contextual fear conditioning paradigm in mice, we found that pharmacological induction of depolymerization of actin filaments through an intra-hippocampal injection of BMS-5 –a potent inhibitor of LIM kinase, which is in turn an inhibitor of ADF/Cofilin activity– causes an impairment in memory consolidation and reconsolidation. On the other hand, when favoring stabilization of actin filaments by intra-hippocampal injection of Jasplakinolide immediately before a short reminder session that usually elicits memory reconsolidation, the formation of an extinction memory was facilitated. On top of that, we found an increase in P-Cofilin/Cofilin ratio in synaptoneurosome-enriched hippocampal extracts obtained after a reconsolidation eliciting reminder, implying a diminished depolymerization activity by this factor, therefore favoring stabilization of actin filaments when this phase of memory is taking place. Our results support the importance of actin cytoskeleton dynamics underlying the memory trace.

P83.-Effect of emotional states upon risky decisión making in youngs Argentines: preliminary results

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The main goal of this study was the evaluation of the effect of positive, negative and neutral emotional states upon risky decision making in young Argentines. 91 undergraduate students (18-27 years old) were assessed (M(Age)=21,92; SD±2,09). For emotional induction film clips were used and to assess emotional experience, Self Assessment Manikin (SAM) and Visual Analogue Scale (VAS) were reported before, during and after induction. To evaluate risky decision making, Balloon Analogue Risk Task (BART) was administered. Repeated measures ANOVA showed an interaction effect of time and type of induction on VAS scores [F(4, 90)=2.89; p.05; ŋ2p =.14]. Post hoc analysis indicated that participants under a positive emotion won more points in BART than participants under neutral or negative emotion. Scores in BART are considered as a measure of risk because indicate larger pumpings in every balloon. This result is coherent with several studies that indicated that youngs under positive events and with a positive urgency trait shows more risky behaviors.

P84.-Activity regulated cytoskeleton-associated protein is required for consolidation of overlapping object, but not spatial memories in the Perirhinal cortex

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Successful memory involves not only remembering information over time but also keeping memories distinct and less confusable. The ability to separate the components of memories into distinct memory representations relies on pattern separation, a computational process by which differences are amplified. Pattern separation has been investigated in the dentate gyrus of the hippocampus and shown to occur in a spatial domain (DG), but little is known about this process in other brain regions like the perirhinal cortex (Prh) that process a different type of information (ie. non-spatial object memories). In this work, we used a PRH-dependent task and manipulated the load of pattern separation during information encoding. We showed in male rats that consolidation of pattern-separated object memories (and not spatial memories) depends on the expression of the gene Arc is required in the PRH for separable storage of overlapping, but not distinct, object representations, and also the neurotrophin BDNF is required for this pattern separation process, which is identical to its role in the DG., and that interaction between Arc and the neurotrophin BDNF is necessary for successful pattern separation. We provide novel evidence regarding the proteins involved in pattern separation outside the DG and suggest that, despite the anatomical differences, similar mechanisms underlie pattern separation in the DG and Prh that are engaged depending exclusively on the similarity of the stimuli.

P85.-Novelty improves LTM after reconsolidation through a behavioral tagging process.

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Last year we introduced that memory reconsolidation occurs through a behavioral tagging process. We demonstrated this showing that reconsolidation blockade, induced by the infusion of the protein synthesis inhibitor emetine (EME) after retrieval, in either the spatial object recognition (SOR) and the inhibitory avoidance (IA) tasks, can be rescued by previous exploration to a novel open field (OF) that provides the proteins required for the process to occur. Here we stepped forward by studying how does the novel experience, in the context of memory reactivation, affects LTM performance after reconsolidation. We observed that SOR reconsolidation established a different memory with the new position of the object during the reactivation session. Also, EME infusion after memory reactivation blocked the reconsolidation inducing amnesia for the original and the new memory. Interestingly, the exploration of a novel OF 1h before memory reactivation rescued the LTM for both the original and the new position of the object. Besides, the same exploration performed before a reactivation session in normal conditions (without EME) improved the LTM after the reconsolidation. Moreover, this effect depended on protein synthesis induced by the novel experience. Similar effects were observed in the IA task. As whole, our results show that experiences close to memory reactivation can improve LTM performance, by taking advantage of the behavioral tagging process underlying the reconsolidation.

P86.-5-HT2a receptor in mPFC controls context-guided reconsolidation of long- term object memory in perirhinal cortex

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The object recognition memory retrieval is a complex process that required the interaction of multiples structures. It has been proposed that mPFC interacts with the hippocampus (HIP) during contextual-guided versions of the spontaneous object recognition paradigm. Using a pharmacological disconnection experiment, we have shown that mPFC 5-HT2aR modulation and HIP interacts in an ipsilateral way during the resolution of an object-in-context recognition memory task. Since the information regarding the identity of the object could be stored in other structures such as the perirhinal cortex (PRH) then, the mPFC-HIP interaction could control the reactivation/reconsolidation in the PRH. To test this idea, we infused a 5-Ht2aR antagonist (MDL) in mPFC before the reactivation phase and immediately after a protein synthesis inhibitor (EME) in the PRH or dorsal dHIP. We also evaluate the interaction between the ventral hippocampus (vHIP) and the mPFC using a disconnection approach. We infused MDL in mPFC and muscimol in the vHIP before the retrieval and EME in the PRH after the reactivation session. We found that blocking 5-HT2aR signaling in the mPFC affects the reconsolidation in the PRH but not in the dHIP. In the disconnection experiment, only contralateral infusions made memories for both objects susceptible to the action of EME. Our results suggest that the interaction between mPFC 5-HT2a modulation and HIP activity controls the reconsolidation of object memory traces in PRH.

P87.-Sleep Accelerates Memory Re-Stabilization

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Consolidated memories can be reactivated by the presentation of a memory-cue (reminder) returning to a labile state followed by a process of re-stabilization known as reconsolidation. Thus, if amnesic agents are presented inside the reconsolidation time window (when the memory is still labile) the memory is impaired. However, if they are presented outside (~6 hours after reminder presentation), it has no effect on re-stabilization. Sleep is known to support the consolidation of newly encoded memories and it is also suggested that sleep has a beneficial effect on reconsolidation. Here we ask whether sleep accelerates re-stabilization of consolidated memories protecting reactivated memories from interferences. Participants learned a list of non-sense syllable pairs on Day 1. On Day 2, they received a reminder and they were allowed to sleep a 90 min diurnal-nap or they stayed awake for the same period of time or for 10 hours. After that, they received an interference task (new list of syllables). We found that the memory performance was impaired only when the interference task was given 90 min after the reminder (inside the time window of reconsolidation). There was no impairment when it was given after 90 min sleep or 10 hours after the reminder presentation (outside the reconsolidation time window). This finding suggests that a short-nap after reactivation during wakefulness accelerates memory re-stabilization.

P88.-mTOR controls hippocampal long-term inhibitory avoidance memory retrieval

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Understanding how stored memories emerge is a central question in the study of memory that is just beginning to be addressed. Although controversy concerning molecular events required for memory retrieval, protein synthesis has been recently investigated during this memory stage. Mammalian target of rapamycin (mTOR), a central regulator of protein synthesis in neurons, has been implicated in synaptic plasticity and memory. Using inhibitory avoidance (IA), a fear-motivated and hippocampus-dependent task, we evaluate the role of mTOR in memory retrieval. Infusion of a selective mTOR inhibitor,rapamycin, into the dorsal hippocampus 15min but not 3h before a test session carried out 24h post training impaired memory expression in a reversible way. We observed the same result using emetine, a general protein synthesis inhibitor. Then, we analyze if the effect depends on the age of the memory studied. mTOR inhibition 15min before test at 7 or 14 days, but not at 2h impaired memory retrieval. As previously seen in our laboratory with pretest hippocampal inactivation induced by muscimol, infusion of rapamycin 15min before test at 28 days did not cause temporal amnesia. Rapamycin infused in retrosplenial cortex, another structure required for IA memory retrieval, also impaired memory retention. Our results support the idea that ongoing protein synthesis mediated by mTOR pathway is necessary for long but not for short term memory retrieval when memory still depends on the hippocampus.

P89.-Becoming Anxious: How Threat Conditioning Affects Negative Valenced, Positive Valenced And Cognitive Systems

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Classical conditioning is the process by which the representation of two stimulus become associated and then, one of them (CS) is capable of predicting the occurrence of the other (US).Neurobiological basis of anxiety disorders were studied in laboratory settings using threat conditioning (TC). Although, little is known about how the formation of a fear memory affects other cognitive and behavioral systems associated with these type of mental disorders. Anxiety manifest as a persistent and generalized defensive system, activated when predicted aversive events are perceived as a threat and uncertain. Here we aim to study how an aversive implicit memory (TC) in humans could affect other valenced and cognitive systems such as those mentioned. To reach such goal, we used different anxiety inventories (BAI and STAI) to discard potential symptoms, electrodermal activity as our implicit memory measure, after that conditioning groups were evaluated on negative valence, positive valence systems and cognitive systems using several different tasks. In Experiment 1 we compared trained and untrained groups which underwent TC followed by the valenced and cognitive tasks in the same day. In Experiment 2, we used the same design evaluating the different cognitive systems 48 hs later. We revealed that the formation of a fear memory affects some cognitive and behavioral systems which are involved in the etiology and maintenance of anxiety disorders.

P90.-Stiatal role in the exploration/explotation balance

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Little is known about the subjacent mechanisms regulating the balance between exploitation and exploration. It is presumed that the striatum is implicated in the action selection process by integrating information coming from different cortices like prefrontal, orbitofrontal and anterior cingulated cortex. Our aim is to analyze striatal neural activity during a virtual foraging task where animals must decide between exploiting a depleting water patch and search for another, richer one. The task consists of a virtual linear track with short rewarded areas followed by longer unrewarded corridors. Two visually distinct rewarded areas are associated with different reward probabilities. Mice are implanted with tetrodes in the dorsal striatum and a metal plaque used to restrain the animal's head. Mice run on a cylinder and their movement is detected and translated into its position in the virtual corridor. Water deprived mice virtually navigate the track until the rewarded zone is reached, where the animal needs to lick a port a certain number of times to obtain a drop of water. Currently, we trained 7 mice to run on a virtual corridor and to stop in the rewarded areas and lick for a drop of water. We recorded striatal single units and local field potential as well as the position of the mice and relevant events during the task. Our results also reveal that mice are able to learn the task in hand by running towards the rewarded area and licking the port to obtain the reward.

P91.-Pattern Separation in humans in a virtual reality environment

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The mechanism by which the ability to separate the components of memories into distinct complex memory representations that are unique and less easily confused is called ‘‘pattern separation”. The objective of this work is to study this mechanism in humans in a virtual reality environment, which allows us to develop a task similar to that studied in rodents in our laboratory. The task consists of collecting separate flags from different angles and then recognize the middle flag. Preliminary results show that in sedentary people there is an angle at which it is not possible to differentiate the memories of the location of the flags (since they are too similar) whereas for another angle this does not happen. In this way, the results of the experiments in humans will benefit from those that occur in parallel in rodents and vice versa. It is a translational proposal that can undoubtedly have an impact on the knowledge of the biological bases of human cognition, mental health and cognitive improvement policies.

P92.-Modulatory effect of novelty on episodic memory and creativity tasks

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Recent studies in neuroimaging show that imagination, creativity, and episodic memory share neural networks. Motivated by this and based on previous results from our laboratory, we decided to study the effect of novelty in memory and imagination. For this we used a declarative memory task (Rey-Osterrieth complex figure), a convergent thinking task (Remote Association Test), a divergent thinking task (Uses Alternative Test) and an imagination of scenes task. The latter is evaluated across different age ranges from 6 to 90 years. Preliminary results show an enhancing effect of novelty on both retrieval of declarative memory and on divergent thinking. On the other hand, in the convergent thinking task, a positive effect was only observed in the more difficult items, but not in the easier ones. In the task of imagination of scenes, children (5-6 years) and elderly people (70-90 years) obtained similar scores, smaller than those found in adolescents (13-14 years) and young adults (20-30 years). Interestingly, novelty increased the number of reported entities by children to values that matched the ones observed in the rest of the groups. In conclusion, novelty enhanced retrieval of a declarative memory, divergent thinking and also convergent thinking, but only for the more difficult items. Surprisingly, novelty was able to increase imagination of scenes in children. These results could point at new strategies to improve memory and imagination in humans.

P93.-Contextual learning and the development of memory systems in the infant rat

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It's common to think about development as a period of immaturity. It doesn't mean that infants are immature but as a society, we consider that there's only one stage of maturity (the adulthood). We can find this social conception of development into neurocognitive theories. In cognitive neuroscience it's common to assume different memory systems and to describe their development through the study of contextual learning and the functional development of the hippocampus. For instance, the absence of recovery-from-extinction effects in preweanling rats has been related to the immaturity of the hippocampus, which in turn is linked to a simple memory system. This relationship has been confirmed in an experiment designed to show up that the administration of MK-801 (that blocks extinction learning in adult rats) does not affect extinction in infant rats (Langton, et al 2007). In the present study, we analyzed the relationship between MK-801 and extinction learning in infant rats, from an ecological model. Given that immaturity isn't a valid explanation in this model, our experimental designs were different to the one used by Langton et al., and they allowed us observing that MK-801 doesn't block extinction learning, but it produces conditioned motor responses interfering with the behavioral index of memory. These results are analyzed in the framework of the discussion between the ecological and the neuromaturational model of development and in terms of the construction of meanings.

P94.-Influence of The Words of Action in the Consolidation Processes in Different Memory Tests

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Consolidation is a process whereby a certain episode is labile during a limited time window after coding, which over time becomes an increasingly resistant memory to interference (McGaugh, 2000). In contrast to consolidation, it is believed that the reactivation returns the memory to a new labile state which will allow that episode to be susceptible to change. These memories are retained in memory through a process similar to the initial consolidation of the episode, that is, they are reconsolidated (Nader & Hardt, 2009; Stickgold & Walker, 2005). Research indicates that in order for this new memory footprint to be reconsolidated, time is needed; Therefore, studies on the process of reconsolidation in episodic memory carry an experimental design that is developed over three days. On the first day coding takes place. The second day, the memory is reactivated and manipulated. Finally, the third day a memory test is performed. The purpose of the present study was to investigate the impact of motor activity on the consolidation / reconsolidation process of movement related information and to see its effects on a free recall test and on another recognition test.

P95.-The influence of stress on fear memory extinction is not associated with dendritic spines remodeling in the ventral hippocampus.

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Fear extinction results in the suppression of the fear response once the conditioned stimulus does not predict the threatening event anymore. Different anxiety disorders have typical deficits in both extinction memory formation and expression. Ventral Hippocampus (VH) is critically involved in the processing of the aversive information as well as in the expression fear extinction memory. The aim of the present work was to evaluate whether the structural plasticity of CA1 VH accompanied the characteristic extinction memory formation and the influence of stress on the extinction memory. Stressed animals were fear conditioned to context and later trained in an extinction paradigm (repeated context re-exposures without foot-shock). Animals were sacrificed for preparation 1 day after conditioning (before extinction) or 1 day after extinction. Prior stress exposure induced a deficit in the formation of the extinction fear memory. With respect to structural plasticity, and on the contrary to the higher density of dendritic spines observed in CA1 Dorsal Hippocampus after fear conditioning, returning to basal levels after extinction training, CA1 VH presented no changes in the number or the morphology of dendritic spines, regardless of the fear conditioning, extinction training or stress condition. Thus, changes in the dynamic of the extinction fear memory might not be supported by synaptic structural remodeling in VH.

P96.-Cognitive Enhancer effects of chronic administration of fluoxetine are mediated by 5-HT2aR in mice

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In recent years, a body of studies have shown that some serotoninergic drugs have a role as cognitive enhancers. It has been proposed that, like in the case of LSD, this effect could be mediated by the serotonin type 2a receptor (5-HT2aR),. However, little is known about the possible cognitive enhancer effect of other serotoninergic drugs used in medical practice. Fluoxetine (FLX) is a selective serotonin reuptake inhibitor, well known for its antidepressant effects and for being widely prescribed in the treatment of different psychiatric disorders. We intended to analyze if chronic administration of FLX presented cognitive enhancer effects and the role of 5-HT2aR in this effect. For this purpose, we administrated a chronic oral dose of fluoxetine (10mg/kg) to Wild Type (WT) and 5-HT2aR knockout. mice (KO). After 4 weeks of FLX administration, we performed a novel object recognition task. The results showed that a 3 min training session is not enough to generate a long term NOR memory (24 h delayed) independently of the genotype. Interestingly, FLX treatment allowed WT mice to solve the NOR test. However, we didn't see this effect in KO mice. This result suggests that fluoxetine might have a role as a memory enhancer and that requires 5HT2A signaling.

P97.-Evaluation of Dopaminergic System Activity In Rats Treated With Cannabinoids and Consume of Artificial Sweeteners

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Nonnutritive sweeteners are sweet substances that no offer energy input to consumers. Sucralose is a nonnutritive artificial sweetener, sweetening food products and beverage. It is known that sweet foods have been implicated in the activation of mesolimbic reward pathway due to strong hedonic components, in fact many researchers have found sucrose has the same impact in dopaminergic system as some drugs of abuse like cocaine, this activation can be detected trough the accumulation of ΔFosB. To sense sweetness is necessary the activation of the heterodimer taste receptor T1R2-T1R3, in last years has been discovered that cannabinoids enhance the preference to sweet. Having this as a reference we hypothesize, that animals treated chronically with cannabinoids alter sucralose intake and modify their dopaminergic system. Whereby our aim is evaluate the sucralose consume of Wistar male rats treated chronically with cannabinoids and assess activity in dopaminergic areas like prefrontal cortex, amygdala and accumbens nucleus trough immunodetection of ΔFosB. Animals are being treated for 20 days with an intraperitoneal injection of anandamide (1mg/kg bw), vehicle injection (DMSO 95% and tween 5%), or without injection, sucralose consume or only water consume. Daily consume of food, water, sucralose solution (0.02%) and weight are measure in each group. The preliminary results suggest that an activation of dopaminergic system exists for the differential expression of DFosB.

P98.-Acute Ethanol Exposure Induces Anxiety Like-Behaviors In Infant Rats: Omega 3 As A Protective Factor

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Introduction: Literature shows that prenatal alcohol exposure can have teratogenic effects on brain structure and function as well as long lasting neuro-behavioral effects including enhanced anxiety-like responses. Omega-3 polyunsaturated fatty acids, the essential fatty acids found in fish oil, have protective effects against ethanol-induced neurotoxicity. Objective: the aim of this study was to explore the potential protective effects of Omega 3 against the increased anxiety-like behavior induced by acute ethanol exposure in infant rats. Method: A 20% solution of ethanol in saline was administered to postnatal day 7 (PND) Wistar rats in two separate treatments, 2 hours apart, each treatment delivering 2.5 g/kg (sc); control rats were treated with saline only. Another group was administered with one dose of Omega3 (720mg/kg, i.g) 15' after the last alcohol injection. Control Omega3 group was considered. Behaviors related to anxiety were analyzed in the open-field task at PND 14. Results: acute ethanol exposure at PND 7 leads an increase in anxiety-like behaviors. Omega3 administration, a single dose, ameliorates the acute alcohol effects. Discussion: This is the first study to demonstrate that an acute ethanol exposure occasioned behavioral alterations that persist in the offspring. Furthermore, Omega3 ameliorated the ethanol-induced effects in rats. Omega3 administration may have therapeutic effects to reverse or mitigate some of ethanol´s damaging consequences.

P99.-Fight outcome modulates an associative memory in the crab Neohelice granulata

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A new area of study has emerged with the aim of studying the effects induced by social relations in processes such as learning and memory. Cognitive abilities of an animal can not be studied and understood if it is not in function of the ecological pressures that mold its behavior. In this sense, several studies have demonstrated that aversive social events can modulate memory. Recently, we studied the influence of an agonistic encounter on an aversive learning paradigm based on a Contextual Pavlovian Conditioning (CPC) that occurs immediately after a paired fight. Results revealed a differential modulation, losers showed significantly higher memory retention than the respective winners. Thus, we propose that the agonistic experience differently modulated the crab's memory consolidation. Taking this together a new question arises in terms of the physiological mechanisms that are involved. A prior hypothesis is that differential stress levels as a consequence of the fight outcome could be implicated. To address this issue we measured glucose levels, after the fight. We found glucose increase between animals that were involved in an agonistic encounter and control animals. No differences between losers and winners were found. Our ongoing research combines the agonistic encounter with an appetitive paradigm. We expect to determine whether their different memory abilities extend to other types of protocols or are only noticeable feature in the aversive memory.

P100.-Effects of handling during a critical period on an animal model of autism

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Autism spectrum disorders (ASD) are characterized by reduced sociability, diminished communicative skills and repetitive behaviors. To identify the physiological mechanisms that underlie this disorder, we used a mouse model of ASD: the prenatal exposure to valproic acid (VPA).

Previous results from our group show that weaning VPA mice at postnatal day 21 (PD21) with control mice reverts the reduction in sociability observed in adult VPA mice reared with other VPA peers. These evidences suggested that there is a critical period between PD21 and PD60, when sociability can be determined. To narrow this critical window, we aimed to study the physiological and behavioral consequences of a procedure called handling (H) and carried it out between PD21 and PD34. H was reported to produce long-term behavioral and immune alterations, and can even counteract the effects of prenatal infections.
We observed that H reverts some of the behavioral alterations observed in our model: increases sociability and diminishes self-grooming. It also reverts the effects of VPA observed in the forced swimming test and open field test. We will evaluate neuroinflammation and alterations in the piriform cortex, as they were identified previously as candidates in our VPA model. We hope that this study will help us identify a possible physiological mechanism underlying the effects of prenatal VPA exposure on behavior and their rescue by handling.

P101.-Waiting for reward: An animal model for studying binge like behavior

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Increasing the intake of highly palatable food in a short time is one of the most important features of binge eating episodes. These are usually related to the previous experimentation of negative emotions. The objective of this study was to explore some aspects of binge eating behavior in a new animal model that involve exposure to frustrating events due to the delay of an expected reinforcement. Adult male Wistar rats were used. In Experiment 1 it was observed that animals trained to receive a highly palatable reinforcer (32% sucrose solution) express a significant intake increase if they are re-exposed to the reward after a 2 min delay, as compared to a control group without delay. In Experiment 2 we explored whether the magnitude of the intake increase is dependent on the state of frustration. Specifically, a group of animals were evaluated upon re-finding a 16% sucrose solution after a delay, which represents a less stressful condition since the discrepancy between the obtained and expected reward is lower. The effect of increased intake by delayed reinforcement was replicated in animals trained with 32%, while no increase intake was observed in animals trained with 16%. These data suggest that the state of frustration produced by delayed reward would involve an increase in the motivational value of the expected reward. This could be one of the behavioral mechanisms underlying the intake increase after frustrating situations.

P102.-Layer IV-Va neurons of the granular retrosplenial cortex (A29) project and control the activity of layers II-IV neurons of dysgranular retrosplenial cortex (A30) during contextual fear memory processing

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Retrosplenial cortex (RSC) is connected with the hippocampal formation and neocortical areas, and has a role in cognition and spatial navigation. It is subdivided in two main regions, A29 and A30, according to their cytoarchitectural organization and connections. It is unknown how these subdivisions are functionally integrated. MK801-treatment was used as a non-invasive method for selective elimination of layers IV-Va neurons of A29 (A29MK801). Immunolabeling of GABA-associated proteins parvalbumin and calretinin revealed that MK801-treatment does not affect these neuronal populations in A29. This suggest that A29MK801 are not GABAergic neurons. Microinjections of the retrograde tracer Fluoro-Gold (FG) in superficial layers of A30 showed FG positive neurons (FG+) exclusively in layers IV-Va of A29 distributed similarly to A29MK801 neurons. MK801 treatment dramatically reduced the number of FG+ in layers IV-Va of A29. These data indicate that A29MK801 neurons establish efferent projection to layers I-IV of A30. cFos and EGR-1 expression during contextual fear memory (CFM) encoding and retrieval indicate A29 and A30 involvement during memory processing with a different activation pattern. Ablation of A29MK801 neurons after consolidation of CFM reduces freezing and IEGs expression in A30, without affecting A29 and other related areas. Together, our results indicate A29MK801 neurons involvement in fear memory processing and their relevance in the interaction between A29 and A30.

P103.-Evaluation of behavioral phenotypes before and after transgene suppression in a conditional TDP-43 mouse model of Frontotemporal dementia /Amyotrophic lateral sclerosis

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Mislocalization and aggregation of TDP-43 are two common features of frontotemporal dementia (FTD) as well as amyotrophic lateral sclerosis (ALS). We developed transgenic mice conditionally overexpressing human wild-type TDP-43 protein (hTDP-43- WT) in forebrain neurons, a model that recapitulate key features of FTD/ALS. After post-weaning transgene (TG) induction during 1 month, these mice display an early behavioral phenotype, including impaired cognitive and social function with no substantial motor abnormalities. In this study we evaluated the behavior before and after 2 weeks of TG suppression. hTDP-43-WT mice evaluated in the Y-maze test displayed normal spatial and working memory both before and after the suppression protocol. This indicates that TG suppression prevents the installment of early cognitive deficits. TG suppression also prevented the development of the mild spasticity observed in mice expressing the TG for 1 month. Both locomotion and exploratory behavior (open field test) and motor coordination (rotarod test) were indistinguishable from controls before and after TG suppression. Since the results of these tests were consistent with the ones seen after 1 month of TG expression, the suppression protocol had no unspecific effects on motor behavior. No social deficits were found before TG suppression. These results contribute to our understanding of FTD/ALS and provide valuable information for susceptibility windows in therapeutic strategies.

P104.-Are CB1R and CB2R interacting in the regulation of anxiety?

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The neuromodulatory role of the endocannabinoid system contributes on maintaining the homeostasis of physiological states including mood and emotion. Changes in the expression of the CB1 receptor (CB1R) gene have been related to depressive effects. Mice lacking CB1R exhibited a behavioral state analogous to depression in experimental animals. Previous results, showed that CB1R knock-out mice (CB1-/-) presents an increase in CB2 receptor (CB2R) expression and altered neuronal plasticity. The aim of the study is to evaluate the effect of CB2R agonist (JWH015) and antagonist (AM630) in behavioral paradigms of anxiety and depression in CB1 receptor wild-type mice (CB1+/+) and CB1-/-. CB1+/+ and CB1-/- mice were divided into four groups and were injected with Vehicle, JWH015, AM630 or JWH015+AM630. Open field test (OF) and forced swimming test (FST) were performed 30 minutes and 2hours after injection, respectively. In OF test, time spent in periphery was decreased by JWH015 and increased by AM630 in CB1+/+ meanwhile time spent in central zone was increased by JWH015 and decreased by AM630 in CB1+/+. No differences were observed in CB1-/-. In FST, time of immobilization was increased in CB1-/- respect to CB1+/+. Treatment with agonists or antagonist did not show any differences in CB1-/- or CB1+/+. Since CB2 agonist, JWH015 has an anxiolytic effect in CB1+/+ but has no effect on CB1-/-, we proposed that CB1R and CB2R could be interacting in the regulation of anxiety.

P105.-c-Fos immunoreactivity in hypothalamus and reward system of young rats after social novelty exposure

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Enriched environments are benefical during youth, since they help to develop cerebral plasticity and decrease the chances to suffer certain diseases. This environments are compose of various types of stimuli that can be classified, in a rough way, in social and non-social, and in turn, in novel and familiar. Doing an analysis of the changes that social novelty causes over c-Fos production (a neural activity marker protein) in the brain, in comparission with other type of socio-ambiental stimuli, we observed that, during novel social encounters between young rats, there is a significant increase of c-Fos expression in the hypotalamus PVN, principal producer of pro-social hormones, oxytocin and vasopressin, and also, in the hedonic hotspots of the reward system, the Nacc and the VP. Our results agree with previous behavioral and physiological observations, wich show preference for social novelty, and participation of the hypotalamus and reward system diuring socialization in adult rodents and humans. This work could be a precedent to new enriched environment studies, manipulating the social variable, aiming to observe its effects over some deseases asociated to the reward system, such as addictions.

P106.-Role of the serotonergic receptor 2a (5-HT2a) in Cognitive Flexibility

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Living organisms inhabit environments that are being permanently modified, so adapting their behavior to such changes could determine their survival. The concept of "cognitive flexibility" refers to this ability, and the processes that mediate it involve cortical regions of the brain such as the prefrontal and the orbitofrontal cortex.
Given that serotonin (5-HT) has been identified as an important player in decision making, it would be reasonable to assign the serotonergic system a major role in processes of cognitive flexibility. Pharmacological experiments support this statement. However, it is still a question which are the receptors that mediate these processes.
One of the most important post-synaptic receptors of the serotonergic system is the type 2A receptor (5-HT2aR). This receptor is highly expressed in the limbic system as well as frontal regions of the cortex and has been associated with various psychiatric disorders. The lack of specific antagonists makes complex the identification of its function. Then, we would assess the role of the 5-HT2aR using protocols of extinction and reversal learning as measures of cognitive flexibility in genetically modified mice. Since cognitive rigidity is a common behavior symptom of many psychiatric disorders, it has clinical relevance to identified its underlying neurobiological substrate in order to generate new and specific pharmacological tools.

P107.-Neuroprotective potential of Insulin-like Growth Factor 1 (IGF1) in a rat model of sporadic Alzheimer's disease

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Alzheimer's disease (AD) is the most prevalent neurodegenerative pathology with no efficient therapy. Our objective is to develop biotechnological therapeutic strategies for preventing and/or overcoming the degenerative changes in the brain with experimental AD. In this context, we implemented gene therapy for Insulin-like Growth Factor 1 (IGF1), a potent neuroprotective molecule, in rats. We evaluated the effectiveness of IGF1 gene transfer to reverse or at least attenuate the deleterious effects caused by the intracerebroventricular (icv) injection of streptozotocin (STZ), an experimental model of sporadic AD. Animals were submitted into three experimental groups: Sham, STZ and STZ+IGF1. STZ and STZ+IGF1 groups received 3 mg/kg STZ-icv and, 7 days later, the STZ+IGF1 group received an adenovirus vector-expressing IGF1 icv. During the last two weeks until the end of the study (day 24 post-STZ-icv) we performed different behavioral tests. STZ treated rats were deficient in all tests. Interestingly, STZ+IGF1 group improved their hippocampus-dependent learning and spatial memory performance in the Barnes Maze. Anxiety-like and depression-like behaviour were also attenuated in the Marble Burying and Forced Swimming test, respectively, by exposure to IGF1. In this study, we concluded that brain over-expression of IGF1 protected against behavioral impairment in our AD rat model. Thus, IGF1 emerge as promising therapeutic molecule for AD treatment.

P108.-An hypothesis-driven analysis of brain functional connectivity during the acute effects of 3,4-Methylenedioxymethamphetamine (MDMA)

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In spite of its discovery during the early 20th century, the notable psychoactive properties of the substituted amphetamine 3,4-Methylenedioxymethamphetamine (MDMA, also known as "ecstasy") were first discovered and documented in the 1970's by the pioneering work of the american chemist Alexander Shulgin (Shulgin, 1986). These psychoactive effects include strong feelings of well-being and empathy along with mild to moderate stimulation and occasional perceptual distortions (Peroutka et al., 1988). The classification of MDMA as a Schedule 1 substance in 1970 halted ongoing investigations on its effects on brain activity and on its promising use as an adjoint for psychotherapy. Recently, the first contemporary neuroimaging study of MDMA performed by the Imperial College Group (Carhart-Harris et al., 2015) adopted an exploratory approach to reveal the alterations in global brain activity produced by the the substance (using a sample group of 25 individuals in combination with a double-blind placebo comdition). Here, we adopt a hypothesis driven approach based on the selection of regions of interest from the Neurosynth database (http://neurosynth.org/), corresponding to terms related to the subjective effects of MDMA (e.g. "empathy", "love", "emotion", "peace", "serotonin", etc). Using these regions as centers of coordinates for seed functional connectivity analysis, we revealed a core set of functional changes that could underlie the subjective acute effects of MDMA.

P109.-A novel and fully automatic spike sorting implementation with variable number of features

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The most widely used spike sorting algorithms are semiautomatic in practice, requiring manual tuning of the automatic solution to achieve a good performance. In this work, we propose a new fully automatic spike sorting algorithm that is able to match, or even improve, the performance of semiautomatic solutions with supervised intervention from expert users. We achieved this by incorporating: 1) a set of heuristic criteria inspired by the expert actions following the solution from semiautomatic algorithms, and 2) an improved feature selection method that increases the number of units that can be isolated from a single electrode recording. We evaluated the performance of the proposed method with real and simulated data. With the real data, the algorithm retrieved, in a fully unsupervised way, nearly 95% of the clusters isolated by the sorting experts while keeping a low number of false positives. With the simulated data, the algorithm managed to correctly isolate up to 18 neurons from a single channel, where 20 neurons were simulated. The new implementation presented here significantly outperformed the experts' sorting considering the number of hits obtained, while reducing the number of false positives by 40%.

P110.-Sturmian -Wavelets: an effective tool to analyze eye tracking data

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Eye tracking people while performing cognitive tasks allows one to gain novel insights regarding the brain structure and operation. However, movements associated with cognitive tasks are entangled with the mobility information related to the dynamics of the eye as a rigid body [1], the movement of the different parts of the internal eye structure, and also the noise produced by the eye tracker itself. In this contribution we present a novel Sturmian-Wavelets model which mathematically is able to separate out the cognitive information. Priorly used in physics [2], the Sturmian functions are chosen here to form a basis to represent the information associated to the eye dynamics. With kernel polynomials associated to these functions we define a Wavelet basis and use them to analyze time series, finally extracting the relevant cognitive information.

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P111.-An explanation for post saccadic oscillations on eye tracking data

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The analysis of the data obtained from eye tracking experiments during the performance of a cognitive task requires the knowledge of a wide variety of phenomena. The information associated to the cognitive task is entangled with many other phenomena. Commercial eye trackers, as the EyeLink 1000, obtain the position of the eye by registering the border of the pupil. The dynamics of the eyeball [1] and their internal structures, such as the iris and crystalline, influence the data obtained. The relevant cognitive information is also mixed with the noise produced by the eye tracker itself.

In this contribution we present a model which explains the post saccadic oscillations appearing on the EyeLink type eye trackers. The model describes, first, the dynamics of the eyeball, while the iris is represented as a driven damped harmonic oscillator mounted on it. The results allows to describe all the characteristics of the saccadic movements: the relation between the peak velocity and the saccadic size, the shape and size of the overshoot, the amplitude and period of the oscillations, among others.

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P112.-The analysis of a large-scale database of neuroimaging activation maps reveals a hierarchical correspondence between spontaneous and evoked brain activity patterns

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Since the seminal work by Biswal et al. (Biswal et al., 1995) - later expanded using multivariate methods by Beckmann and colleagues (Beckmann et al., 2005) - it is known that spontaneous brain activity recorded using fMRI presents a spatio-temporal organization consistent with well-defined neural systems. This correspondence was revealed for the first time by Smith and colleagues (Smith et al., 2009), who compared the independent components obtained from a database of fMRI task activation maps (http://www.brainmap.org/) with those obtained from resting state fMRI data. The striking correspondence between both sets of components suggested that spontaneous brain activity recapitulates spatio-temporal patterns that might be required for the rapid reaction to environmental demands. Here we investigate a database (http://neurosynth.org/) comprising 413429 maps obtained from 11406 studies. Combining graph-theoretical tools with modularization optimization algorithms, we performed a hierarchical clustering of these maps and observed task-positive and negative clusters at a coarse-level, which were then subdivided into maps associated with well-defined functions. In contrast with the work by Smith et al., the correspondence between task-derived maps and resting state networks was only manifest at an intermediate resolution. This result suggests that the wandering of brain activity around a hypothetical landscape of attractor states can only occur at a certain spatio-temporal grain

P113.-Towards a new protocol for study pattern separation in humans within virtual reality enviroment

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We present a computational kit to create neuroscience experiments in virtual immersive environment like a CAVE (Computer Assisted Virtual Environment). The virtual scenarios should be as similar to the real ones as possible, to improve experiences. The purpose of this work is to study the response of the human central nervous system in similar situations avoiding external factors (such as weather) or distraction. Protocols about perception, attention, cognition and memory is designed and implemented in CAVE. To examine pattern separation, the participant searches and collects objects inside CAVE using spatial strategies. All information about each participant trajectory, virtual scene configuration, location of objects indoors, and answers to particular questions regarding the experience is automatically collected.

P114.-Metric on the color space mediated by adaptation process

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In spatially uniform and temporally stationary conditions of luminosity, the ability of discrimination for trichromat humans depends on the compared colours. For example, it is pretty much easier to discriminate two orange chromas whose wavelengths differ in a quantity $\delta \lambda$, that two green chromas with the same difference. In previous work, we developed a theoretical model which explains this inhomogeneities in term of the physiological properties of the retinal cones. The absorption of photons is a stochastic process which variability depends on the wavelength. This variability puts a limit to the discrimination of the electrical signals that represent the two compared colours. There are recent experiments that extends the previous studies to the situation where illumination is not spatially uniform (the colour of the sorround is controlled in the experiment) , neither temporally stationary (the stimulus are shows for a brief period). The results show that the capacity of discriminating colour depends strongly on these conditions. On this work, we extend the previous theoretical models by including the spatial and temporal structure of the stimulis used in the more recent experiments. We show that, as response to the chroma of the surround, the visual system generates a representation such that the test colour moves away from the colour of the surround, distorting in this way the directions in colour space where it is easier or harder to make discriminations.

P115.-Testing the spacing effect on Mate Marote: a cognitive training software designed for large-scale educational interventions

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Mate Marote is an open source cognitive-training software aimed at children between 4 and 8 years old. It consists of a set of computerized games specifically tailored to train executive functions (EF): a class of processes critical for purposeful, goal-directed behavior, including working memory, planning, flexibility, and cognitive control. In previous studies we showed that (1) less than 7 hours of training elicited transfer to some (but not all) facets of EF, (2) the academic performance of children living at risk was boosted by the intervention, and (3) the quality of play and behavioural patterns in unsupervised interventions are comparable to the data collected in one-to-one supervised designs. The spacing effect in learning is well known. However, the effect of distributed practice on cognitive training has never been tested. In the present study we show that children performance in the EF tests obtained in controlled school environments with their own teacher are enhanced when children had played spaced versus massive designs, one session a week. In this unsupervised experiment, the gameflow, the instructions and the feedback were entirely provided by the platform and teachers only had to ensure the correct login of each children. This results represent an important step towards the ultimate goal of the investigation: the implementation of the platform in large-scale educational interventions as an online free resource which improves cognitive functioning.

P116.-AN INTEGRATED MODEL FOR MOTOR CONTROL OF SONG IN CANARIES

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Birdsong is a learned motor behavior that emerges from the interaction between a nervous system with a peripheral vocal device. The neural substrate that controls song production is known as the song system and consists of an interconnected structure of neural nuclei that is bilaterally organized, with anatomically indistinguishable structures in each hemisphere. These nuclei ultimately project to the periphery, (i.e. expiratory and inspiratory muscles and syringeal muscles) and therefore oversee the generation of complex motor gestures necessary for phonation. The vocal organ, or syrinx, is a bipartite structure that contains two pairs of phonatory membranes (labia) that can be controlled independently to produce complex sounds. Then, to vocalize, a bird must coordinate these motor gestures that regulates the tension of the labia, the airflow, and the gating patterns. In this work, we present a computational model that puts together the neuronal substrate with the biomechanics into an integrated model for birdsong production: First, we propose a computational model whose variables are the average activities of different neural nuclei of the song system of oscine birds. As an output of this model, two variables represent the air sac pressure and the tension of the labia during canary song production. Then, we show that these time dependent gestures can drive a biomechanical model of the vocal organ into synthesizing realistic canary like songs.

P117.-Modulation of glial cells activation in Parkinson's Disease induced by Lipopolysaccharide (LPS)

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Parkinson's Disease (PD) is a progressive neurodegenerative disorder which manifests as a motor disorder, characterized by slowness of movements, rigidity and tremor. Motor dysfunction of PD is due to dopamine loss in the neostriatum and due to the neurodegeneration of dopaminergic neuron's cell bodies of the Substantia Nigra pars Compacta (SNPC). Evidence suggests that chronic neuroinflammation, mediated by activated microglial and astroglial cells in the SNPC, could be essential for the degenerative process. It has been shown that intranigral LPS injection in rodents induces activation of glial cells, which release neurotoxic and pro-inflammatory factors that damage nigral dopaminergic neurons. Based on this evidence, our objectives were the following: *Generate a PD in vivo model by injecting LPS unilaterally in SNPC in order to characterize its impact on the motor function. *Implement gene therapy for IGF1 in order to evaluate its neurorestorative effect on rats' motor performance, on glial activation and on inflammatory response. Our results show that IGF1 gene therapy is capable of restoring motor deficit present on a PD model induced by LPS. Moreover, we observed a significant increment of both GFAP+ (astrocytes) and Iba1+ (microglia) cells on the ipsilateral hemisphere of rats injected with LPS. In conclusion, IGF1 gene therapy can modulate glial activation and improve motor impairment caused by LPS injection.

P118.-Synchronized HVC activity in auditory perception in canaries

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Songbirds have been the focus of neuroethological research of the principles underlying vocal production, perception and learning. A birdsong's brain presents specialized neural nuclei dedicated to these tasks (the 'song system'). Telencephalic nucleus HVC is sensorimotor: it is required for song production and its neurons present a highly selective response to auditory presentations of the bird's own song (BOS). Previous works showed that in zebra finches (Taeniopygia guttata), the elicited auditory response presents a similar firing pattern to the one measured while the bird is singing, suggesting a shared coding mechanism for the motor production and sensory perception of song.
With the advent of multielectrode arrays, it is possible to obtain high-quality neural data across many recording sites simultaneously. In this work, we studied HVC activity using a 32-channel silicon probe by measuring the auditory response to BOS in head-fixed, urethane-anaesthetized canaries (Serinus canaria). Spike sorting allowed us to isolate many single units from each protocol and we found that population firing patterns tend to be highly correlated, even among cerebral hemispheres. Since auditory responses to BOS could be used as a proxy for neural activity during singing, these results may also inform the neural code for song production. Finally, we studied the relation between local field potentials (LFPs) peaks and bursts of activity of single units at HVC.

P119.-Modelling temperature manipulations in the brain during birdsong production

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The neural mechanisms in the birdsong motor pathway that lead to the generation of respiratory patterns are a matter of extensive debate. In a top-down control paradigm, vocal gestures emerge from a unique timescale ruled by the telencephalic nucleus HVC, which engages other brain regions downstream. Another possibility is that the generation of motor instructions is distributed throughout the neural network, flowing both upstream and downstream. In this circular architecture, the song results from the integration of more than one timescale. In order to disambiguate these views, we used local focal cooling of HVC in canaries to manipulate the timescale present there. Within the frame of the circular model, we fitted the experimental pressure patterns of four recurring types of syllables, which form a full song. We show that at least two separate timescales must be taken into account to reproduce them, as one timescale is manipulated and the other remains unchanged. The modifications -stretching and breaking- of the syllables were quantitatively reproduced in this frame.

P120.-From EMG to frequency modulation in the zebra finch song

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Behavior requires the central nervous system (CNS) to control a set of biomechanical devices. The instructions from the CNS are electrical in nature, and need to be translated by these devices. In the case of birdsong, a delicate and fast control of a set of muscles is required to control the configuration of the syrinx (the avian vocal organ), and the respiratory system. In particular, the syringealis ventralis muscle (vS), controls the tension of the vibrating labia, which modulate the airflow to produce sound. However, the translation of the instructions into acoustical features is complex and species specific. In the case of zebra finch, although the mean fundamental frequency in a syllable is correlated to the mean electromyographic (EMG) activity of vS, it is not trivial to account for the fast frequency modulations, or to interpret bursts of activity between syllables.
In this work we present a biomechanical model of the dynamics of the vS muscle and the labia. The model is driven by the EMG activity of the vS muscle and allows to calculate the frequency modulation produced by the stretching of the labia.
We show that even using small segments of data, the parameters of the model can be fitted, and the predicted frequency for different types of syllables and frequency ranges is in agreement with the measured sound.

P121.-Development of a low cost eye tracker

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The registration of the eye movements is turning into common practice in games, business, marketing, science, and other areas. It is also turning into an important tool for diagnosis of diverse medical or psychological conditions like AAD, Autism, Alzheimer desease, etc. Among the various types of eye movements, the most important ones for the diagnosis are the saccadic. Most of the commercial eye trackers like those produced by EyeLink and Tobii are expensive and even prohibitive for most of the health institutions. This make difficult the use of these equipments widely on clinical and health institutions.
In this contribution we present a low cost eye tracker developed to be accurate enough to make a precise registration of the saccadic movements with the only requirement of essentially any common webcam. Possibilities in this direction has already been studied and reported [1]. We worked on a custom-made Javascript code that localize pupils positions in real time, with a featured-based method. Different type of information processing can be performed with a set of in-browser tools on the web page front-end. Some preliminary results are presented using the eye-tracker in an experiment consisting of fixating gaze on a grid of equispaced points over a large screen.

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P122.-HVC neural activity supports a circular model for birdsong production

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Songbirds are a well-established animal model for the study of vocal production, perception and learning. During singing, the respiratory system and the vocal organ are driven by neural instructions from a set of nuclei dedicated to song production. Telencephalic nucleus HVC (used as a proper name) plays a key role in the production of motor commands that drive the periphery. In canaries (Serinus canaria), the interaction between air sac pressure and muscle tension necessary for song production has been previously studied in detail. Recently, these biomechanical motor gestures have been obtained as solutions to a neural population model of the song system. This model makes specific predictions about the timing of the sparse activity in the neural nucleus HVC during the production of motor gestures. We developed a tetrode array to chronically record extracellular activity in HVC of singing canaries. We were able to isolate single units from the recorded data and found a set of neurons locked to singing behavior for different phrases. We analyzed spike time delay with respect to syllable onset for specific phrases and found that neurons fire at a particular instance within a syllable and robustly for all syllables within a phrase across renditions. Spike times from different syllables from two birds occur at note transitions within the syllable. These findings support the predictions from the neural population model.

P123.-Modulation of glutamate release induced by GABAergic and glycinergic inhibitors during excitotoxic damage in a model of spinal injury

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In the spinal cord high extracellular glutamate concentration-evoked excitotoxic damage has large negative impact on loss of locomotor function and neuronal death. We have shown that the glutamate analogue kainate largely destroys neurons via excitotoxicity with a modest white matter damage (Mazzone et al, 2010). Our present objective was to determine the relative role of glutamate and GABA neurotransmission in the process of excitotoxicity. Using an in vitro model of excitotoxicity evoked by kainate on mouse organotypic spinal slice cultures, we investigated the timecourse and extent of endogenous glutamate release following 1 h application of kainate using a commercially available biosensor placed in the ventral horn area of such slices. We have analyzed the effect of different pharmacological inhibitors of glycinergic and GABAergic receptors, i.e. strychnine (0.4 µM), bicuculline (20 µM) and gabazine (20 µM) on this phenomenon. A strong release of endogenous glutamate induced by kainate to mimic spinal injury in vitro could be reliably monitored on a real-time basis. Our data indicate that blocking GABA receptors by bicuculline potentiated glutamate release, while no effect was observed with gabazine or strychnine. Thus, this method can offer an advantageous approach to explore the role of inhibition in controlling excitotoxicity and to test the mechanism of action and time-dependence of neuroprotective drugs aimed at blocking glutamate release. Supported by ICTP, CONICET.

P124.-Mesenchymal stem cell therapy improves motor performance in a rat excitotoxic spinal cord injury model

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Spinal cord injury (SCI) is a very common tissue destroying condition that leads to permanent or temporal loss of motor and autonomic functions as well as sensory capacity of the organs innervated by the injured spinal cord segment. In recent years, mesenchymal stem cells (MSC) therapy has generated promising results due to their anti-inflammatory, immunomodulatory and neuroprotective properties, although their ability to functionally replace neurons and glial cells remains highly discussed. The goal of the present work was to determine whether intracerebroventricular injection of MSC modifies the behavioural performance of rats affected by an excitotoxic SCI model. Male Sprague Dawley rats were intraparenchymally injected with 1mM KA at the C5 cervical segment. Three days later, 10 µl of either MSC (6x103 cells/µl) or saline were injected by intracerebroventricular via into the fourth ventricle. Motor and sensitive abilities were evaluated at days 3, 7 and 14, post KA injection (pi). We found that sensory evaluation showed no significant difference between both groups at any day pi. However, motor performance was significantly better in KA-MSC animals than in KA-injected animals. Intracerebroventricular injection of MSC showed a beneficial motor effect on KA- injected animals, thus indicating a potential use of the MSC therapy on the rat excitotoxic spinal cord model. Further studies are needed to correlate clinical with possible morphological changes.

P125.-Deep hypothermic shock reverses the damage caused by perinatal asphyxia in the rat's striatum

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The striatum is particularly vulnerable to perinatal asphyxia (PA). The main cells of this structure are the median spiny neurons, which are GABAergic calbindin (CB) positive neurons. At the time of delivery GABA has excitatory properties and the excitotoxicity process could be mediated through GABA-GABA synapses. The GFAP is an astrocyte protein that is overexpress after brain injury. The present work aims to quantify CB and GFAP after exposure to PA in the striatum and to evaluate the therapeutic effect of a short and deep hypothermic shock after asphyxia. The uterus was removed by caesarean section and the fetuses were exposed to hypoxia (19 min at 37 C˚) by immersion in water and, also, exposed to a temperature of 10 C˚for 30 min in case of the hypothermic group. Four experimental groups of 3-4 rats each were formed. The labeling of CB, GFAP, neuN, DAPI was measured in adult rats. In the PA group there was a significant decrease in CB positive neurons and an increase in GFAP expression compared to control. Treatment with post-asphyxia hypothermia prevented changes in CB and GFAP showing expression levels similar to control. The quantification of NeuN, DAPI did not show differences between groups. Perinatal asphyxia generates a decrease in the GABAergic cells of the striatum and increase a marker of brain insult as GFAP. Hypothermia seems to reverse this damage. Deep hypothermia could be a superlative option to reduce severe disability generated by the PA.

P126.-Neuroendocrine control of puparium morphogenesis

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Drosophila larvae undergo a dramatic change in body shape at the end of the larval growth period when the thin, flexible and transparent cuticle of the larvae is transformed into the puparium. This remodeling is achieved by a series of muscular contractions such as retraction of the anterior segments and body contraction, and accompanied by structural remodeling of the cuticle. Even though the onset of the metamorphosis is known to be under the control of ecdysone, other molecular players have been shown or hypothesized to act downstream of it to mediate different aspects of these behavioral and morphogenetic processes. Serendipitously, we observed that animals lacking the relaxin-receptor like G-protein coupled receptor Lgr3 produce a thin and elongated puparium, indicating that Lgr3 is required for proper puparium morphogenesis. This activity is separable from the previously described role for Lgr3 during larval development, where it has been shown to act in a subpopulation of CNS neurons to coordinate growth with developmental timing by inhibiting ecdysone biosynthesis, in a Drosophila insulin-like peptide 8 (Dilp8)-dependent fashion. Rather, our results are consistent with Lgr3 acting in a distinct population of neurons that respond to a developmentally-triggered surge of carcass-derived Dilp8 peptide that occurs at the onset of pupariation. Hence, the Dilp8 and Lgr3 constitute a new neuroendocrine pathway directly contributing to puparium morphogenesis.

P127.-Unbalanced Corticostriatal Connectivity in a Mouse Model of Neonatal Dopamine Dysfunction

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Neurodevelopmental psychiatric disorders as attention deficit hyperactivity disorder (ADHD) might stem from alterations of dopamine (DA) regulation of the corticostriatal system. Previously, we found that neonatal DA depleted mice (proposed as an ADHD mouse model) showed alterations in exploration of novel environments and deficits in the capacity to exploit opportunities and social behavior. These behavioral changes were accompanied by a reduction in corticostriatal connectivity and a contraction of medium spiny neuron (MSN) dendritic tree. In order to understand whether the neonatal DA lesion affects differentially the activity of the direct (dMSN) and the indirect MSN (iMSN), here we performed in vivo juxtacellular recordings of individual MSN in transgenic mice showing dMSN-type-specific expression of the fluorescent protein tomato allowing us to indentify the cellular identity of the recorded cell. We examined the in vivo MSN response to cortical inputs from prelimbic and M2 cortical areas. We found that the neonatal DA neuron lesion did not affect the response of dMSN and iMSN to prelimbic inputs. Interestingly, we also found that lesion mice dMSN were more responsive to M2 inputs with no changes in iMSN response. Together, our results suggest that DA is essential during postnatal development for the normal functional and structural maturation of the corticostriatal system, and the correct balance of corticostriatal inputs to the direct and indirect pathways.

P128.-Connexin switch in glial network maturation

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Olfactory bulb innervation by olfactory sensory neurons (OSNs) refines post-natally and is a sensory activity-dependent process. OSNs associate to olfactory ensheathing cells (OECs), specialized glia organized in connexin 43 gap junction mediated networks. We propose that glial networks refine simultaneously with neuronal circuits. Previous results showed that OEC networks exist at neonatal ages, and that OEC sensitivity to meclofenamic acid (MFA, gap junction blocker) is comparable at neonate and juvenile stages. MFA-sensitivity is absent in OECs with deletion of the gap junction protein Cx43 at juvenile and adult ages. Strikingly, OECs show minimal Cx43 expression at P0-3 and higher levels from P4-30, suggesting a connexin switch during circuit refinement. By means of dye-coupling experiments we show that OEC network size diminishes with age. Surprisingly, dye-coupling is affected at P7 but not at P3 Cx43 KO OECs, indicating Cx43 independence at P3. To assess the molecular bases of these results, we used mice expressing a fluorescent reporter in OECs. mRNA was extracted from OEC-enriched samples by laser microdissection microscopy. We were able to specifically detect OEC markers and avoid contamination with neuronal transcripts. Cx29, a putative candidate to mediate OEC networks in the absence of Cx43 was not detected. These results suggest that OECs mature with the neuronal circuit, reflected in network selectivity and the molecular bases for connectivity.

P129.-Voltage Activated Conductances in Motoneurons, and their Influence on Motor Circuits

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Motoneurons have been conceived as mere output units of networks that control motor behaviors; however, several evidences suggest that they play active roles in shaping motor patterns. In leeches the motoneurons responsible for the elongation of their body, CV (circular ventral) neurons, are linked to the crawling central pattern generator (CPG) via a positive feedback connection. Intrinsic properties of neurons can markedly shape the output of the circuits inwhich they participate. CV motoneurons exhibit a low threshold spike (LTS) on topof which a burst of action potentials is fired. In the present work we aim at analyzing the properties of the CV LTS, and develop tools to analyze the role of this phenomenon on crawling. The results suggest that the LTS of CV motoneurons exhibits a threshold close to the resting potential of the neurons, depends on Ca2+]o, and NNC 55-0396, a blocker of T-type Ca2+ channels, inhibits it.

P130.-Ghrelin Signaling Diferentially Activates Non-Dopaminergic Neurons of the Ventral Tegmental Area Subregions

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The ventral tegmental area (VTA) together with the nucleus accumbens (Acb) form the mesolimbic pathway, which is involved in the regulation and processing of the rewarding aspects of food consumption. The VTA comprises different neuronal populations, including dopaminergic, GABAergic and glutamatergic neurons. The VTA and Acb are both divided in three different sub-divisions with differential connectivity. Ghrelin is a peptidic orexigenic hormone secreted from stomach that binds to a G-protein coupled receptor, the growth hormone secretagogue receptor (GHSR). GHSR is expressed in several brain nuclei involved in food intake regulation, including the VTA. In this study, we investigated the ability of ghrelin to reach and activate VTA and Acb sub-divisions. We found that peripherally administered ghrelin fails to reach and increase the levels of the marker of neuronal activation c-Fos in both the VTA and the Acb. We also found that centrally administered ghrelin reaches VTA neurons and increases c-Fos in different sub-divisions of the VTA and Acb. Finally, we show that dopaminergic neurons of the VTA fail to increase c-Fos in response to centrally administered ghrelin. Thereby, we conclude that central ghrelin is able to reach the VTA and to activate VTA and Acb sub-divisions, and that VTA neurons activated by ghrelin are not dopaminergic neurons.

P131.-Neuronal projections from the lateral neocortex to the amygdala

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Cognitive function is a product of the concerted and synchronized activity of many brain areas with a proposed hierarchical relation. Previous results indicated that the lateral neocortex is necessary for contextual fear memory reconsolidation and suggested a functional connection with the amygdala, a key structure for processing emotional information. To further investigate the synaptic connections between these areas, we first used an optogenetic-based strategy in which we expressed the light-activated cation channel rhodopsin in the lateral neocortex on the left side of the brain and implanted an electrode array plus optic fiber in the amygdala in this hemisphere. We observed changes in amygdalar local field potential upon light stimulation in almost half of the electrodes. Furthermore, we performed paired-pulse stimulation and found a deflection of the paired pulse ratio when diminishing the pulse delay, indicating monosynaptic connectivity. To evaluate the possibility of a direct morphological connection between the areas we performed retrograde labeling studies. Overall, our results support a monosynaptic connection between the lateral neocortex and amygdala.

P132.-Experience-dependent retinal protection against acute ischemia

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Ischemia is a key component of several retinal diseases that are leading causes of irreversible blindness. At present, there are no effective strategies to prevent retinal ischemic damage (ID). Enriched environment (EE) is a paradigm that involves sensory, cognitive, motor, and social stimulation. The aim was to analyze whether the previous exposure to EE prevents acute retinal ID. Adult male Wistar rats were exposed to standard environment (SE) or EE for 1 or 3 weeks before ischemia. Retinal ischemia was induced by increasing intraocular pressure to 120 mm Hg for 40 min. After ischemia, both groups were housed in SE for 3 weeks, and subjected to functional (by electroretinogram (ERG) and anterograde transport to central visual areas) and histological analysis. The number of retinal ganglion cells (RGCs) was assessed by Brn3a-immunoreactivity. In animals housed in SE, ID induced a significant decrease in ERG a- and b- wave amplitude and oscillatory potentials and anterograde transport, whereas the previous exposure to EE prevented these alterations. Two weeks after ischemia, a significant decrease in the total retinal thickness, the number of RGCs as well as an increase in Iba1 and ED1 immunoreactivity were found in retinas from animals housed in SE, whereas in ischemic retinas from animals housed in EE, these parameters were significantly preserved. These results suggest that the exposure to EE decreases retinal vulnerability to ID.

P133.-Analysis of Single-Unit Activity and Local Field Potentials during the Progression of Epileptogenesis on an Experimental Epilepsy Model

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Epileptic seizures are sudden changes in neural activity that interfere with the normal functioning of the neural network, expressed through hypersynchronic discharges. The aim of this study is to analyze how single-unit activity (SUA) and local field potentials (LFP) would be affected during the progression of epileptogenesis. Male Wistar rats were implanted with a bipolar macroelectrode in the CA1 region of right ventral hippocampus, through which they were kindled, and eight microwires were placed in the CA1 region of right dorsal hippocampus (rdH). SUA and LFP were recorded continuously during the rapid kindling protocol. SUA and LFP ictal and interictal activity of rdH were analyzed. We found heterogeneous changes in neuronal firing rate during electrographic seizure activity. Different patterns of neuronal activity were observed. Some neurons increase and others decrease their firing rates, while many units did not change. The interictal firing rate becomes higher according as epileptogenesis progresses. These different degrees of stereotypical firing patterns during seizures might depend on whether or not neurons are actually being recruited by the propagating wave of seizure spread. The combined study of SUA and LFP can provide new insights into the process of transition to seizure, allowing us to assess precisely the dynamic changes involved in epileptogenesis. Future studies are needed to understand how these patterns would be involved in epileptogenic networks.

P134.-Reward-related signaling in the dorsal striatum

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The ability to predict rewarding outcomes is essential for learning and consolidating stimulus-reward associations. The striatum is part of the basal ganglia and it is involved not only in the motor control of a sequence of actions but also in coding other aspects related to a task such as cues that are associated to a reward, estimation of time, reward-prediction error, etc. Here we used tetrodes to record striatal activity in a self-initiated rewarded task. Briefly, after a minimum inter-trial interval of 2.5 s, water-deprived rats must enter a nosepoke and, following a visual cue, emit an eight-licks sequence onto a tube to receive water. Behavioral analysis shows that subjects quickly learn to perform lick sequences but have more difficulties in the control of their timely emission, as they prematurely enter the nosepoke. Premature entries reset the timer, reducing the reward rate, but with training animals learn the action-outcome association, improving their performance in the task. In electrophysiological records we found bracketing-like activity in beginning and the ending of the trials and also activity related to the visual cue and the delivery of the reward. Interestingly, we found neuronal activity modulation that correlates with the length of the ITI, both for correct trials and premature entries with sequences. These findings show that the striatum is coding multiple aspects of the task.

P135.-Influence of young vs. mature adult-born dentate granule cells on CA3 in vivo

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The hippocampal dentate gyrus is among the few areas of the adult mammalian brain that constantly incorporates new neurons. Ex vivo experiments revealed that young granule cells (GCs) are more excitable than mature GCs, while both populations evoke similar postsynaptic potentials on their main target neurons in CA3. However, the influence of young vs. mature GCs on CA3 in vivo remains unknown. Here we show CA3 neuronal activity recorded while mice explored different environments, with or without optogenetic stimulation of young and mature GCs of the same cohort (longitudinal analysis). Our preliminary data suggest that stimulation of mature GCs evokes greater local field potentials in CA3 than young GCs. Furthermore, only the mature population evokes greater responses at 1 Hz than 0.1 Hz, suggesting differential facilitation effects. Ongoing experiments explore this phenomenon at higher stimulating frequencies and varying intensities. On the other hand, we identified three frequency bands in the local field potential that coordinate their amplitude with theta oscillations. Preliminary analyses suggest that exposing mice to an enriched environment potentiates the coupling at high frequencies but reduces it at low frequencies. This effect is partially reverted upon stimulation of adult-born GCs. These results suggest that CA3 information processing is dissimilarly affected by adult born GCs at different maturational stages.

P136.-Neuromodulators in the processing of afferent inputs in the dentate gyrus

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Neurogenesis in the adulthood continuously provides the dentate gyrus (DG) of the hippocampus with pools of granule cells (GC) which integrate into the preexisting network. The maturation process of this newborn neurons is well characterized and is similar to the maturation of GC during development. It has been shown that newly born GC are necessary for many types of memory but how these neurons contribute to the hippocampal function is under intense investigation. As inputs arrive to DG, they activate both excitatory and inhibitory neurons, and the excitation to inhibition (E/I) balance results in a pattern of population activity. Immature 4 week old GC have specific processing features, as they exhibit a higher E/I balance compared to mature GC. Thus, even though this population of neurons represents only 3-6 % of the total GC, their contribution to processing could be important due to their higher activity, their higher spiking rate and their higher plasticity. Neuromodulatory circuits projecting to the DG could modulate E/I balance in GC, providing a new level of plasticity for information processing of afferent stimulation.

P137.-Effects of cortical parvalbumin positive neuron dysfunction on the physiological properties of prefrontal cortex pyramidal neurons

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The underlying circuit mechanisms involved in cognition require a balanced interplay of interneurons and pyramidal neurons (PN). In the PFC, executive control and cognition correlates with gamma oscillations and with membrane potential (mp) subthreshold oscillations. Importantly parvalbumin interneurons (PV) are required for the generation of gamma oscillations and the balance of excitatory and inhibitory (E/I) inputs producing mp subthreshold oscillations. Thus a dysfunction in the PV activity may alter the PN physiology and the E/I balance. Such dysfunction is believed to be present in neurodevelopmental illnesses like schizophrenia, thus the study of PV dysfunction in PFC circuits is highly relevant for the understanding of cognition in health and disease. We focused on the effects of PV dysfunction on the morphology, membrane properties and E/I balance of PNs in mouse mPFC using a mouse line where the NMDAR is eliminated from corticolimbical PV neurons early on, showing molecular and behavioral markers resembling schizophrenia. We found a reduced and less complex dendritic tree and an increased excitability in PNs of KO mice. Furthermore whereas the E/I balance was not altered in the spontaneous activity of acute slices, the miniature events displayed a reduced IPSC and normal EPSC frequencies, increasing the E/I balance. These results suggest that PV dysfunction early on, impacts the maturation of the circuit altering both functional and structural characteristics of PNs

P138.-Study of cortical oscillatory activity in the development of dyskinesias associated to L-Dopa treatment in a rodent model of Parkinson's disease

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Prolonged treatment with L-Dopa in Parkinson's disease (PD) often leads to the emergence of abnormal involuntary movements known as L-Dopa-induced dyskinesias (LIDs). Recent findings in a rodent model of PD have shown that dyskinetic symptoms are linked to the occurrence of a prominent 80Hz oscillatory local field potential (LFP) activity within the primary motor cortex. Additionally, L-Dopa treatment decreases exaggerated beta (13-30Hz) oscillatory activity, which is exacerbated in parkinsonian state and has been associated with rigidity and bradykinesia. Despite of this, the correlation between motor symptoms and oscillatory activity in the development of LIDs is not fully understood; mainly because the animal’s behavior in the "on" state is a major constraint for multi-electrode chronic recording studies. To solve this and with the purpose to characterize the relationship of beta and high gamma (70–110Hz) cortical activity with parkinsonian state and the development of LIDs, we design a new setup based on a mouse spherical treadmill where animals could walk freely but had the head restrained of movement. This system allowed us to record cortical LFP and spike signals by means of high density electrodes in hemiparkinsonian mice as well in animals with LIDs, both in “on” as in “off” states. Movements were also tracked in order to correlate them with brain activity. Preliminary results showing a characterization of the oscillatory activity in the beta range will be presented.

P139.-Design of an affordable and easy-to-implement one photon microscope for imaging of neural activity during behavior

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Fluorescence microscopy of proteins such as GCamp6 has made it possible to observe neural activity of large neural populations. In particular, recently developed miniaturized one-photon microscopes enable the simultaneous recording of hundreds of genetically targeted neurons in behaving animals, with stability of months. However, commercially available microscopes are prohibitively expensive, while Do It Yourself alternatives have two main drawbacks. On one hand, they require a complex logistics that makes difficult their implementation in developing or peripheral countries. On the other, the manufacturing process requires specialized skills, such as experience with soldering ultra-small surface-mount device components. Here we test an open source prototype and propose several improvements adapted to the needs of Latin American laboratories. As a proof of principle, fluorescence images of fixed YFP-expressing mouse brain slices taken with the miniaturized prototype are shown to match those obtained with standard bench fluorescence microscopes. Based on the experience of building this prototype, we discuss several improvements regarding the design of the microscope body, the optics and the imaging hardware. Together, these improvements will make this technology affordable to neuroscience laboratories with no previous knowledge in microscopy or specialized skills in the assembly of electronic components.

P140.-Analysis of the encoding properties of nucleus accumbens neurons during learning of a self-paced operant conditioning task

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The available behavioral and anatomical evidence points strongly toward a role of nucleus accumbens (NAc) in promoting behavioral responses associated with reward and it has been proposed to function as a limbic-motor interface. Recordings in NAc in animals performing operant conditioning tasks have revealed phasic responses, in partially overlapping subpopulations, correlated with different aspects of the task, including motor responses and reward associated cues. However, little is known about how this responses evolve place during learning of a behavioral task. To unveil the evolution of encoding properties of NAc neurons along the acquisition of an operant conditioning task we implanted Long-Evans male rats with a microelectrode array in the NAc. Rats were motivated by water restriction to obtain water droplets from a lick tube located within a recessed “nose-poke” in a standard behavioral chamber. Rats were daily trained using a protocol in which trials were self-paced by the animal. Animals were required to lick 8 times for a water reward to be presented. To differentiate reward receipt from expectancy, half of the total correct trials were rewarded, half unrewarded. We identified different subpopulations of units responding to environmental salient events and motor responses. Interestingly, signaling properties and population composition of the NAc responses evolved along the learning of the task, supporting the notion that NAc participates in the learning process.

P141.-Minocycline prevents chronic stress-induced vulnerability to cocaine self-administration

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Clinical evidence supports the idea of individuals that suffer stressing events along their lives are vulnerable to developing substance use disorders (SUDs). Here, we demonstrated how exposure to chronic stressful life events can facilitate the acquisition of cocaine self-administration (SA). We also attempted to prevent SA behavior by minocycline pre-treatment. Thus, rats were exposed to chronic restraint stress (2 hs daily) during seven days. A week after that, animals were implanted with indwelling jugular catheters. A week after surgery, rats began daily 2 hs cocaine SA sessions for ten days. Four days before the onset of SA paradigm, the minocycline (30 mg/kg/12hs) or vehicle (DMSO 5%) daily treatments started, which were carried out until the end of the SA behavior. SA consists of a fixed ratio 1 schedule (FR 1) in which one response on the active lever yielded one intravenous cocaine infusion (0.2 mg/infusion, followed by a 10 s timeout period), paired with a tone and a light cue. An inactive lever was also available each session. SA criterion was defined as the first day animals obtaining more than ten infusions of cocaine. Our results point out a facilitation of the acquisition of cocaine SA as well an augmented intake of cocaine induced by chronic stress, which was interestingly abolished by minocycline. These findings constitute a starting platform to study the mechanisms underpinning the comorbility between stress and SUDs.

P142.-Big data analysis of whole striatum transcriptome after L-DOPA or Pramipexole treatment in a rat model of Parkinson's disease

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L-DOPA is the most effective treatment of Parkinson's disease (PD), but it frequently produces response fluctuations and abnormal involuntary movements after long-term treatment. Pramipexole is a D2/D3 dopamine receptor agonist which has a lower efficacy but also a lower propensity to induce motor complications. Therefore, it is likely that different molecular changes underlie these specific pharmacological responses. Transcriptomic technologies have aided large-scale research to elucidate the link between a specific gene or a cluster of genes and a particular biological mechanism. We used DNA microarray technology to assess whether the striatal gene expression profiles of hemiparkinsonian rats treated with L-DOPA or Pramipexole show statistically significant differences. To produce a model of early PD, rats received a unilateral injection of 6-OHDA in the striatum and were treated with L-DOPA or Pramipexole for three weeks. Differences in gene expression were assessed using the empirical Bayes moderated t-statistic. Overall, more than a thousand of genes were differentially expressed. The PD map of the University of Luxembourg was used as an exploratory tool to point out the localization of differentially expressed genes within biological pathways and compartments refining gene selection. This analysis will reveal new genetic striatal networks possibly contributing to the therapeutic effects of the most common treatments for PD.

P143.-Understanding ADHD dopaminergic neurotransmission: the p35 KO mice have a preserved D1 but an altered D2 function

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Attention-deficit hyperactivity disorder (ADHD) is a behavioural condition characterized by atypical levels of inattention, hyperactivity and impulsivity. A recent study suggest a global prevalence of 3,4 % in children, being the most diagnosed psychiatry disorder at present. Previous studies from our lab have demonstrated that transgenic mice lacking p35 protein (p35KO), the specific activator of Cyclin dependent kinase 5 (Cdk5) exhibit behaviors resemble those described in animal models of ADHD. P35 KO mice display hyperactivity and less anxiety-like behaviors. Besides, these mice have an increased striatal dopamine (DA) level. These behavioral and biochemical phenotypes are reverted by Methylphenidate and d-Amphetamine, drugs used in ADHD treatment. Since locomotor activity is dependent on dopaminergic neurotransmission, we decided to study the function and expression levels of the two main DA receptor, D1 and D2, in the p35 KO mice. We found that striatal D1 and D2 contents are similar between p35 KO and Wild Type (WT). To test D1 and D2 function, we used pharmacologic agonist (SKF81297/Quinpirol respectively) and antagonists (SCH23390/Haloperidol respectively) drugs. We found that p35 KO mice have a preserved D1 but an altered D2 function, since a low dose of the antagonist Haloperidol (0,03 mg/kg) induces an increase in WT locomotor activity and a decrease in p35 KO. These results may help us to elucidate the mechanism underlying the hyperactivity of this ADHD model

P144.-High dose ketamine increases glutamatergic neurotransmission in the prelimbic cortex of female rats

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Ketamine, a noncompetitive NMDA receptor antagonist, has potent psychomimetic effects, being able to accentuate the psychotic state of schizophrenic patients. One of the brain areas affected by its use is the prefrontal cortex, as the performance on tasks dependent upon their activity is deeply influenced by administration of ketamine. As in schizophrenia, these changes may be modulated by hormonal factors, and can be explained by the influence of female sex hormones. Attentional disturbances can be analysed by prepulse inhibition (PPI), heavily regulated by cortical-limbic circuits in rats. In this study we examine the effects of chronic administration and withdrawal of ketamine on attentional processes of female Wistar rats, tested at different stages of the estrous cycle, as well as the effects of pharmacological modulation of glutamatergic systems of the prelimbic cortex (PL). We confirm the hypothesis that PPI varies throughout the estrous cycle in rodents and the menstrual cycle in women, and is increased by estrogen treatment. Our results also show that the NMDA agonist alone in PL has no effect on PPI, but in association with the high dose of systemic ketamine was able to reverse the PPI deficit, independent of the estrus cycle phase. In conclusion, high doses of ketamine are able to increase glutamatergic neurotransmission in the PL in female rats. Financial Support: FAPESP (2014/09685-9).

P145.-Oral administration and behavioral testing of an inhibitor of serotonin synthesis

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Adult hippocampal neurogenesis can be enhanced by factors like serotonin (5-HT) depletion. Indeed, chronic administration of para-chlorophenylalanine (PCPA), an inhibitor of the 5-HT rate-limiting enzyme, results in increased survival of hippocampal newborn neurons, without affecting proliferation. We thus aim to dissect the role of 5-HT in the neurogenic multistep process, and in order to avoid intraperitoneal injections, experimental conditions for PCPA oral administration were set up. C57Bl/6J, male, 6-week old mice received PCPA (aprox. 100 mg/kg) by means of palatable yeast and jelly cubes, during 5 or 8 weeks. Brain and plasma samples were recovered to analyze 5-HT level. Neurogenic parameters were studied by immunohistochemistry and determined by unbiased stereologically counting. To study the role of PCPA-enhanced neurogenesis in the ability for pattern separation, we have previously performed 2 approachs: the Contextual fear discrimination learning test and the Object location task (OL). No difference were found between control and treated mice in any of these 2 tests. We now set up the Object Pattern Separation task, a recently developed test similar to the OL, but with more resolution. We suspect that this test may allow us to find subtle differences. These results will prove useful for a future proposal of replacement in the way of administration of PCPA and to implement this new test when studying animal models of enhanced neurogenesis.

P146.-LiCl treatment during cocaine abstinence leads to modifications on Wnt/B-catenin pathway in mesocorticolimbic areas.

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Cocaine addiction is a chronic relapsing disorder characterized by the loss of control over drug-seeking and taking. Recently, we reported that Wnt/b-catenin pathway's activity, in the prefrontal cortex (PFC), is important in the early stages of cocaine-induced neuroadaptations. Also, we found that a cocaine challenge after a period of abstinence, increased the pathway activity in the in the nucleus accumbens (NAcc). Moreover, we have shown that LiCl administered before each cocaine injection prevented the development of sensitization by restoring b-catenin levels in the PFC, CPu, and Amygdala, and prevented the expression of sensitization keeping the levels of b-catenin increased in the NAcc.
Thus, to elucidate if LiCl treatment during abstinence in animal models may prevent the expression of cocaine induced sensitization, all animals received one injection of cocaine or saline per day for 7 days. Then, they were administered with LiCl or saline for 7 days and 2 weeks later received a final cocaine challenge on day 28. Locomotor activity was measured after cocaine injection on days 1, 7 and 28. Then animals were sacrificed and their brains removed to evaluate b-catenin levels in PFC and NAcc.
Our results showed that LiCl treatment during abstinence exacerbated the response to cocaine on day 28, while preliminary data indicate that b-catenin levels are decreased in PFC. Ongoing studies are aimed to evaluate if LiCl during abstinence also modifies b-catenin levels in NAcc.

P147.-Influence of chronic restraint stress on cocaine-induced glutamate release in the nucleus accumbens

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Cross-sensitization between stress and drugs of abuse may be explained by long-term neurobiological changes in the mesocorticolimbic dopamine (DA) and glutamate (GLU) transmissions; specifically, within Nucleus Accumbens (NAc), the major limbic-motor integration area. In this sense, previous results from our lab have demonstrated that after two weeks of a single exposure to restraint stress a challenge of cocaine induced locomotor sensitization and a parallel increase in extracellular DA levels in Core compartment of NAc, meanwhile GLU levels in this area were not modified. The present study attempted to determinate the long-term effect of chronic restraint stress pre-exposure in extracellular levels of GLU in NAc Core in response to cocaine. Wistar rats were exposed to repeated (2h for 7 days) restraint stress and two weeks after the last stress session, all animals were implanted with probes of microdialysis in NAc Core. The day after surgery, GLU dialysate samples were collected and quantified by HPLC. After cocaine administration (15 mg/kg, i.p.), animals pre-exposed to chronic stress did not show increased extracellular glutamate levels in NAc Core, similarly to our results obtained following pre-exposure to acute stress. These findings could be explained in the framework of a dysregulation of GLU homeostasis induced by stress. The current study provides neurochemical basis in order to investigate the mechanisms underpinning the comorbidity between stress and drug abuse.

P148.-The kinase Fyn has an important role in NMDA receptor regulation in L-DOPA induced dyskinesia in a mouse model of Parkinson's disease

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Levodopa (L-DOPA) induced dyskinesia (LID) is a side effect of Parkinson's disease (PD) treatment. A great challenge is to reduce the development of LID without affecting the restorative effect of dopamine stimulation. It has been established that DA stimulation increases the phosphorylation at tyrosine 1472 of NR2B, regulatory subunit of NMDAR, which is one target of the Src kinase Fyn. Our aim is to address the role of Fyn in the NMDAR activation under L-DOPA stimulation in a mouse model of PD and the role of Fyn in the genesis of LID. We developed a model of PD in Fyn-KO and WT mice by induction of dopaminergic death by means of unilateral injection of 6-OHDA, and mice induced to developed LID by daily treatment with L-DOPA. Dopaminergic denervation was confirmed by immunodetection of TH in the SN. ΔFosB, TH, pNR2B were determined in the striatum by WB. Fyn-KO mice show a significant reduction in NR2B phosphorylation concomitant with a LID reduction, as shown by behavioural tests and ΔFosB levels reduction. In an independent set of experiments, WT mice were injected with 6-OHDA and randomly assigned to receive Amantadine (NMDA receptor antagonist), Saracatinib (Src kinase inhibitor), both, or vehicle together with L-DOPA. The three groups were compared in their ability to develop LID and the expression of molecular markers of LID.

Neurochemistry and Neuropharmacology

P149.-Molecular Function of Heteromeric Nicotinic Receptors Containing the α7 Subunit and its Duplicated Form

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The α7 nicotinic receptor subunit gene, CHRNA7, codes for a subunit that forms the homomeric α7 receptor, which is involved in learning and memory. In humans, exons 5-10 of CHRNA7 were duplicated and fused to the FAM7A gene, given rise to the CHRFAM7A gene. The product of the resulting chimeric gene, dupα7, is a truncated subunit that lacks part of the ACh binding site. We here combined cell expression, confocal microscopy, western blot, and electrophysiological recordings in HEK cells to understand the functional role of the dupα7 subunit. We found that cells transfected with dupα7 cDNA express the dupα7 protein but show neither surface binding of an α7 specific antagonist nor agonist-elicited currents. To determine if dupα7 assembles with α7 into functional receptors, we used an α7 subunit carrying mutations in determinants of conductance (α7LC) as a reporter of receptor stoichiometry. Co-expression of α7LC with dupα7 or the reverse combination, α7 with dupα7LC, allowed detection of single-channel openings elicited by ACh, indicating that α7 and dupα7 subunits co-assemble into functional heteromeric receptors. The analysis revealed that a minimum of two α7 subunits is required for forming functional receptors and that activation of the heteromeric receptors occurs through the α7/α7 interface. Our results contribute to the understanding of the functional significance of the partial duplication of the α7 gene.

P150.-Enriched environment as a non-pharmacological tool to prevent changes in hippocampal oxidative state induced by different noise exposure schedules at an early developmental age

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Previous results showed different hippocampal (HC)-related behavioral alterations in noise-exposed rats. In addition, enriched environment (EE) housing was effective to prevent most of them. However, data of HC oxidative state after noise exposure have not been obtained yet. Thus, the aim of the present work was to test a potential noise effect on HC oxidative state through the measurement of endogenous antioxidant enzymes in rats exposed to different schedules as well as the possible prevention of these changes by rearing in an EE. 7-days-old rats were exposed to noise (95-97 dB, 2h) for one (N1) or five (N5) consecutive days. After weaning, groups of rats were transferred to EE or standard cages. One week later, levels of Trx1 and Trx2 -two antioxidant enzymes from the thioredoxin family- were tested. Results showed that Trx1 levels were increased in N1 and N5 rats. In contrast, rearing these animals in an EE was effective in preventing these changes. On the other hand, Trx2 levels were increased only in N5 animals and EE was successful in preventing these changes. These findings suggest that an oxidative imbalance might be triggered after noise exposure, being Trx1 more susceptible to noise impact since only one exposure was enough to alter its levels. Conversely, several consecutive noise exposures might be necessary to generate changes on Trx2 levels. Finally, EE seems to be an effective strategy to reverse noise-induced changes in HC oxidative state.

P151.-Rac1 is essential for the expression of behavioral sensitization induced by chronic stress in nucleus accumbens

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It is well known that there is a high rate of co-occurrence of substance abuse disorders and stressful life experiences. It has been shown that both drug administration and exposure to stress induce adaptations at the level of synapses involving modifications in the density and morphology of dendritic spines that are regulated, at least in part, by a small GTPase known as Rac1. Evidence from our laboratory revealed that repeated stress alters the capacity of a subsequent cocaine injection to modulate dendritic spine morphology and actin dynamics in the NA core. Moreover, the pharmacological inhibition of actin polymerization in the NA prevents stress cross-sensitization with cocaine. Thus, the main goal of this project is to evaluate whether changes in Rac1 signaling induced by chronic stress, facilitate the development of sensitization to cocaine. For this purpose, we have generated lentiviral particles containing a constitutive active form of Rac1 (CA-Rac1) to express in NA, and explore its function during cross-sensitization between stress and cocaine. Thus, Wistar rats will be exposed to chronic restraint stress two hours daily during 7 days. Stressed and control animals will be administered with an intra-accumbens injection of CA-Rac1 before a challenge with cocaine, when behavioral sensitization will be evaluated. Our data suggests that the expression of the active form of Rac1 is sufficient to prevent the expression of cross-sensitization between stress and cocaine.

P152.-Study of the role of yerba mate (Ilex paraguariensis) as a neuroprotective factor to dopaminergic neurons in a mouse model of Parkinson's disease

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The clinical signs of Parkinson's disease (PD) are a consequence of the degeneration of the dopaminergic neurons in the substantia nigra. Since the mechanisms that underlie this neuronal degeneration have not been fully clarified, currently there is no preventive therapy for PD. However, an inverse association was found between coffee intake or smoking and the occurrence of PD. Similarly, a case-control study conducted in Argentina in 2013 revealed that consumption of 'mate' also has an inverse association with the risk of developing PD. Mate is a drink widely consumed in several South American countries, made with yerba mate (YM), obtained from the plant Ilex paraguariensis. We propose to characterize the extract of YM by HPLC and to quantify the concentrations of the main bioactive components (caffeine, theobromine, chlorogenic acid and rutin), and to evaluate if the consumption of YM provides a benefit on the survival of dopaminergic neurons in a mouse model of PD. The extract of YM was obtained by 'cebada simulada' and the main bioactive components were quantified by HPLC. Wild type mice with a moderate lesion of the nigrostriatal system are currently under treatment, receiving water or 'mate' as their only source of fluid in their feeding bottle. These results could contribute to the development of novel therapeutic interventions, using YM in association with the frequently used antiparkinsonian drugs and to have thus a direct impact on the quality of life of patients.

P153.-Ghrelin Action in the Ventral Tegmental Area Increases Locomotor Activity Independently of Food Intake Regulation

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Ghrelin is a stomach-derived octanoylated peptide hormone that regulates a variety of central functions via its action on a specific ghrelin receptor that is highly expressed in the brain. Here, we investigated if ghrelin´s effects on food intake and locomotor activity in mice involve the action of the hormone on the ventral tegmental area (VTA), a midbrain area known to regulate both functions and express ghrelin receptor. We found that: 1) subcutaneously-injected ghrelin increases both food intake and the level of the marker of neuronal activation cFos in the hypothalamic arcuate nucleus (ARC) while it fails to increase cFos levels in the VTA. In addition, subcutaneously injected ghrelin fails to affect locomotor activity in mice without access to food; 2) centrally-injected ghrelin increases food intake as well as cFos levels in the ARC and the VTA. In addition, centrally-injected ghrelin increases locomotor activity in mice without access to food; 3) intra-VTA injected ghrelin fails to affect food intake and cFos levels in the ARC while it increases locomotor activity as well as the cFos levels in the VTA. Thus, our results show that ghrelin action at the ARC increases food intake without effects on the locomotor activity while ghrelin action at the VTA increases locomotor activity without effects on the food intake. We conclude that the ghrelin effects on food intake and locomotor activity are neuroanatomically dissociated.

P154.-Sex differences in X-linked gene expression in embryonic hypothalamic neurons

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Although sex hormones are usually considered the main architects of sexual dimorphisms, recent studies have demonstrated that sex chromosomes can also induce sex differences in somatic gene expression in the absence of hormonal differences. Ngn3 is a Notch regulated gene that, in developing neurons, is involved in neurite extension and remodeling. Previous results showed that hypothalamic neurons carrying the XX sex chromosomes present a higher expression of Ngn3 and a faster rate of development than XY neurons, irrespectively of gonadal hormones. Using the Four Core Genotypes (FCG) mouse model, here we analyzed the expression of X-linked genes involved in neuronal growth and differentiation which are probable candidates to regulate Ngn3 expression. By qPCR, we have evaluated the expression of Ddx3x, Eif2s3x, Kdm6a, Syp, Mecp2 and Usp9x in primary hypothalamic cultures from E15 FCG mice. Ddx3x, Eif2s3x and Kdm6a showed higher expression levels in XX neurons than in XY neurons, regardless of the embryo sex. Importantly, Kdm6a is an epigenetic regulator codifying for a histone demethylase, whereas Ddx3x and Eif2s3x codify translation regulators. Thereby, it is possible to hypothesize that some of these genes might be regulating Ngn3 expression and neuronal development. Further experiments blocking these X-linked genes are required to determine the effect of this specific down regulation over Ngn3 and neuronal development. Financial support: CONICET, ANPCyT and SECyT-UNC.

P155.-The neurohormone tyramine modulates the intestinal release of insulin like-peptides (ILPs) to coordinate systemic stress response in C.elegans.

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The nervous system plays a pivotal role in the coordination of systemic stress response. Our results demonstrated that in C.elegans the neuronal release of tyramine (TA) (the invertebrate counterpart of adrenaline) inhibits the systemic response to long-term stressors. We found that the intestinal adrenergic-like receptor TYRA-3 is involved in the tyraminergic control of stress response. We also observed that the insulin receptor DAF-2 is essential for this response, suggesting the compromise of the conserved insulin/insulin-like growth factor signaling (IIS) pathway. However, the identity of the signals that connect these pathways remains unknown. Our screening of the 40 insulin like-peptides (ILPs) revealed that null mutants of INS-3 and INS-7 are as resistant to thermal and oxidative stress as tdc-1 (incapable of synthetizing TA) and tyra-3 null mutants. We also found that INS-3 and INS-7 co-localize with TYRA-3 in intestine. Moreover, INS-3 is down-regulated upon oxidative and thermal stress. The analysis of double null mutants (tdc-1 or tyra-3 with ins-3 and/or -7) suggest that these genes acts in the same pathway to modulate stress response. Therefore, we propose that TA inhibits the systemic stress response by allowing the release of INS-3 and INS-7, which in turn activate DAF-2 in different worm cells. This study will contribute to understand molecular mechanisms involved in neuronal regulation of stress response in a multicellular organism.

Sensory Systems

P156.-Early and late onset of inflammation affects AT2R expression levels and subcellular localization in different subpopulations of nociceptors

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Pharmacological evidence suggests that the type 2 receptor for angiotensin II (AT2R) plays a role in relieving neuropathic pain, an effect that has been attributed to both inhibition (by EMA401) and activation (by mycolactone) of the receptor. Thus, more research is needed to uncover the underlying mechanisms. We injected Complete Freund's Adjuvant (CFA) into the hindpaw of female Wistar rats and analyzed the effect 1 (CFA1) and 4 (CFA4) days thereafter. We combined immunohistochemistry with a detailed quantification analysis to examine a) subcellular localization and b) relative levels of AT2R. We found that AT2R was restricted to both small and medium size dorsal root ganglion neurons that either bound IB4 or expressed TrkA or both. These markers indicated that AT2R expressing neurons were C and A-delta nociceptors. The intracellular localization of AT2R varied amongst the neurons. We observed two patterns: retracted to the peri-nuclear region or evenly distributed to the cell membrane. Membrane-associated staining is likely to reflect functional AT2R whereas cytoplasmic distribution reflects receptor synthesis and availability. Hence, we measured both signals and compare them across neuronal sizes. At CFA1 the receptor level increased significantly only at the cell edge of small neurons, whereas at CFA4 AT2R levels increased only at the edge of medium neurons. This pattern could partly explain the dual behavior observed for AT2R in pathological pain models.

P157.-Strength of the efferent olivocochlear system modifies the activity of a central auditory nuclei

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The auditory system in many mammals is immature at birth but precisely organized in adults. Spontaneous activity in the inner ear comes into play to guide this process. This spontaneous activity is modulated by an efferent pathway that descends from the brain. In this work, we used a mouse model with enhanced medial efferent activity (Chrna9L9'T, KI) to understand the role of the olivocochlear efferent system in the correct establishment of auditory circuits. Wave III of auditory brainstem responses (which represents synchronized activity of synapses within the Superior Olivary Complex) was smaller in the KI suggesting a central dysfunction. In order to analyze this functional observation, we studied the underlying mechanism on brain slices containing the medial nucleus of the trapezoid body (MNTB) where neurons are topographically organized along a medio-lateral axis. Various MNTB physiological properties with a tonotopic organization in WT mice were abolished in the KI. Additionally, slice recordings evidenced synaptic alterations on the MNTB in agreement with the ABR recordings. Our results suggest that medial efferent activity before hearing onset is involved in the refinement of the tonotopic map of the MNTB.

P158.-Visual stimuli induce retinal neuroprotection against acute retinal ischemia

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Enriched environment (EE) is a complex combination of inanimate and social interaction. EE boosts exploratory conduct, voluntary physical exercise, sensorial and cognitive functions, and social interaction. We have previously shown that EE induced neuroprotection against unilateral retinal ischemia in adult rats. However, the relative contribution of each component to the effects of EE is still controversial. Our aim was to dissect the individual contributions of the EE repertoire components in its protective effect against retinal ischemia. The social and exploratory components by themselves were unable to protect the retina against unilateral ischemia. However, when ischemia was bilaterally induced, regardless of motor activity, the protection triggered by EE was abolished, suggesting that the visual input within EE was necessary for retinal neuroprotection. To confirm this hypothesis we induced unilateral ischemia and housed animals in a standard laboratory cage surrounded by monitors showing black/white contrast or grey patterns during the 12 h light phase. Contrast patterns achieved retinal protection against unilateral ischemia. Finally, we administered a Trk-b receptor antagonist (ANA-12) to animals with unilateral retinal ischemia exposed to contrast patterns. ANA-12 prevented the retinal protection against ischemia, further suggesting that visual stimuli, likely in a BDNF dependent manner, could account for the retinal protection induced by EE.

P159.-Perception of relevant components in odor mixtures depends on experience

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In nature, olfactory stimuli are present as mixtures in which their elements differ in their meaning. This meaning may even change among individuals from the same species but with different experiences. We studied honey bees, as they are generalist foragers that depend on olfaction and on their own experience to find food sources.
In previous works we studied the neural representation of mixtures and pure components and found that the representation of a mixtures is shifted toward the representation of the learned components and away from components that have no predictive value. Here we asked if these changes do have a correlate at the behavioral level.
In a first experiment we trained bees using appetitive conditioning toward pure odors and after that we tested them using mixtures that contain that odor. We found that bees are highly efficient in detecting the rewarded component embedded in the mixture.
In a second experiment we trained the bees using pure odors, and then, we retrained them again but using as conditioned stimulus a mixture that contains the learned odor plus a novel odor. Finally, the bees were tested with the novel odor alone. A second group of bees underwent only the learning session with the mixture. We found that learning the novel odor was affected in animals that had a previous experience. These result are consistent with the hypothesis that odor and mixture perception is adjusted by experience.

P160.-DETECTING MINORITY COMPONENTS IN A BINARY MIXTURES: THE ROLE OF OLFACTORY SENSORY ADAPTATION

Nicolás Pírez [2°], Federico Gascue [1°], Fernando Locatelli [2°]

1° Departamento de Fisiología, Biología Molecular y Celular, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina, 2° Departamento de Fisiología, Biología Molecular y Celular, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina e Instituto de Fisiología Biología Molecular y Neurociencias, UBA-CONICET, Argentina
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The olfactory system is an excellent model system to study how contextual information is detected and processed by the nervous system. The coding of olfactory information undergoes multiple changes due to prolonged or repeated exposures to odorants. Sensory adaptation is defined as a phenomenon by which the sensitivity towards a stimulus is rapidly decreased after a prolonged exposure to it; it is followed by a complete recovery after the disappearance of the stimulus. Here, we use Apis mellifera to study the effect that the olfactory sensory adaptation has on the capability of animals to detect minor components embedded in binary mixtures. By means of behavioral experiments, we were able to show that olfactory sensory adaptation reduces the learning level of pre-exposed stimuli, while enhancing the learning of stimuli that would be normally overshadowed by the major component of the mixture. Additionally, by performing calcium imaging experiments to measure odor induced signals in the olfactory system, we were able to show that the glomerular activation patterns elicited by a binary mixture, changes after pre-exposure of the animal to one of the components, resulting in a representation that drastically favors the underrepresented (or minor) component of the mixture. These results suggest that olfactory sensory adaptation is critical to allow detection of minor components present in complex in mixtures, and that it increases the sensibility of the animal to certain stimuli.

P161.-CB1 Receptor Agonist Protects The Retina From Light Induced Retinal Degeneration

Manuel Soliño, Ester María López, Laura Caltana, Alicia Brusco, Juan José López-Costa

IBCN ¨Prof. E. De Robertis¨, UBA-CONICET; Fac Med, UBA.
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Endocannabinoids are neuromodulators whose effects are mediated by G protein coupled receptors named CB1 and CB2. CB1 agonists play a neuroprotective role in glaucoma models of retinal injury. Light induced retinal degeneration (LIRD) is a model that resembles other human retinal degenerative diseases as AMD. The aim of this work was to evaluate the potential neuroprotective effect of the modulation of CB1 receptor in LIRD. The right eyes of Sprague Dawley rats were intravitreally injected either with ACEA (CB1 agonist), or AM251 (CB1 antagonist) while the left eyes received vehicle as controls. Later, rats were subjected to continuous illumination (12.000 lux) for 24 hs. Retinas were dissected out and processed by Western Blot (WB) using either antibodies to GFAP or to activated Caspase 3. The optical density data were statistically analysed using Student´s t-test and differences were considered significant when $p<0.05$. The eyes treated with ACEA showed retinas with significant lower levels of activated Caspase 3 and GFAP. Conversely, the eyes treated with AM251 showed retinas with significant higher levels of activated Caspase 3 and GFAP. The administration of ACEA previous to illumination stress was neuroprotective (decreased apoptosis and glial reactivity), while AM251 worsened retinal damage (increased apoptosis and glial reactivity) in LIRD. Although further work is needed, CB1 receptor agonism may be considered a potential neuroprotective strategy in AMD.

(Supported with grant form University of Buenos Aires, UBACYT 200-20130100675BA).

P162.-Interaction between sensory feedback and attention in a finger tapping task

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In the present work we investigate the effects of attention and sensory feedback on finger tapping performance. Subjects must synchronize to an auditory metronome and, after an abrupt tempo change, must resynchronize to the new tempo. It is expected that both, an increased level of attention and the addition of sensory feedback, will improve task performance. Preliminary results (N = 4) show that under this paradigm of augmented attention the mean asynchrony decreases and the resynchronization velocity increases with respect to a basal/normal level of attention. On the other hand, the presence of additional auditory feedback also decreases the mean asynchrony, but contrary to what is expected diminishes the resynchronization velocity after a tempo change.

P163.-Activation of presynaptic GABAB receptors minimize depression and enables sustained transmission at high rate stimulation of cholinergic olivocochlear-hair cell synapses

Carolina Wedemeyer [1°], Eleonora Katz [1°2°], Ana Belen Elgoyhen [1°3°]

1° Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Hector Torres" - INGEBI (CONICET), 2° 2Dpto. de Fisiología, Biología Molecular y Celular, FCEN, Universidad de Buenos Aires, 3° Instituto de Farmacología. Facultad de Medicina- UBA
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During development, medial olivocochlear (MOC) neurons transiently innervate cochlear inner hair cells (IHCs). Although acetylcholine (ACh) is the main neurotransmitter at this synapse, an abundant GABA innervation is also present. Electrical stimulation of MOC efferent fibers triggers the release of ACh, but also activates presynaptic GABAB receptors, that in turn reduce the amount of ACh released. GABA-mediated mechanism is through the inhibition of P/Q type Ca2+ channels. We are now studying the consequences of GABAB-mediated inhibition in the short-term plasticity of this synapse. Inhibitory synaptic currents (IPSC) were recorded in IHCs of acutely isolated organs of Corti at P9-P11, while MOC fibers were electrically stimulated. In control condition, 10 pulses applied at high frequency (50 Hz) resulted in a progressive decrease on IPSC amplitudes throughout the train (P10/P1= 0.54). On the contrary, the specific GABAB agonist baclofen, increased the facilitation rate and eliminated depression at the same frequency (P10/P1= 1). Moreover, application of CGP35348, a GABAB antagonist, produced a bigger depression even at low stimulation frequencies (10Hz). These results suggest that the activation of presynaptic GABAB receptor, minimizes depression and would enable sustained transmission during high-frequency stimulation at the MOC-inner hair cell synapse.

P164.-Kv7 channel openers and non-steroidal anti-inflammatory drugs decrease striatal cholinergic interneuron excitability

Rodrigo Manuel Paz, Cecilia Tubert, Agostina Stahl, Gustavo Murer, Lorena Rela

Grupo de Neurociencia de Sistemas, IFIBIO Houssay, Facultad de Medicina, UBA-CONICET
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Striatal cholinergic interneurons (SCIN) have emerged as key modulators of the striatal circuitry controlling voluntary movement. SCIN dysfunction has been involved in the genesis of movement disorders such as Parkinson's disease (PD) and L-DOPA-induced dyskinesia (LID). Therefore, a better understanding of SCIN physiology may provide new potential therapeutic targets for PD and LID. SCIN are autonomous pacemakers and display spike frequency accommodation in response to sustained current injection. Previous work found that blockade of Kv1 channels strongly increase SCIN excitability but the contribution of other voltage-dependent potassium channels has been less studied. Here we aim to disclose the role of Kv7 currents in SCIN excitability. Blockers of Kv7 channels had no effect on SCIN response to somatic current injection and spontaneous tonic firing but increased EPSP summation induced by intrastriatal electrical stimulation. Retigabine, a Kv7 channel opener, markedly decreased SCIN excitability, which was restored by subsequent addition of XE991. Non-steroidal anti-inflamatory drugs (NSAIDs) may behave as Kv7 channel openers. Interestingly, diclofenac and meclofenamic acid reproduced the effect of retigabine in a dose-dependent manner but XE991 failed to reverse this effect, suggesting that NSAIDs decrease SCIN excitability through a Kv7 independent mechanism. These results implicate Kv7 channels and NSAIDs targets as key regulators of SCINs excitability.

P165.-Histamine potentiates acid sensing ion channels (ASICs) currents at the giant Calyx of Held synapse.

Carlota Gonzalez Inchauspe, Osvaldo D. Uchitel

Instituto de Fisiología Biología Molecular y Neurociencias (IFIBYNE UBA CONICET)
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ASICs play an important function in physiologic processes and signal transduction associated with local and global extracellular pH variations during normal and pathological neuronal activity. We have identified homomeric ASIC1a-mediated currents during synaptic transmission at the calyx of Held synapse, suggesting an acidification of the synaptic cleft due to the co-release of neurotransmitter and H+ from synaptic vesicles. ASIC-1a current amplitudes are small relative to glutamatergic AMPA mediated excitatory postsynaptic currents. It is possible that some endogenous ligands may modulate ASICs and enhance their responses to physiologically significant levels. Indeed, we have found that micromolar concentrations of histamine significantly potentiate ASIC-1a currents. This potentiation may be due a shift of the activation dependence of ASIC-1a channels to less acidic conditions, increasing pH sensitivity. Histamine is involved in the immune and inflammatory response, and it also plays a role of a neurotransmitter in the central nervous system, regulating numerous physiological functions. The fact that histamine can target ASIC-1a channels is of great relevance since both histamine and ASIC receptors are implicated in many pathologies such as epilepsy, Alzheimer's disease, attention-deficit hyperactivity disorder, schizophrenia and multiple sclerosis.


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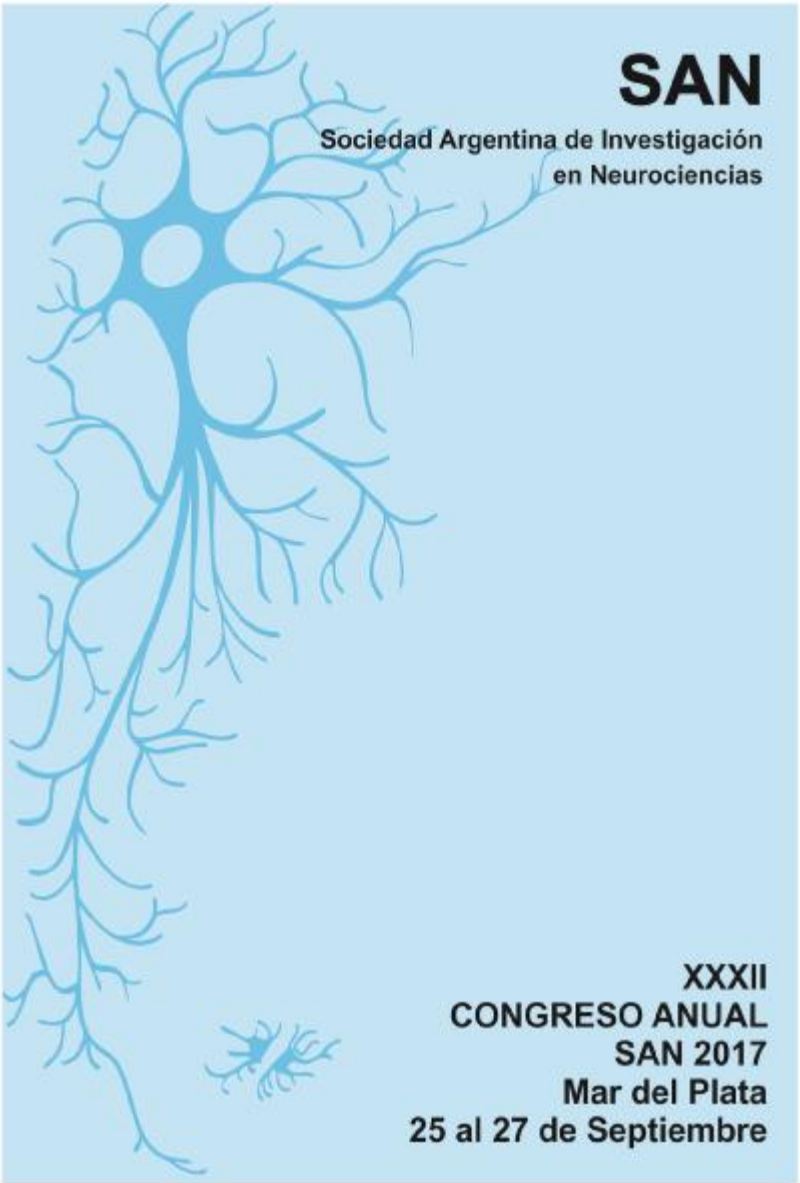

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Sociedad Argentina de Investigación en Neurociencias

XXXII CONGRESO ANUAL SAN 2017

Mar del Plata

25 al 27 de Septiembre

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XXXII Congress of the Argentine Society for Research in Neuroscience
Mar del Plata – September 25-28 , 2017

Curso Pre-Congreso

"Análisis Comportamental en Modelos Animales de Desórdenes Psiquiátricos"

Sabado 23/9

15:00h Acreditación

16:30-18:30h ¿Qué es un modelo animal?

19-21h Presentación de tests conductuales

Domingo 24
9-11h Modelos de ansiedad y depresión

11:30-12:30 Discusión de papers (ansiedad y depresión)

12:30-13:30 Lunch

14-16h Comportamientos sociales y modelos de autismo

16:30-18:30 Discusión de papers (autismo)

19-21 Modelos de esquizofrenia

Lunes 25
9-10:30 Discusión de papers (esquizofrenia)

11:00-12:30 Discusión general (orden de tests, estandarizacion y reproducibilidad, etc)

XXXII Congress of the Argentine Society for Research in Neuroscience

DAY 1 / Monday, 25th

09:00 - 15:00 Registration

15:00 - 15:05 Welcome by Organizers

15:05 - 15:55 **SPECIAL LECTURE / ROOM A**
Chair: Damian Refojo, IBIOBA-Max Planck Institute, Buenos Aires, Argentina, and Sebastian Kadener, Hebrew University of Jerusalem, Israel *and Brandeis University Waltham, MA, USA*

Michael Rosbash, Brandeis University, Waltham, USA
"Circadian Rhythms and RNA: Past, Present and Future"

16:00 – 18:30 **Symposium I and Symposium II**

SYMPOSIUM I / ROOM A
"Epigenetic: Interface between the environment and genome"
Chair: Eduardo Cánepa, FCEN, University of Buenos Aires

*"**Epigenetic signature of prenatal stress on adult offspring"***
Marcela Brocco, IIB, San Martín University, Buenos Aires, Argentina

"***Prenatal stress programs sex specific predisposition to Binge Eating through hypothalamic epigenetic adaptations at multiple levels"***
Mariana Schroeder, Max Planck Institute of Psychiatry, Munich, Germany

*"**DNA methylation dynamics and phenotypic plasticity in mouse models"***
Juan Young, University of Miami, USA

"Early life adversities and the epigenetic programming of gene expression"
Eduardo Cánepa, University of Buenos Aires, Argentina

SYMPOSIUM II / ROOM B

"Exocytosis and endocytosis in neuroendocrine cells"
Chair: Fernando Marengo, University of Buenos Aires, Argentina

"The actin binding protein cortactin regulates actin polymerization and exocytosis in neuroendocrine chromaffin cells"
Ana María Cárdenas, Valparaiso University, Chile

"Rab3A regulates the stability of exocytotic fusion pores in human sperm"
Claudia Tomes, Cuyo University, Argentina

"Immediately Releasable Pool (IRP) Exocytosis, Endocytosis and Vesicle Replenishment in Mouse Chromaffin Cells"
Fernando Marengo, University of Buenos Aires, Argentina

18:30 – 18:55 Coffee break

19:00 – 20:00 **EDUARDO DE ROBERTIS LECTURE / ROOM A**
Chair: Agustín Anastasia, Instituto de Investigación Médica Mercedes y Martín Ferreyra, Córdoba, Argentina

*"**Criticality in brain (and biological) function"***
Dante Chialvo, UNSAM University, Argentina

20:00 Welcome Reception / **ROOM C**

DAY 2 / Tuesday, 26th

08:30 – 11:00 **Symposium III and Symposium IV**

SYMPOSIUM III / ROOM A
"Decentralizing the central dogma: new perspectives of RNA function in neurobiology"
Chair: Damian Refojo, IBioBA-Max Planck Institute, Buenos Aires, Argentina

*"**RNA profiling ofcircadian neurons and behavior"***
Michael Rosbash, Brandeis University, Waltham, USA

"A Multi-step Transcriptional and Chromatin State Cascade Underlies Motor Neuron Programming from Embryonic Stem Cells"
Esteban Mazzoni, New York University, USA

"***Rounding the circle: Unravelling the molecular and physiological functions of circRNAs"***
Sebastián Kadener, Hebrew University of Jerusalem, Israel *and Brandeis University Waltham, MA, USA*

"**Small, Circular and Essential: Control of Neuronal Maturation by microRNAs and circRNAs"**
Damian Refojo, IBIOBA, Buenos Aires, Argentina

SYMPOSIUM IV / ROOM B
FALAN Young Investigator Symposium (FALAN-YI) 2017 – "Preclinical assessment of promising genetic, pharmacological and environmental treatments for alcohol consumption"
Chair: Ricardo Pautassi, INIMEC-CONICET, Córdoba University, Argentina

"**Inhibition of depressant effects of ethanol by mutations and small molecules affecting the glycine receptor"**
Luis Aguayo, University of Concepción, Chile

"**Intracerebral Stem Cell Administration Inhibits Chronic and Binge Alcohol Intake in Rats"**
Fernando Ezquer, del Desarrollo University, Santiago, Chile

"**An update on CRF mechanisms underlying alcohol use disorders and dependence"**
Isabel Quadros, Sao Paulo University, Brasil

"**Environmental Enrichment enhances alcohol intake in female adolescent rats"**
Ricardo Pautassi, INIMEC-CONICET, Córdoba University, Argentina

11:00 – 11:25 Coffee break

11:30 – 13:30 **Short talk by students I and II**

SESSION I / ROOM A
Chair: Abel Carcagno, Leloir Institute, Buenos Aires, Argentina

"An integrated model for motor control of song in canaries" - **Rodrigo Alonso**, Dinamic Systems Lab,, DF, FCEN, UBA.
"Enriched environment preserves visual functions and reduces neuroinflammation of the optic nerve" - **Marcos L. Aranda,** NROE, CEFyBO, UBA/CONICET.
"Blockade of D1/D5 dopaminergic receptors in the VTA promotes the persistence of weak appetitive memories" - **Fernando Castillo Díaz**, Laboratorio de Memoria, IBCN, FMED-UBA.
"The surprising effects of acute downregulation of a GABA receptor in Drosophila sleep behavior" - **Florencia Fernández**, IBioBA-CONICET-MPSP
"Activity regulated cytoskeleton-associated protein is required for consolidation of overlapping object, but not spatial memories in the perirhinal cortex" - **Magdalena Miranda**, INECO
"Neuromodulators in the processing of afferent inputs in the dentate gyrus" - **Mora Ogando**, IBioBA-MPSP-CONICET

SESSION II / ROOM B
Chair: Mariela Chertoff, FCEN, UBA, Buenos Aires, Argentina

"Analysis of NMDAR subunits expression after GluN2A knockdown in mature primary neuronal cultures" - **Maria Florencia Acutain**, IBCN, CABA
"Murine hippocampal encephalopathy derived from hemolytic uremic syndrome (HUS) produced by shiga toxin 2 (STX2) from enterohemorrhagic Escherichia coli (EHEC)" - **Clara V. Berdasco**, IFIBIO, UBA-CONICET
"Tetraspanins as promoters of TrkA receptor tyrosine kinase activation, downstream signaling and biological responses to NGF" - **Facundo N. Ferrero Restelli**, IBCN, UBA-CONICET.
"Perinatal malnutrition deregulates PRC2 catalytic subunits and Kdm6b expression" - **Estefanía A. Fesser**, Neuroepigenética Lab, QB, FCEN, UBA.
"The membrane glycoprotein M6a endocytic/recycling pathway involves clathrin-mediated endocytosis and affects neuronal synapses" - **Micaela D. Garcia**, IIB-UNSAM.

"Neural crest derivatives in the liver during development and in fibrogenesis"
R**omina Sierra**, IIMT CONICET- Austral University.

13:30 Lunch break

15:30 – 16:25 **HÉCTOR MALDONADO LECTURE / ROOM A**
Chair: Arturo Romano, IFIBYNE-FCEN, UBA, Buenos Aires, Argentina
"How are memories formed and stored for years to come?"
Rodrigo Quian Quiroga, Research Chair at the University of Leicester, UK.

16:30 – 19:00 **Poster session I: ODD NUMBERS / ROOMS A, C & D**

19:00 Asamblea Anual SAN

DAY 3 / Wednesday, 27th

08:30 - 11:00 **SYMPOSIUM V / ROOM A**
LOCAL SENIOR RESEARCHERS LECTURES
Chair: Mario Guido, CIBIQIC, FCQ, UNC, Córdoba, Argentina, and Liliana Cancela, IFEC, UCQ, UNC, Córdoba, Argentina

"Biological events associated with stress-induced resistance to the fear memory labilization/reconsolidation process"
Victor Molina, Córdoba University

"Generation of neuronal diversity through temporal and spatial patterning in the developing spinal cord"
Guillermo Lanuza, Leloir Institute, Buenos Aires.

"From the central nervous system to the circadian timing system: new paradigms on the road?"
Estela Maris Muñoz, IHEM, Mendoza

"Circadian rewiring of adult networks in Drosophila"
M. Fernanda Ceriani, Leloir Institute, Buenos Aires.

11:00 – 11:25 Coffee break

11:30 – 13:30 **Young Investigator Symposia I & II**

YOUNG INVESTIGATOR SYMPOSIA I / ROOM A
Chair: Antonia Marin Burgin, IBioBA-Max Plank Institute, Buenos Aires, Argentina

"Changes in NMDAR-GluN2A expression as marker of long term memory consolidation"
Baez, M. Verónica, FMED – UBA, Buenos Aires
"Signatures of conscious processing in the resting-state brain activity dynamics"
Sitt, Jacobo, ICM Research Center, Hôpital Pitié-Salpêtrière, France
"Prior stress promotes the generalization of contextual fear memories: Involvement of the gabaergic signaling whithin the basolateral amygdala complex"
Bender, Christian, IFEC-CONICET-UNC, Córdoba
"Role of microRNAs in the establishment of cognitive and emotive deficits derived from perinatal protein malnutrition"
Berardino, Bruno, FCEN-UBA, Buenos Aires

YOUNG INVESTIGATOR SYMPOSIA II / ROOM B

Chair: Alejandra Pacchioni, FCBF, UNR, Rosario, Argentina

"A Local Network Activated by Experience Accelerates the Integration of New Dentate Granule Cells"
Giacomini, Damiana, Leloir Institute, Buenos Aires
"The dentate gyrus role on spatial working memory"
Piatti, Verónica, IIBBA, Buenos Aires
"A novel therapeutic target for neurodegeneration and vascular damage in Retinopathies"
Barcelona, Pablo, FCQ, UNC, Cordoba
"Role of insulin like-peptides in neural control of stress response"
Veuthey, Tania, INIBIBB-DBByF-UNS. Bahia Blanca

13:30 Lunch break

15:30 – 17:55 **Poster session II: EVEN NUMBERS / ROOMS A, C & D**

18:00 – 18:30 **SAN AWARD: Best Doctoral Thesis in Neuroscience 2017**
ROOM A
Chair: Lorena Rela, IFIBIO, FMED, UBA, Buenos Aires, Argentina

"Spatio-temporal map of output connectivity of adult-born dentate granule cells"
Silvio G. Temprana, present address: University of California Berkeley, USA

18:30 – 19:30 **RANWEL CAPUTTO LECTURE / ROOM A**
Chair: María Fernanda Ceriani, Leloir Institute, Buenos Aires, Argentina

"Time in the Brain. Biological Rhythms Clocks in the Lab, to Infinity and Beyond"
Diego Golombek, UNQ, Quilmes, Argentina

19:30 – 19:45 **SAN AWARD to best talks by students & Closing remarks**

21:00 Party in "Espigón de Pescadores".

LECTURE ABSTRACTS

Monday, 25th - 15:05 - 15:55 SPECIAL LECTURE / ROOM A

Circadian Rhythms and RNA: Past, Present and Future

Michael Rosbash
BrandeisUniversity, Waltham, MA, USA

There is a long history of circadian rhythm research, but the modern era began with the now famous Konopka and Benzer 1971 publication on Drosophila. It began the molecular genetics revolution that founded modern behavioral genetics, in mammals as well as flies. I will discuss past history, the present research landscape, describe some important unanswered questions and try to anticipate some future directions.

Monday, 25th - 19:00 – 20:00 EDUARDO DE ROBERTIS LECTURE / ROOM A

Criticality in brain (and biological) function

Dante R Chialvo
Center for Complex Systems & Brain Sciences (CEMSC3), CONICET & Universidad Nacional de San Martın, Buenos Aires, Argentina

It is increasingly accepted that the working brain stays at an intermediate "critical" regime, in between the extremes of highly synchronized states and weakly correlated dynamics. In the last decade, evidence of such criticality has been collected at very different scales, from molecules to single cells, from cortex cultures to full brain neuro-imaging. This viewpoint, introduced by us in the 90's, proposes that some of the most fundamental properties of the functioning brain are only possible because it is spontaneously posed at the border of such (critical) instability. I will first describe briefly the main argument, illustrated with the most significant results, and then explore the implications of this view for the functioning brain.

Tuesday, 26th - 15:30 – 16:25 HÉCTOR MALDONADO LECTURE / ROOM A

How are memories formed and stored for years to come?

Rodrigo Quian Quiroga
Centre for Systems Neuroscience, University of Leicester, United Kingdom

Intracranial recordings in patients suffering from intractable epilepsy allow studying the firing of multiple single neurons in awake and behaving human subjects. These recordings are typically done in the hippocampus and surrounding cortex, an area known to be critical for memory functions. Using the unique opportunity to record directly from such neurons in the human brain, about 10 years ago we found what has been named 'Concept Cells' or 'Jennifer Aniston Neurons' – neurons that represent specific concepts, responding to particular persons or objects, such as Jennifer Aniston, Luke Skywalker or the Sydney Opera House. In this talk will show more recent work on how these neurons are involved in forming and storing declarative, and particularly episodic memories - the memories we have of our life experiences.

Wednesday 27th - 18:30 – 19:30 **RANWEL CAPUTTO LECTURE / ROOM A**

Time in the Brain. Biological Rhythms Clocks in the Lab, to Infinity and Beyond

Diego A. Golombek

Universidad Nacional de Quilmes / CONICET, Buenos Aires, Argentina.

Biological timing encompasses several orders of magnitude, ranging from the microsecond to the year. Among these frequencies, circadian (i.e., about 24 h) rhythms and interval timing (i.e., in the second-to-minute range) have been thoroughly studied in several organisms. In mammals, circadian rhythms are generated in the main biological clock located in the hypothalamic suprachiasmatic nuclei (SCN) which are entrained by environmental signals such as the light-dark cycle through a dedicated retinohypothalamic tract. Most, if not all, physiological and behavioral variables exhibit such circadian variations, which resonate throughout the body thanks to peripheral oscillators. Here we will focus on the signal transduction mechanisms responsible for mammalian entrainment, specifically involving the cGMP/nitric oxide pathway. In addition, as an example of circadian control, we have demonstrated diurnal changes in immune parameters which, in turn, feedback into the SCN in order to fine-tune the biological clock. Experimental models of circadian desynchronization result in severe metabolic disruption, which might represent a window into human situations which compromise entrainment, such as chronic jet lag or shift work. Indeed, in recent years, the importance of an adequate internal (i.e., among organs) and external (i.e., between the body and the environmental) synchronization has been accepted. Diverse diseases involve a varying degree of circadian disruption which, when adequately targeted, might improve the outcome and quality of life of human patients.

SYMPOSIUM ABSTRACTS

Monday 25th - 16:00 – 18:30 SYMPOSIUM I / ROOM A
"Epigenetic: Interface between the environment and genome"
Chair: Eduardo Cánepa, FCEN, University of Buenos Aires

Epigenetic signature of prenatal stress on adult offspring

Marcela A. Brocco[1] Melisa C. Monteleone[1], María Eugenia Pallarés[2], Marta C. Antonelli[2]

[1]. Instituto de Investigaciones Biotecnológicas - Instituto Tecnológico de Chascomús (IIB-INTECH).Universidad Nacional de San Martín - Consejo Nacional de Investigaciones Científicas y Técnicas(UNSAM-CONICET)

[2]. Instituto de Biología Celular y Neurociencias "Prof. Eduardo De Robertis", Facultad de Medicina, Universidad de Buenos Aires.

Prenatal stress (PS) strongly impacts on offspring, affecting gene expression and adult behavior. We studied the epigenetic signature (gene expression, microRNA levels, methylation status) in the hippocampus of adult offspring of pregnant rats subjected to PS. Our previous work showed that chronic stress alters the mRNA levels of GPM6A, a neuronal glycoprotein involved in filopodium extension. Now, we observed that PS also affects gpm6a expression. PS significantly modified the microRNA-133b levels, as well. Moreover, microRNA-133b was validated as a gpm6a regulator. In addition, PS significantly altered the bdnf, mef2a, suv39h1 and tet1 mRNA levels. Together with a reduced total 5-hydroxymetylcytosine content, our findings suggest that part of the long-lasting PS effects are linked to changes in plasticity genes and in the chromatin methylation pathway. Notably, PS altered the methylation pattern within two CpG islands in the gpm6a gene. PS-induced molecular changes alter neural connectivity, increasing the risk for neuropsychiatric disorders. Because of their antidepressant-like effects, histone deacetylase inhibitors (HDACi) are being broadly studied. We treated primary neuron cultures with the HDACi apicidin. It increased GPM6A expression and induced filopodium extension. In summary, PS affected the epigenetic machinery resulting in long-term effects. We propose gpm6a as a novel target for epigenetic regulation and for pharmacological manipulation to revert PS effects.

Prenatal stress programs sex specific predisposition to Binge Eating through hypothalamic epigenetic adaptations at multiple levels

Mariana Schroeder, Mira Jakovcevski, Tamar Polacheck, Maya Lebow, Yonat Drori, Shifra Ben-Dor and Alon Chen

Max Planck Institute of Psychiatry, Munich, Germany

Binge eating (BE) is a common aberrant form of eating behavior, characterized by overconsumption of food in a brief period of time. Recurrent episodes of BE constitute the BE disorder, which like all eating disorders mostly affects females and is frequently associated with early-life adversities. In the present study, we show that prenatal stress (PNS) in the form of corticotropin releasing factor (CRF) overexpression in late gestation predisposes female offspring to BE-like behavior that coincides with hypomethylation of hypothalamic miR-1a locus and downstream

dysregulation of the melanocortin system through Pax7/Pax3. Moreover, exposing the offspring to a diet balanced in methyl donors during adolescence can prevent the dysregulation and predisposition from being triggered. We demonstrate that gestational programming, per se will not lead to BE-like behavior, but pre-existing alterations due to stress-related prenatal programming are revealed only when challenged during adolescence. We provide experimental evidence for long-term epigenetic hypothalamic abnormalities stemming from PNS in predisposing specifically female offspring to BE disorder as well as a potential non-invasive prevention strategy.

DNA methylation dynamics and phenotypic plasticity in mouse models

Juan Young
University of Miami, USA

DNA methylation is a stable epigenetic modification with a critical role in transcriptional regulation. Experience-dependent gain or loss of DNA methylation reshapes the genomic landscape of brain cells, potentially participating in the dynamic regulation of neural circuits. We will discuss the possible roles of DNA methylation in experience-dependent modulation of phenotypic plasticity in mice. Current evidence focusing on the effects of environmental manipulation (administration of drugs of abuse; environmental enrichment) on the brain epigenome and phenotypic manifestations in mice will be presented. We will also discuss whether epigenetic processes may be involved in the passage of induced traits between generations. Overall, current findings suggest that environmental exposures of sufficient biological impact are associated with long-lasting epigenetic changes. These epigenetic changes are a likely mechanistic platform linking the effects of developmental exposure to behavioral and neurobiological phenotypes.

Early life adversities and the epigenetic programming of gene expression

Eduardo T. Cánepa
Departamento de Química Biológica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires and CONICET

The quality of brain architecture is established early in life through a series of dynamic interactions in which environmental conditions and personal experiences have a significant impact on the establishment of genetic programming. Current work suggests that epigenetic mechanisms of gene regulation could explain how early life experiences can leave indelible chemical marks on the brain and influence both physical and mental health later in life even when the initial trigger is long gone. When it comes to the effects of adverse environmental stimuli on individual health there are two main and seemingly contradicting views. The “cumulative stress” hypothesis sustain that the stress exposure during a lifetime are accumulative and predispose individuals to be more vulnerable to aversive challenges later in life. The mismatch hypothesis, on the other hand, states that aversive experiences early in life trigger adaptive processes, thereby rendering an individual to be better adapted to aversive challenges later in life. A third and integrative hypothesis considers that specific genes or genetic variants may predispose an individual to be more

susceptible to environmental influences. Finally, as an interface mechanism between genetic and environment several features of epigenetic should be considered when discussing health inequalities: epigenetic traits are established early in development and their effects on health persist throughout the life course; epigenetic are highly responsive to environmental changes which are affected by social institutions; there are evidences that epigenetic traits can be transgenerationally inherited.

Monday 25th - 16:00 – 18:30 SYMPOSIUM II / ROOM B

"Exocytosis and endocytosis in neuroendocrine cells"

Chair: Fernando Marengo, University of Buenos Aires, Argentina

The actin binding protein cortactin regulates actin polymerization and exocytosis in neuroendocrine chromaffin cells

Arlek M. González-Jamett, María José Guerra, Ximena Baez-Matus, Jacqueline Vásquez-Navarrete, **Ana M. Cárdenas**

Valparaiso University, Chile

Cortactin is an actin-binding protein that promotes actin polymerization in synergy with the nucleation promoting factor N-WASP. In the present work we examined the role of cortactin in the Ca2+-induced formation of actin filaments and exocytosis. With this aim we expressed in bovine chromaffin cells different cortactin domains or mutants enable to interact with proline-rich domain (PRD)-containing proteins, like including N-WASP, or to be phosphorylated by Ca2+-dependent kinases, such as ERK1/2 or and Src. Our results show that the activation of nicotinic receptors in chromaffin cells promotes cortactin translocation to the cell cortex, where it colocalizes with actin filaments. We further found that, in association with PRD-containing proteins, cortactin contributes to the Ca2+-induced actin filament formation and to regulate fusion pore dynamics and number of exocytotic events induced by activation of nicotinic receptors. However, whereas the actions of cortactin on fusion pore dynamics depend on the availability of monomeric actin and cortactin phosphorylation by ERK1/2 and Src kinases, this actin binding protein regulates the extent of exocytosis by a mechanism independent of actin polymerization, and that is determined by its phosphorylation by ERK1/2. Together our findings point out a role for cortactin as a critical modulator of actin filament formation and exocytosis in neuroendocrine cells.

This work has been supported by the grants FONDECYT 1160495 and P09-022- F from ICM-ECONOMIA, Chile.

Rab3A regulates the stability of exocytotic fusion pores in human sperm.

Claudia Nora Tomes

Instituto de Histología y Embriología de Mendoza (IHEM) "Dr. Mario H. Burgos" CONICET. Universidad Nacional De Cuyo. Facultad de Ciencias Médicas, Argentina

Secretory cells undergo regulated exocytosis in response to physiological signals. At the final stage of exocytotis, a fusion pore opens between the plasma and a secretory vesicle membranes; typically, when the pore dilates the vesicle releases its cargo. My lab uses the exocytosis of the acrosomal vesicle of human sperm (the acrosome reaction or AR) as model system. Each sperm contains a single, very large and

electron dense granule whose contents are secreted by regulated exocytosis at fertilization. The acrosomal membrane fuses at multiple points with the plasma membrane that overlies the anterior part of the head. Joining of pores originates hybrid plasma membrane-outer acrosomal membrane vesicles. The AR is completed when vesicles and acrosomal contents are shed. The exocytosis of the acrosome depends on members of the standard fusion machinery, including small GTPases and SNAREs. Geranylgeranylated and active Rab3A elicits the AR per se. Its carboxy-terminus domain is necessary and sufficient to promote exocytosis whereas its amino-terminus prevents calcium-triggered secretion. because it stabilizes open fusion pores. Sperm SNAREs engage in α-SNAP/NSF-sensitive complexes at a post-fusion stage. In other words, vesiculation is not spontaneous; rather, post-fusion regulation of the pores determines their expansion and the success of the AR.

Immediately Releasable Pool (IRP) Exocytosis, Endocytosis and Vesicle Replenishment in Mouse Chromaffin Cells

Fernando D. Marengo

Instituto de Fisiología, Biología Molecular y Neurociencias, (CONICET). Departamento de Fisiología y Biología Molecular y Celular. Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina

IRP is a pool of vesicles selectively released by brief stimuli. Consequently it might be responsible of chromaffin cell secretion at basal action potential frequency. We previously determined that IRP exocytosis is mainly dependent on a tight coupling between its vesicles and P/Q Ca 2+ channels via the synprint site of the channel. Using membrane capacitance measurements, we recently analyzed the process of exocytosis recovery after the application of an action potential like stimulus (AP ls). The exocytosis triggered by AP ls (ETAP) represents a fraction of IRP (11±2 fF), and recovered with a time constant of 0.730.11 s, what is fast enough to maintain synchronous exocytosis at 0.2-0.5 Hz stimulation. We noted that this recovery process is partially dependent on the transference of vesicles from upstream pools. However, since we regularly observed a fast endocytosis (τ=0.71±0.21 s) after ETAP, we studied the possibility that this process might be also involved in ETAP recovery. When we inhibited fast endocytosis with dynasore, nitrendipine, an anti-dynamin monoclonal antibody, or the dynamin inhibitory peptide GST-Dyn 829-842 , ETAP recovery was delayed respect to the control condition. The application of the same antibody also provoked the progressive inhibition of synchronous exocytosis during low frequency AP ls stimulation. Therefore, we conclude that a fast dynamin-dependent endocytosis is involved in rapid ETAP recovery and in the maintenance of exocytosis at basal APls frequencies.

Tuesday, 26th - 08:30 – 11:00 SYMPOSIUM III / ROOM A
"Decentralizing the central dogma: new perspectives of RNA function in neurobiology"
Chair: Damian Refojo, IBIOBA-Max Planck Institute, Buenos Aires, Argentina

RNA profiling of circadian neurons and behavior
Michael Rosbash
BrandeisUniversity, Waltham, MA, USA

The Drosophila circadian clock functions within 75 pairs of central brain neurons. They are arranged in 7-8 subgroups, each of which is in a specific location with a set of defined anatomic features. We are expanding our understanding of several of these subgroups, including their contributions to behavior, their regulation of sleep and their circuitry. To this end, we have used neuronal purification and deep sequencing "around the clock" to analyze and profile RNA from several of these circadian subgroups as well as from specific non-circadian neurons. The profiling and subsequent characterization has identified molecules that are expressed in discrete neuron subgroups and contribute to specific behavioral modalities.

A Multi-step Transcriptional and Chromatin State Cascade Underlies Motor Neuron Programming from Embryonic Stem Cells
Esteban Mazzoni
New York University, New York, USA

Direct cell programming via overexpression of transcription factors (TFs) aims to control cell fate with the degree of precision needed for clinical applications. However, the regulatory steps involved in successful terminal cell fate programming remain obscure. We have investigated the underlying mechanisms by looking at gene expression, chromatin states, and TF binding during the uniquely efficient Ngn2, Isl1, and Lhx3 motor neuron programming pathway. Our analysis reveals a highly dynamic process in which Ngn2 and the Isl1/Lhx3 pair initially engage distinct regulatory regions. Subsequently, Isl1/Lhx3 binding shifts from one set of targets to another, controlling regulatory region activity and gene expression as cell differentiation progresses. Binding of Isl1/Lhx3 to later motor neuron enhancers depends on the Ebf and Onecut TFs, which are induced by Ngn2 during the programming process. Thus, motor neuron programming is the product of two initially independent transcriptional modules that converge with a feedforward transcriptional logic.

Rounding the circle: Unravelling the molecular and physiological functions of circRNAs
Sebastian Kadener
Hebrew University of Jerusalem (Jerusalem, Israel) and Brandeis University Waltham, MA, USA

Circular RNAs (circRNAs) are a very abundant type of newly described RNA species. Two of them work as miRNA sponges and one buffers the activity of a RNA binding protein, but no function has been assigned for the other thousands of circRNAs expressed across the animal kingdom. Recently, work from our lab has uncovered the mechanism by which these molecules are produced. Moreover, we identified the splicing factor muscleblind as the first modulator of circRNAs production. Here we will present new data regarding the molecular and physiological functions of circRNAs. First, and by combining state of the art methodologies, we demonstrate that a subset of circRNAs produce proteins in neural tissue. Interestingly, we found that circRNAs are translated by membrane-bound ribosomes and that this translation is regulated by FOXO in the fly brain. Second, by generating and testing a collection of 75 fly strains in which specific circRNAs are downregulated we demonstrated their functionality in vivo. We observed that downregulation of eight circRNAs resulted in total/ partial developmental lethality and that downregulation of other four circRNAs resulted in distinct defects in locomotor activity, circadian rhythms and sleep patterns. Moreover, for two of those circRNAs we have investigated the molecular mechanism mediating these defects. Together, our results constitute the first proof of functionality of circRNAs at the organismal level and provide a methodological approach to tackle this issue comprehensively.

Small, Circular and Essential: Control of Neuronal Maturation by microRNAs and circRNAs

Damian Refojo

IBioBA-Max Planck Institute of Buenos Aires, Buenos Aires, Argentina

MicroRNAs (miRNAs) are conserved noncoding RNAs that function as posttranscriptional regulators of gene expression. The current toolkit to investigate the role of miRNAs in vivo is very limited. We developed a transgenic miRNA sponge mouse line that allows the conditional inactivation of the miR-9 family (the most abundant miRNA in the brain) in a spatio-temporal-controlled manner. Using this novel approach, we found that miR-9 controls dendritic growth and synaptic transmission in vivo mostly by repressing the transcriptional repressor REST. Recently studies also indicate that a new class of non-coding RNA, the circular RNAs (circRNAs) might also exert fundamental roles in neuronal development and function. Recent profiling studies suggest that circRNAs are enriched in the brain, increase with neuronal maturation and are abundant in synapses. A first description about the role of the most abundant circRNAs in neuronal development and function will be discussed.

Tuesday, 26th - 08:30 – 11:00 SYMPOSIUM IV / ROOM B

FALAN Young Investigator Symposium (FALAN-YI) 2017 – "Preclinical assessment of promising genetic, pharmacological and environmental treatments for alcohol consumption"

Chair: Ricardo Pautassi, INIMEC-CONICET, Córdoba University, Argentina

Inhibition of depressant effects of ethanol by mutations and small molecules affecting the glycine receptor

Aguayo LG, Muñoz, B. San Martin, L. Guzman, L.
University of Concepcion, Concepcion, Chile

Alcohol abuse is a worldwide problem that causes major social, medical and economic burdens. Therefore, the search for novel, mechanistically oriented therapies is of utmost importance. Basic residues in the intracellular loop of the glycine receptor (GlyR) 1 subunit (316-320 and 385/386) are important for the receptor´s sensitivity to low concentrations of ethanol (5-50 mM). The pharmacological effects of the mutations are specific for ethanol, since the sensitivity to neurosteroids, isoflurane, propofol and Zn2+ are unchanged. Therefore, we generated and studied a Knock In (KI) mouse for 1 GlyRs with mutations in residues 385/386 of the receptor. The KI mice had normal behavior and most importantly did not display a hyperexcitable phenotype demonstrating that the mutation is primarily silent. The study of spinal and brainstem neurons with electrophysiological techniques showed that native GlyRs were less affected by ethanol- and G--mediated modulations. The data also showed that a tonic 1GlyR-mediated current in accumbal neurons, that modulates neuronal excitability, was exclusively sensitive to ethanol only in WT mice. Behavioral studies demonstrated that the KI mice have higher binge drinking and conditioned place preference indicating that GlyRs in the nAc may have a protective role against abuse. Interestingly, the mice exhibited a reduced loss of righting reflex (LORR) time when compared with WT. Results from the DID protocol showed that the KI mice went into binge drinking from day 1 of exposure, drinking three times more than the WT mice. In conclusion, we identified important amino acids that participate in the modulation of GlyR by ethanol. The study opens a novel opportunity for pharmacotherapy development to treat alcohol use disorders.
Supported by Fondecyt DPI 20140008 grant

Intracerebral Stem Cell Administration Inhibits Chronic and Binge Alcohol Intake in Rats

Fernando Ezquer[1] ,María Elena Quintanilla[2], Paola Morales[2] , Marcelo Ezquer[1] Mario Herrera-Marschitz[2] and Yedy Israel[2]
[1]Centro de Medicina Regenerativa, Facultad de Medicina Clínica Alemana-Universidad del Desarrollo, Santiago, Chile
[2]Instituto de Ciencias Biomédicas-Universidad de Chile, Santiago, Chile.

Alcohol use disorders are accompanied by hippocampal neuronal damage, cognitive deficits and binge-drinking relapse. Neuroinflammation appears to be partly responsible for these dysfunctions, perpetuating chronic alcohol drinking. Studies in

rodents show that chronic ethanol intake, involving the action of lipopolysaccharide and likely salsolinol, leads to neuroinflammation and production of oxidative stress, which act synergistically.In these animals, the administration of N-acetyl cysteine, a strong antioxidant, inhibits chronic ethanol intake by 60-70%, indicating that the reduction in reactive oxygen species (ROS) and inflammatory molecules in the brain has a direct impact on alcohol intake. However, the inhibitory effect of N-acetyl cysteine on alcohol intake required daily administration and disappeared 96-hours after discontinuing its administration. Mesenchymal stem cells (MSCs) of allogeneic origin have emerged as a promising tool for the treatment of a variety of neurodegenerative diseases since these cells can secrete a broad range of neuroprotective factors but also anti-inflammatory cytokines and ROS scavengers. Using an animal model of high alcohol-intake, we demonstrated that the single intra cerebro ventricular administration of MSCs obtained from bone marrow or adipose tissue of alcohol-naïve rats markedly inhibits chronic alcohol intake. Furthermore, MSC administration resulted in an 80-85% reduction of alcohol binge-drinking upon ethanol re-access compared to untreated rats. A marked inhibition of re-access intake (60%) continued 40 days after the single MSC administration (four cycles of alcohol deprivation and re-access), suggesting a marked remodelling or inhibition of the brain reward systems. The inhibitory effect of MSCs on alcohol intake was already significant 24 hours after its administration. Thus, it is likely that these early effects are due to the release of soluble factors by the MSCs.This study constitutes the first proof-of-principle demonstration that the intracerebral administration of MSCs inhibits chronic ethanol intake and virtually reverses the ethanol relapse-like phenotype observed following alcohol deprivation. We are presently evaluating if the intracerebral administration of human-derived MSCs into alcoholic rats is able to replicate the therapeutic effect.

Supported by Fondecyt # 1170146; # 1130012, #1150589, #1150850, Conicyt ACT1411 and Millennium Initiative #P09-015-F.

An update on CRF mechanisms underlying alcohol use disorders and dependence

Isabel Marian Hartmann Quadros, Giovana Camila Macedo, Liz Paola Domingues, Cristiane Aparecida Favoretto.

Department of Psychobiology, Escola Paulista de Medicina, Universidade Federal de São Paulo. São Paulo, SP, Brazil

Alcohol is the most commonly used and abused substance worldwide. The emergence of alcohol use disorders, and alcohol dependence in particular, is accompanied by functional changes in brain reward and stress systems, which contribute to escalated alcohol drinking and seeking. Corticotropin Releasing Factor (CRF) systems, including the closely related peptides Urocortins, have been critically implied in the transition towards problematic alcohol drinking and alcohol dependence. After repeated and chronic exposure to alcohol, rats present hyperactive extra-hypothalamic CRF activity, as indicated by increases in CRF immunoreactivity and/or increases in mRNA for CRF and its receptors in amygdala nuclei and the BNST. Consistently, increased alcohol seeking and intake can be attenuated after the administration of antagonists to CRF type 1 receptors (CRFR1),

particularly in animals with extensive history of alcohol exposure or escalated drinking. While blocking CRFR1 attenuates alcohol drinking, this effect can also be achieved with the activation of CRFR2 signaling, suggesting opposite roles for CRFR1 and CRFR2 in the modulation of excessive alcohol intake. However, manipulation of CRF receptor signaling in different brain regions may reveal differential effects and interactions between CRFR1 and CRFR2. Pharmacological studies start to unveil a role for both CRF receptors within brain reward pathways, as well as CRF binding protein, as critical modulators of escalated alcohol drinking. Moreover, CRF/Urocortin signaling is also recruited during other alcohol-related effects, including alcohol-induced behavioral sensitization, alcohol-escalated aggression and alcohol withdrawal-related anxiety. While effects of alcohol on the HPA axis, the amygdala and other stress-related structures have been more widely characterized, promising contributions of CRF/Urocortin signaling in brain reward pathways and other structures are starting to emerge and will be discussed.

Environmental Enrichment enhances alcohol intake in female adolescent rats

Ricardo Pautassi, Luciana Berardo, María Carolina Fabio
Instituto de Investigaciones Médicas M. y M. Ferreyra (INIMEC-CONICET-UNC), Córdoba, Argentina

There is considerable interest in the use of enriched environments (EE) to prevent development of alcohol (i.e., the drug also known as ethanol) and other drug disorders. Exposure to EE, which in rodents involve larger-than-usual home cages with interactive objects, including tunnels, toys and running wheels that provide opportunity for voluntary physical activity, reduces alcohol drinking, alcohol-induced behavioral sensitization (Rueda et al., 2012) and the rewarding effects of this drug (de Carvalho et al., 2010) and cocaine (Solinas et al., 2009. There are, however, conflicting results, with a few, yet intriguing, studies (e.g., Fernandez-Teruel et al., 2002) indicating greater ethanol intake after prolonged EE exposure. In this work, we assessed ethanol intake in adolescent rats, males and females, exposed to maternal separation during infancy (postnatal days 1-21) and environmental enrichment (EE) during adolescence (postnatal days 21-41). Ethanol intake was tested in 12, two-bottle daily sessions, spread across 30 days. We found a significant, two fold increase (i.e., approximately 6.0 vs 3.0 g/kg/24h) in ethanol intake in males – but not in females -- that had been exposed to EE than in control counterparts, an effect that was not modified by maternal separation. In other experiments we assessed several effects of EE that could explain its promoting effect upon ethanol intake. Ethanol-induced sleep time, sedation and aversion were unaffected by EE, which also did not modify anxiety response patterns. EE, nevertheless, resulted in greater novelty seeking and risk taking behaviors, which were evaluated in a modified version of the concentric square field test. These results put a cautionary note to the use of enriched environments as a means to prevent alcohol initiation, at least during adolescence, a developmental stage characterized by high levels of sensation seeking and novelty response. It is possible that exposure to EE further exacerbates this age-typical behaviors, thus increasing the risk for alcohol initiation and escalation. Future studies should take into account this potential side-effect of EE.

Wednesday, 27th - 08:30 - 11:00 SYMPOSIUM V / ROOM A
LOCAL SENIOR RESEARCHERS LECTURES
Chair: Mario Guido, CIBIQIC, FCQ, UNC, Córdoba, Argentina, and Liliana Cancela, IFEC, UCQ, UNC, Córdoba, Argentina

Biological events associated with stress-induced resistance to the fear memory labilization/reconsolidation process

Victor A. Molina
Instituto de Farmacología Experimental (IFEC)-CONICET. Facultad de Ciencias Químicas. Universidad Nacional de Córdoba

It is well known that consolidated fear memories can enter into a labile state after reactivation followed by a restabilization process defined as reconsolidation. Reactivation-induced destabilization renders memories sensitive to pharmacological interference within a limited time window. Our findings revealed that prior stress resulted into a memory trace that was insensitive to pharmacological interference. Moreover, we observed an enhanced expression of both Zif-268 and the subunit GluN2B-two molecular markers of the labilization/reconsolidation process-following reactivation.in the Basolateral Amygdala Complex (BLA) in control animals. However, no elevation was evidenced in stressed animals.D-cycloserine (DCS), a partial agonist of NMDA sites, administered prior to reactivation restored the vulnerability to the drug interfering effect and the elevation of Zif-268 in the BLA of stressed animals.

We also explored the role of the GABAergic signaling within the BLA on stress-induced resistance. The intra-BLA infusion of Midazolam (MDZ) prior to stress prevented such resistance. In addition, the blockade of GABA-A receptors in BLA prevented the drug interfering effect, similar to that observed with stress exposure. Overall, evidence suggests that the GABAergic signaling within BLA, at the moment of memory encoding, is determinant for the induction of fear memory resistance to the onset of the labilization/reconsolidation process.

Generation of neuronal diversity through temporal and spatial patterning in the developing spinal cord

Guillermo Lanuza
Developmental Neurobiology Lab. Leloir Institute, IIBBA-CONICET. Buenos Aires, Argentina

Considerable progress has been made in understanding the mechanisms that control the production of specialized neuronal types. However, how differentiation timing contributes to neuronal diversity in the developing spinal cord is still a pending question. We have found that the CerebroSpinal Fluid-contacting Neurons (CSF-cNs), an enigmatic cell type of the central canal, arise from unique unrecognized late

neurogenic events in the mouse spinal cord. The genetic program that sustains neuronal differentiation at the gliogenic phase of development are unknown. In this work, we identified that the transcription factors Ascl1, Gata3 and Gata2 sequentially control the specification of CSF-cNs. Through expression analysis and mouse genetics, we discover that Ascl1 is restricted to progenitors that give rise to CSF-cNs. By temporally dissecting Ascl1 activity in vivo, we found that this proneural protein confers neurogenic potential to late progenitors by suppressing ependymal fate, and initiates CSF-cN differentiation. Furthermore, we discover that, downstream of Ascl1, the acquisition of the precise CSF-cN identity depends on the postmitotic action of Gata3 and Gata2. In summary, we demonstrate that Ascl1-Gata3/2 are essential components of the temporally restricted transcriptional program that controls spinal cord late-born neuron specification.

From the central nervous system to the circadian timing system: new paradigms on the road?

Estela M. Muñoz

IHEM-UNCuyo-CONICET–Mendoza, Argentina.

Now it is known that every cell possesses the molecular machinery to generate its own circadian oscillations. In multicellular organisms, however, a circadian timing system synchronizes each cell to temporal cues according to its need, which modulates overall physiology and behavior. The circadian system is a multisynaptic circuit that transduces photic information into chemical signals, and the pineal gland is one of its key components. How the whole circadian system is developed, and what allows this system to be plastic and adaptive, along with its precision, are questions that are still not fully answered. It has therefore been of special interest for us to study the cellular, molecular and genetic mechanisms behind the ontogeny and plasticity of circadian clocks. We have been using the highly rhythmic pineal gland from conventional and genetically modified rodents, as a biological model. Furthermore, we have been comparing pineal ontogeny to the development of the central nervous system (CNS). Differential mechanisms that involve common players such as transcription factors, have emerged from these comparative studies. The participation of constantly ‘activated’ microglial cells on pineal ontogeny and homeostasis has also been characterized, as compared with a more complex spectrum of microglia phenotypes in the brain. Recently published data and future avenues will be presented in this talk. It is expected that a better knowledge of normal development of the circadian system will facilitate our understanding of associated pathologies, including developmental disorders and neurodegenerative diseases.

Circadian rewiring of adult networks in Drosophila

M. Fernanda Ceriani

Laboratorio de Genética del Comportamiento. Instituto Leloir. IIB-BA CONICET, Buenos Aires, Argentina

Oscillations between day and night are dominant, at times neglected, evolutionary driving forces. To cope with such challenges, biochemical timers that run with periods similar to the earth's rotation(¨circadian clocks¨) have evolved. The fruit fly Drosophila melanogaster has been instrumental in understanding how these timekeeping systems work at the molecular level, and to demonstrate that multiple layers of interconnected cellular mechanisms are recruited by the clock to ensure its function. Clock neurons in the brain sustain a cell autonomous clock but rely on the communication among each other for entrainment (i.e., a response to a change in the environmental conditions) and phase adjustments. Aside from neuropeptides and classical neurotransmitters that are differentially released throughout the day, circadian remodeling of the neuronal terminals of clock neurons could contribute to the reconfiguration of the circadian network, necessary to adjust to changes in photoperiod. Such circadian structural plasticity would provide a mechanism by which a neuron can exert sequential control of different target circuits along the day.

Wednesday, 27th - 11:30 – 13:30 YOUNG INVESTIGATOR SYMPOSIA I/ ROOM A

Chair: Antonia Marin Burgin, IBioBA-Max Plank Institute, Buenos Aires, Argentina

Changes in NMDAR-GluN2A expression as marker of long term memory consolidation.

María Verónica Baez

Instituto de Biología Celular y Neurociencia (IBCN)-CONICET

Facultad de Medicina – UBA

NMDA receptors (NMDAR) play a critical role in synaptic plasticity, memory encoding and storage. These receptors are heterotetramers composed by two obligatory GluN1 subunits and two regulatory subunits: GluN2 (A-D) or GluN3 (A-B), being GluN2A and GluN2B the major regulatory subunits in central areas related to cognitive functions (see Shipton and Paulsen, 2014). It was already shown that there is an increase of GluN1 and GluN2A 70’ after 5’ exploration leading to habituation to an open field, in rat hippocampus of young adults Wistar rats (Cercato et al, 2017). We hypothesize that this NMDAR subunits increase could be related to memory tracing; hence, we investigated if those changes would take place following other learning paradigms like an object recognition (OR) or an inhibitory avoidance (IA) task. In this work we showed that 70’ after OR training there was a significant increase in hippocampal GluN1 and GluN2A NMDAR subunits levels. As OR task depends on prefrontal cortex (CPF), we investigated if there was a change in NMDAR subunits at this

structure, however we found that GluN1, GluN2A and GluN2B subunits remained similar to controls, 70' after training. Then we decided to investigate if similar changes occurred after IA training. As IA memory is related to amygdala, we decided to analyze also this structure. Western blot analysis showed that there is an increase in GluN1 and GluN2A subunits 70' after IA training in both hippocampal and amygdala protein extracts. Although, these results did not demonstrate that NMDAR subunits changes are associated to memory consolidation. For this reason, we used 4 months hemyzigous McGill-R-Thy1-APP rats (Leon et al, 2010) where IA LTM is impaired. In those animals, we showed that NMDAR subunits remained similar to controls after IA training, at least, at the analyzed times. These results strongly suggest that changes in hippocampal NMDAR subunits could be a mark for LTM consolidation.

Signatures of conscious processing in the resting-state brain activity dynamics.

Jacobo D. Sitt

ICM Research Center, Hôpital Pitié-Salpêtrière, France

At rest, the brain is traversed by spontaneous functional connectivity patterns. Two hypotheses have been proposed for their origins: (1) they reflect a continuous stream of ongoing cognitive processes and/or (2) they are mere random fluctuations shaped by a fixed anatomical connectivity matrix. In this presentation, I'll show that both sources contribute to the shaping of resting-state networks, yet with distinct contributions during conscious and unconscious conditions. I'll present a series of studies that uses fMRI and dynamical functional connectivity to contrast conscious versus conscious conditions in two different experimental models (anesthesia and brain-injury). In both experimental models, unconscious conditions are characterized by a dominant functional connectivity patterns that inherits the structure of anatomical connectivity. These patterns exhibit inferior small-world properties, and they are also characterized by the disappearance of negative correlations between brain-regions. Conversely, also in both studies, wakefulness is characterized by the sequential exploration of a richer repertoire of functional configurations, often dissimilar to anatomical structure, and comprising positive and negative correlations among brain regions. These results reconcile theories of consciousness with observations of long-range correlation in the unconscious conditions and show that rich functional dynamics might constitute a signature of consciousness, with potential clinical implications for the detection of awareness in anaesthesia and brain-lesioned patients.

Prior Stress Promotes The Generalization Of Contextual Fear Memories: Involvement Of The Gabaergic Signaling Within The Basolateral Amygdala

Complex

Christian Luis Bender

Instituto de Farmacología Experimental de Córdoba. IFEC-CONICET-UNC

Fear generalization occurs when a response previously acquired with a threatening stimulus is transferred to a similar one. However, it could be maladaptive when stimuli that do not represent a real threat are appraised as dangerous, which is a hallmark of several anxiety disorders. Stress exposure is a major risk factor for the occurrence of anxiety disorders and it is well established that influences different phases of fear memory, but its impact on the generalization of contextual fear memories has been less studied. Here, we characterized the impact of acute restraint stress prior to contextual fear conditioning on the generalization of this fear memory and the role of the GABAergic signaling within the basolateral amygdala complex (BLA) on the stress modulatory effects. We found that a single stress exposure promoted the generalization of this memory trace to a different context that was well discriminated in unstressed conditioned animals. Moreover, this effect was dependent on the associative properties and on the order of presentation of the testing chambers (i.e., conditioning vs generalization chamber). Furthermore, we observed that increasing GABA-A signaling by intra-BLA midazolam administration prior to the stressful session exposure prevented the generalization of fear memory, whereas intra-BLA administration of the GABA-A antagonist (Bicuculline) prior to fear conditioning induced the generalization of fear memory in unstressed rats. We conclude that stress exposure prior to contextual fear conditioning promotes the generalization of fear memory and that GABAergic transmission within the BLA has a critical role in this phenomenon.

Role of microRNAs in the establishment of cognitive and emotive deficits derived from perinatal protein malnutrition

Bruno G. Berardino

Laboratorio de Neuroepigenética, Departamento de Química Biológica (QB), Facultad de Ciencias Exactas y Naturales (FCEyN), Universidad de Buenos Aires (UBA)

Early life stress -such as maternal malnutrition- during the critical perinatal period modifies cellular differentiation and neurogenesis programs promoting lifetime social and cognitive disturbances. However, the role of microRNAs in the CNS linking malnutrition with behavioral deficiencies has not been described. First, we found that miRNA biogenesis pathway was affected in low-protein maternally malnourished mice (LP) compared to their normal-protein fed counterparts (NP). Additionally, we found an increase in anxiety-like behavior and impaired memory. Both emotional and cognitive phenotypes in LP mice could be reversed by an enriched environment post

weaning. A global high-throughput sequencing analysis of miRNAs in the hypothalamus suggested three miRNAs (miR-187-3p, miR-132-3p and miR-369-3p) that could be part of the molecular basis of the behavioral phenotype. The expression of miR- 132-3p was shown to be negatively correlated with BDNF expression. Axon guidance pathway was enriched among the pathways to be potentially regulated by the target mRNAs predicted to interact with the altered miRNAs. Consistently, perinatal malnutrition and EE affected myelination and oligodendrocyte morphology. Alterations in the emotional and cognitive behavior of LP mice could have molecular bases in the deregulation of miRNAs that affect axonal targeting, potentially through BDNF. On the other hand, the phenotypic reversal may be due, in part, to the increased efficiency of myelination in face of environmental enrichment. These results suggest that miRNAs could play a role in neuroplasticity, allowing adaptive responses to adverse environments.

Wednesday, 27th - 11:30 – 13:30 YOUNG INVESTIGATOR SYMPOSIA II /ROOM B
Chair: Alejandra Pacchioni, FCBF, UNR, Rosario, Argentina

A Local Network Activated by Experience Accelerates the Integration of New Dentate Granule Cells

Damiana P. Giacomini*, Diego D. Alvarez*, Sung M. Yang, Mariela F. Trinchero, Silvio Temprana, Karina Büttner and Alejandro F. Schinder
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The addition of adult-born dentate granule cells (GCs) in the dentate gyrus is a unique form of network plasticity. GCs develop and integrate into the local networks in a process that lasts several weeks. It has been shown that the level of local networks activity has a positive impact on the maturation speed of adult-born GCs. Here we show that developing GCs in the adult mouse hippocampus display a critical period whereby they are prone to activity modulation long before they acquire cortical excitatory inputs. A brief exposure to an enriched environment (EE) of immature GCs undergoing this critical period for two days, accelerated their functional integration. Furthermore, direct in vivo depolarization of young GCs during the critical period using synthetic DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) was sufficient to also accelerate dendritic growth. In addition, activation of mature GCs by means of the hM3Dq receptor was used to monitor the influence of local circuits on developing GCs. Indeed, in vivo chemogenetic activation of a limited population of mature GCs accelerated the integration of developing GCs. Slice recordings showed that mature GCs recruit GABAergic feedback mediated by parvalbumin interneurons (PV-INs) that depolarizes developing GCs.Accordingly,chemogenetic stimulation of PV-INs accelerated GC integration, while inactivation of PV-INs prevented the effects of EE.In agreement with recent

works we propose that PV-INs are responsible of controlling neuronal maturation. Our results suggest that during EE exposure, mature GCs activate PV-INs, which, in turn, “prime” young GCs promoting their functional recruitment through a disynaptic feedback loop.

The dentate gyrus role on spatial working memory

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The dentate gyrus (DG) has been shown to be critically involved in spatial discrimination and spatial working memory (sWM). The first role has been shown to be dependent on the integrity of the dorsal DG and the neuronal process of pattern separation but little is known about the mechanisms by which the DG supports sWM. Working memory is the ability to transiently store and process information that is relevant for completing goal-directed actions. We first hypothesized that DG´s role in sWM is a consequence of its ability to separate similar inputs to avoid generalization in this transient memory traces before reaching the goal. If this was the case animals with dorsal DG lesion should be impaired in sWM performance. We addressed this hypothesis with selective colchicine lesions of the dorsal, ventral or the entire DG of different Long-Evans rats that were previously trained in asWM task. Contrary to our hypothesis we found that both regions support sWM in equal manner than controls animals. These results suggest a novel DG’s network computation to contribute to sWM. Therefore, we implanted controls and entire DG-lesioned trained rats with an electrode array and recorded the neuronal activity of the DG and its target area, CA3 region, while the animals performed the same task. We found a distinctive firing pattern in the DG from the one previously described in the dorsal DG. Neurons recorded in the entire dentate granule cell layer fired associated to the reward of the sWM task instead of firing in response to a particular location, named place field, only recorded in the dorsal layer. In addition, we observed that sharp-wave ripples, hallmark of hippocampal mnemonic processing, were increased in CA3 of controls rats but not in CA3 of DG lesioned rats during the reward timing of the task. Therefore the entire DG may be able to generate the transient memory traces in CA3 to reach the goal during working memory performance.

A novel therapeutic target for neurodegeneration and vascular damage in Retinopathies

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Propose: The p75NTR is a neurotrophin receptor, which promotes neuronal pruning and death. In the healthy adult retina, p75NTR and proNGF are expressed at very low levels, but they are up regulated in many neovascular and neurodegenerative diseases. Here, we studied the mechanism of action of p75NTR and its ligand in the modulation of vascular and neurodegenerative events on Retinopathies. Methods: Drug-like pharmacological antagonists of p75NTR or biological antagonists of proNGF (anti-proNGF mAb), were administered after disease onset of retinopathy animal models. Drug delivery was performed using various rout of administration. At optimized endpoints we quantify retinal structure by FD-OCT, p75NTR signals by measured TNFα, receptor and ligand kinetics expression by IF, in situ hibridization and biochemical analyses. Neuronal survival was analyzed by TUNEL assay and by counting of BRN3 labeled cells in whole retina. Finally, vascular permeability were quantified by Evans Blue extravasation. Results: p75NTR was up-regulated in Muller glial cells, and it was responsible for promoting production of neurotoxic cytokines such as TNFα and α2M which kill RGCs. In vasculature p75NTR also was up-regulated. The kinetics of p75NTR expression correlated with the disease progression. Pharmacological inhibition of p75NTR or proNGF normalized the levels of neurotoxic cytokines, prevented neuronal fiber loss and RGC death and reduced vascular permeability and decreased retinal avascular area and neovascularization. Conclusion: In retinopathies, the p75NTR mechanisms showed a paracrine regulation on glia and vasculature, impacting on health RGC. Using p75NTR or proNGF antagonists, it was possible to ameliorate the neuronal as well as the vascular components. These studies validate p75NTR as a druggable therapeutic target for retinopathies and potentially for other diseases of the nervous system.

Neuronal control of the systemic stress response in C. elegans

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Homeostasis is the ability of cells and organisms to maintain an internal equilibrium state. It is known that environmental factors disrupt homeostasis. In response to environmental challenges, multicellular organisms trigger conserved and tightly regulated molecular mechanisms to minimize cellular damages, known as “stress response”. Neural coordination of systemic stress response is key to handle unfavorable conditions. The signals that coordinate sensorial stress perception with the response in non-neural cells are still unknown. We proposed to study neural modulation of stress response in C. elegans under different environmental challenges such as heat, oxidative stress or food deprivation. Our studies reveal that neural tyramine release, the invertebrate counterpart for epinephrine, leads to suppression of cellular response to these aggressions. Intestinal expression of the adrenergic-like

receptor TYRA-3 is essential for this inhibition. By analyzing null mutants of insulin receptor DAF-2, we found that this neural regulation of stress response entirely depends on the highly conserved insulin/insulin-like growth factor signaling. We now aim to elucidate the role of the insulin like-peptides (ILPs) in this stress coordination. Our results show that, similar to worms deficient in tyraminergic signaling, ins-3 and ins-7 null mutants are also resistant to thermal and oxidative stress. Strikingly, we found that both ILPs are expressed in the tyraminergic neuron RIM, and co-express with intestinal TYRA- 3. Moreover, INS-3 is down-regulated upon oxidative and thermal stress. Genetic analysis confirms that both ILPs play a key role in neural control of stress response. Our results suggest that environmental stressors, independently of their nature, leads to a common neuronal signaling to coordinate systemic stress response in C. elegans. As most of the pathways involved are conserved throughout the animal kingdom, our findings can be universally significant.

SAN AWARD

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Spatio-temporal map of output connectivity of adult-born dentate granule cells

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The hippocampus is one of the few structures in the mammalian brain where new neurons are added throughout adult life. Adult born neurons integrate into the granule cell layer of the dentate gyrus, providing the circuit with a striking kind of plasticity: the addition of new functional units for information processing. The computational role of these new-born granule cells (nGCs) and their impact on behaviour still remain unknown. Once they are fully mature, nGCs are functionally indistinguishable from granule cells (GCs) born during development, regarding the kind of inputs they receive and how they are activated in response to them. It has been shown that during their maturation they undergo a critical period of enhanced synaptic plasticity and high excitability which may confer the circuit with a temporal window of unique processing capabilities. In order to unveil the circuital relevance of nGCs it is necessary to establish the nature of the postsynaptic networks they recruit. In this work we combine optogenetics, acute slice electrophysiology, and in vivo chemogenetics to activate nGCs at different stages of maturation and study the recruitment of local circuits. We show that young nGCs can efficiently drive distal targets but poorly activate proximal interneurons responsible for feedback inhibition. As nGCs transition towards maturity, they reliably recruit GABAergic feedback loops that restrict spiking of neighbor GCs, a mechanism that would promote sparse coding.

SHORT TALKS BY STUDENTS ABSTRACTS

Analysis of NMDAR subunits expression after GluN2A knockdown in mature primary neuronal cultures

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For several years, NMDA receptors (NMDAR) have been investigated through different approaches because of their role in synaptic plasticity, learning processes and memory. NMDAR are composed by two GluN1 obligatory subunits and two regulatory subunits: GluN2 (A-D) or GluN3 (A-B). In hippocampus and other memory related brain structures GluN2A and GluN2B are the most expressed regulatory subunits, with different expression patterns. While GluN2B is expressed in immature synapses, GluN2A is characteristic of mature and stable synapses. In order to understand the role of GluN2A during memory acquisition and plasticity induction we built two AAV-eGFP vectors: one of them codifying a shRNA anti GluN2A (AAV-sh2A), and the other carrying a shRNA scramble as control (AAV-shSc). In this work we analyzed the specifity of GluN2A knockdown in primary neuronal cultures infected with AAV-sh2A or AAV-shSc. We observed a decrease in GluN2A mRNA by qPCR only in primary cultures infected with AAVsh2A, without changes in GluN1 or GluN2B expression. Interestingly in those cultures, GluN2A decreased expression was accompanied by a significant diminution on GluN1 protein level. On the other hand, GluN2B levels were similar to control cultures infected with the AAV-shSc. These results suggest that GluN2A decrease does not change NMDAR subunit expression at transcription level. However GluN2A decayed levels could activate some postranscriptional regulatory mechanisms that change GluN1 protein levels.

An Integrated Model for Motor Control of Song in Canaries

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Birdsong is a learned motor behavior that emerges from the interaction between a nervous system with a peripheral vocal device.
The neural substrate that controls song production is known as the song system and consists of an interconnected structure of neural nuclei that is bilaterally organized, with anatomically indistinguishable structures in each hemisphere. These nuclei ultimately project to the periphery, (i.e. expiratory and inspiratory muscles and syringeal muscles) and therefore oversee the generation of complex motor gestures necessary for phonation.
The vocal organ, or syrinx, is a bipartite structure that contains two pairs of phonatory membranes (labia) that can be controlled independently to produce complex sounds. Then, to vocalize, a bird must coordinate these motor gestures that regulates the tension of the labia, the airflow, and the gating patterns.
In this work, we present a computational model that puts together the neuronal substrate with the biomechanics into an integrated model for birdsong production: First, we propose a computational model whose variables are the average activities of different neural nuclei of the song system of oscine birds. As an output of this model, two variables represent the air sac pressure and the tension of the labia during canary song production. Then, we show that these time dependent gestures can drive a biomechanical model of the vocal organ into synthesizing realistic canary like songs.

Enriched Environment Preserves Visual Functions And Reduces Neuroinflammation Of The Optic Nerve

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The therapeutic potential of environmental enrichment during neuroinflammation was scarcely examined. Optic neuritis (ON) is an inflammatory, demyelinating, and neurodegenerative condition of the optic nerve, which might induce blindness. We examined the effect of enriched environment (EE) on visual pathway damage provoked by experimental ON induced by bacterial lipopolysaccharide (LPS) injection into the optic nerve from Wistar rats. After LPS or vehicle injection, animals were housed in EE or remained in standard environment (SE) for 21 days. EE housing prevented the decrease in pupil light reflex (PLR), visual evoked potentials, anterograde transport, phosphorylated neurofilament immunoreactivity, microglial reactivity, astrocytosis, myelination, axon and retinal ganglion cell number induced by LPS injection. EE prevented the increase in oxidative damage, nitric oxide synthase-2, cyclooxygenase-2, interleukin-1β and TNFα mRNA levels induced by experimental ON. In addition, EE housing increased optic nerve brain-derived neurotrophic factor levels. When EE housing started at 4 (but not 7) days post-injection of LPS, a preservation of the PLR was observed at 21 days post-LPS, which was blocked by the daily administration of ANA-12 from day 4 to day 7 post-LPS. Moreover, EE housing from day 4 to day 7 post-LPS significantly preserved the PLR at 21 days post-injection. These data suggest that EE preserved visual functions and reduced neuroinflammation of the optic nerve.

Murine Hippocampal Encephalopathy Derived from Hemolytic Uremic Syndrome (HUS) Produced by Shiga Toxin 2 (STX2) from Enterohemorrhagic *Escherichia coli* (EHEC)

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Stx2 from EHEC causes hemorrhagic colitis, HUS and neurological dysfunctions. In the hippocampus, Stx2 produces cognitive deficits in patients. EHEC not only secretes Stx2, but it also releases LPS. The aim of this study was to determine whether a sublethal dose of Stx2 or Stx2 with LPS altered the hippocampal neurovascular unit. Male NIH mice (n=4) were injected iv with either: control (C); 800ηg of LPS (L); 1ηg of Stx2 (S) or 1ηg of Stx2 with 800ηg of LPS (S+L). Fixed brains were subjected to immunofluorescence with lectins to determine the microvasculature profile, anti-GFAP and anti-NeuN to identify reactive astrocytes and neuronal damage respectively. Primary microglial cultures were incubated with either DMEM or 100ηg of Stx2 following immunofluorescence to identify Stx2 and microglial cells (anti-IBA1). The deepest hippocampal deterioration was observed after 2 days of S+L. S and S+L treatments resulted to increase fragmented immunopositive lectin particles (22 ±0.81 C; 29 ±0.8 L; 33 ±1.22 S; 40 ±1.57 S+L), expression levels of GFAP (0.19 ±0.02 C; 0.36 ±0.04 L; 0.52 ±0.02 S; 0.60 ±0.02 S+L) and decreased the thickness of pyramidal layer (59 ±1.3 C; 48 ±1.44 L; 42 ±1.15 S; 36 ±1.5 S+L) all in comparison to C group, $p<0.05$. Stx2 was found inside of activated microglia. Stx2 damaged the microvasculature, affected the astrocytic state and caused neurodegeneration. Also, LPS and activated microglia trigger an inflammatory reaction that may contribute to the observed damage.

Blockade of D1/D5 dopaminergic receptors in the VTA promotes the persistence of weak appetitive memories

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Ventral tegmental area (VTA) dopaminergic neurons innervate the hippocampus and DA neurotransmission has been shown to modulate synaptic plasticity and memory. Dopaminergic inputs to the dorsal hippocampus are involved in the persistence of cocaine-associated memory 12 h after a single dose of cocaine. In this study we use a conditioned place preference (CPP) paradigm in rats using cocaine as a positive reward to analyze which are the structures involved in the persistence of this memory from the first exposure to the drug. Behavioral experiments were carried out with dopaminergic receptor agonists (SKF 38393) and antagonists (SCH 23390) infusions into the VTA, nucleus accumbens (NAcc) or medial prefrontal cortex (mPFC). We found that the blockade of the D1/D5 dopamine receptors in the VTA promotes the durability of a weak memory when it is infused at 12 h or immediately after conditioning. We also found that the neural activity in the NAcc is necessary for the formation of the memory from the beginning. In addition, mPFC may not be involved in this type of appetitive memory. Lastly, we wanted to test whether the VTA is involved in the maintenance of other types of appetitive memories. To do that we developed a food-CPP protocol in which animals were conditioned with food instead of drug. Same results as with cocaine were obtained showing that the memory persistence of appetitive tasks is due to the activation of neural circuits involving VTA.

The surprising effects of acute downregulation of a GABA receptor in Drosophila sleep behavior

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Sleep is a complex and vital behavior regulated by both, circadian and homeostatic mechanisms. The so called sleep homeostat is responsible for sensing the sleep debt that is accumulated during wake. The neural circuits involved in sleep homeostasis are not well described yet, but it has been suggested that GABAergic inputs to the large lateral ventral neurons (lLNvs) of the adult brain of Drosophila melanogaster may have the role of informing those arousal neurons about the sleep homeostat status.
Starting from this point, our aim was to analyze the mechanisms of GABAergic inhibition on those neurons, their influence on sleep behavior and their role on the sleep homeostat. For this, we quantified sleep behavior by inferring it from locomotor activity. In addition, we studied the circadian neuropeptide PDF (pigment dispersing factor) levels in the axonal projections of the lLNvs in order to evidence the effect over neuronal outputs under those circumstances.
Our findings indicate that downregulation of the GABAA receptor Rdl in the LNvs affects sleep behavior in the way it was previously reported. Moreover, we have now confirmed its previously suggested role on the sleep homeostat. However, we have surprisingly found that sleep can be differentially affected by the downregulation of Rdl in the LNvs when the genetic manipulation is performed in a constitutive or an acute way, opening unexpected possibilities of their mechanism of action.

Tetraspanins as promoters of TrkA receptor tyrosine kinase activation, downstream signaling and biological responses to NGF

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Nerve growth factor (NGF) is a target-derived cue that controls many aspects of sensory neuronal development and plays a key role in pain sensation. The identification of signaling molecules that regulate TrkA activation and mediate NGF-dependent axonal growth and target tissue innervation currently represents a major challenge. Here, we identify an essential role of Tetraspanins (TSPANs) in the control of NGF/TrkA activation. In PC12 cells, TSPANs overexpression accelerated neurite outgrowth and promoted TrkA activation by NGF, while TSPAN knockdown inhibited both TrkA activation and neuronal differentiation in response to this neurotrophin. Furthermore, we show that TSPAN is expressed by developing TrkA-positive dorsal root ganglion (DRG) neurons and that downregulation of TSPAN in these sensory neurons inhibits axonal growth in response to NGF. Additionally, We also provide a mechanism by which TSPNs may be regulating the activity of TrkA. Together, these results provide an insight into TSPAN function and establish a new endogenous mechanism to modulate signaling and biological responses induced by NGF and TrkA in neuronal cells.

Perinatal malnutrition deregulates PRC2 catalytic subunits and Kdm6b expression

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Early life adversities such as perinatal malnutrition can modulate neuronal plasticity through epigenetic mechanisms contributing to neurophysiologic and behavioral alterations. However, factors mediating these effects remain still unknown.
To evaluate these factors we used CF1 dams fed with normal protein (NP, casein 20%) or low protein diet (LP, casein 8%) during pregnancy and lactation, and the offspring were analyzed at P56. Using high-throughput sequencing we evaluated the global gene expression profile in medial prefrontal cortex (mPFC) of NP and LP mice. From the analysis of the RNA-seq, demethylase Kdm6b, methytransferases Ezh1 and Ezh2 (PRC2 subunits) and transcription factor Npas4 turned out to be interesting candidates for this study since methylation/demethylation of H3K27 and Npas4 pathway are involved in neurodevelopment and cognitive abilities. RT-qPCPR analysis showed that these four genes were differentially expressed in primary cultures of mouse embryonic fibroblasts (MEFs). Further, Kdm6b and Ezh1 expression were significantly decreased in the mPFC of LP female mice at P56. Predicted microRNAs that potentially regulate Kdm6b or Ezh1 mRNAs were analysed by stem-loop RT-qPCR. miR-138-5p, miR-20a-5p, miR135a-5p and miR-103-3p were not differentially expressed. These results suggest that perinatal malnutrition could affect epigenetic mechanisms, particularly histone methylation, that mediate the development and the cognitive and social deficits in later life.

The membrane glycoprotein M6a endocytic/recycling pathway involves clathrin-mediated endocytosis and affects neuronal synapses

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SNPs or variations in the expression of the gene encoding the neuronal glycoprotein M6a have been associated with psychiatric disorders such as Alzheimer´s disease, depression and schizophrenia. In cultured neurons, M6a positively contributes to neurite extension, axon guidance, filopodia/spine outgrowth, and synapse formation. The endocytic processes of neuronal membrane proteins are linked to the differentiation, growth, signalling and plasticity of neurons. However, the roles of M6a and the precise mechanisms through which M6a internalizes and recycles back to the neuronal membrane are unknown. Here, by in vitro assay, we showed that if 30-40% of M6a is endocytosed, the number of synapses in hippocampal neurons decreases. When re-establishing the levels of M6a at the cell surface, the number of synapses returned to its normal values. M6a internalization involves clathrin-coated pits, AP2 and the 251YEDI254 motif located within the C-tail of M6a. Upon endocytosis, M6a is sorted to EEA 1- and Rab5-positive endosomes and, then sorted back to the cell surface via Rab11- or to degradation via Rab7 and, finally LAMP-1-positive endosomes. Our results demonstrated that the levels of M6a at the cell surface modified the formation/maintenance of synapses, without altering the protein levels of synaptophysin or NMDA-R1. This novel mechanism might be relevant during neuronal development, pruning and/or many of the mental disorders in which the number of synapses is affected.

Activity regulated cytoskeleton-associated protein is required for consolidation of overlapping object, but not spatial memories in the Perirhinal cortex

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Successful memory involves not only remembering information over time but also keeping memories distinct and less confusable. The ability to separate the components of memories into distinct memory representations relies on pattern separation, a computational process by which differences are amplified. Pattern separation has been investigated in the dentate gyrus of the hippocampus and shown to occur in a spatial domain (DG), but little is known about this process in other brain regions like the perirhinal cortex (Prh) that process a different type of information (ie. non-spatial object memories). In this work, we used a PRH-dependent task and manipulated the load of pattern separation during information encoding. We showed in male rats that consolidation of pattern-separated object memories (and not spatial memories) depends on the expression of the gene Arc is required in the PRH for separable storage of overlapping, but not distinct, object representations, and also the neurotrophin BDNF is required for this pattern separation process, which is identical to its role in the DG., and that interaction between Arc and the neurotrophin BDNF is necessary for successful pattern separation. We provide novel evidence regarding the proteins involved in pattern separation outside the DG and suggest that, despite the anatomical differences, similar mechanisms underlie pattern separation in the DG and Prh that are engaged depending exclusively on the similarity of the stimuli.

Neuromodulators in the processing of afferent inputs in the dentate gyrus

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Neurogenesis in the adulthood continuously provides the dentate gyrus (DG) of the hippocampus with pools of granule cells (GC) which integrate into the preexisting network.

The maturation process of this newborn neurons is well characterized and is similar to the maturation of GC during development. It has been shown that newly born GC are necessary for many types of memory but how these neurons contribute to the hippocampal function is under intense investigation.

As inputs arrive to DG, they activate both excitatory and inhibitory neurons, and the excitation to inhibition (E/I) balance results in a pattern of population activity. Immature 4 week old GC have specific processing features, as they exhibit a higher E/I balance compared to mature GC. Thus, even though this population of neurons represents only 3-6 % of the total GC, their contribution to processing could be important due to their higher activity, their higher spiking rate and their higher plasticity. Neuromodulatory circuits projecting to the DG could modulate E/I balance in GC, providing a new level of plasticity for information processing of afferent stimulation.

Neural crest derivatives in the liver during development and in fibrogenesis

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Introduction: We aimed to analyze the phenotype of neural crest derived cells (NCDCs) in the healthy and fibrotic liver, since this issue remains largely unknown. Methodology: We based our study on genetic lineage tracing analyses of NCDCs by using double transgenic mouse lines (embryonic stages: PLP1creERT2-Rosa26YFP and SOX10creERT2-Rosa26YFP; adult: Wnt1cre-Rosa26Tom and GLASTcreERT2-Rosa26Tom). Fibrosis models: intraperitoneal chronic injection of thioacetamide (TAA; 4 and 8 weeks; 3 doses/week) and bile duct ligation (2 weeks). Results: During embryonic stages, only when tamoxifen (Tx) was applied at E12.5, but not at E15.5, some YFP+ cells were also cytokeratin 18+ and alpha-fetoprotein+ but desmin-. In the adult, some Tomato+ cells showed properties of hepatocyte-like cells (HLCs; in GLASTcreERT2-Rosa26Tom this feature was only seen when Tx was applied at P2 but not at P60). In fibrotic livers, the incidence of glia and Tomato+ HLCs was largely increased. Finally, in adult WNT1cre-Rosa26Tom mice which were treated with TAA for 1 week and then injected with the oligonucleotide IMT504 the incidence of HLCs Tomato+ was further increased. Conclusions: NCDCs would be a source of HLCs (NCD-HLCs) during development. In fibrogenesis, numbers of glia and NCD-HLCs were largely increased, with eventual contribution of progenitor cells from the bone marrow. These two mechanisms would influence the worsening of this pathology and occurrence of regenerative events, respectively.

POSTER ABSTRACTS

P1.-Incredible Mind!

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Neuroscience researchers visited 2 elementary schools in Rosario to raise 3rd and 2nd grade students' consciousness about the important role of the brain in our daily life through games and fun activities. Each grade worked in its classroom coordinated by at least 3 members of the team and their teachers. Incredible Mind! consisted in short interventions using visual aid that were alternated with games and fun activities. For instance, after presenting the neuron´s shapes and parts, the students did one or more puzzles with neuron´s parts on a color cardboard. Then, to explain how neurons communicate they were asked to make neuronal circuits with their puzzles on a big poster. After that, and to talk about brain areas and their functions, they were asked to prepare a "brain hat". To do that they needed to paint, cut and glue the brain lobes. Both brain lobes, left and right, with their divisions were draw in a piece of paper. Then, they were asked to put on the "brain hat" and point out the different brain areas while one of the team members described their functions. Finally, they learned about types of memories, perspective and the five senses through fun games. The whole activity was a big success because 3rd and 2nd grades were really engaged and have lots of fun. At the end, the students, their teachers and the school received small presents to remind them about Brain Awareness Week.

P2.-Brain Week in Luján

Erika Schwab* [1°], Laura Montaldo* [1°], Romina Torretta [1°], Tania Valicenti [1°], Mauricio Montenegro [2°]

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This activity was held at the National University of Luján (UNLu), in the context of the Brain Awareness Week sponsored by the Dana Alliance for Brain Initiatives. The activity was carried out under the supervision of teachers, researchers and students. The aim of the event was to disseminate current topics on neuroscience in order to bring a more comprehensive vision, generate a formative space for undergraduate students involved in the organization and guide the event to the Community in general. The event consisted in a series of talks carried out by researchers from different disciplines working in neuroscience. The topics covered the general physiology of the brain, where and how memory is formed and the importance of neuroscience in the process of constructing pedagogical concepts and how all this information is currently used in high performance sport. The talks were open, interactive and for a general audience. Also, a neuroscience fair was held by undergraduate students from UNLu, in which didactic and educational activities were performed about how the brain and nervous system work. As a future perspective we think about continuing the activity every year, spreading the importance of neurosciences, and trying to renew and update the information to be disclose taking into account the scientific innovations in the area and related topics, so that it can be accessible to a diverse audience and not just to specialists in the area.

*Contributed equally to this work

P3.-ConurBAW: the third time, is the charm?

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The Brain Awareness Week at the National University of Quilmes (UNQ) was carried out on April 5st. It was the third BAW event held on the south of the metropolitan area of Buenos Aires. The core of the event was a "Neuro-Fair" with stands prepared by neuroscience research laboratories and scientific popularization groups, covering topics such as sensorial perception, biological rhythms, development of the nervous system, animal laboratory models, and brain anatomy, among others. The stands allowed participants to chat with presenters and engage in games and interactive experiences. The graphical displays and activities were specifically designed for a high-school level audience, aimed to both inform as well as to promote scientific formation.
Also during the day, special talks were held by the BAW organizing team from La Plata (Buenos Aires, Argentina) on electrophysiology, and by Bruno Bianchi about auditory and visual illusions. In the afternoon popularization lectures were presented by the recognized neuroscientists Juliana Leone, Ramiro Vergara, Mariana Feld, Julia Hermida, Cecilia Calero and Pablo Gonzales.We estimate that the event reached an audience of over 2,000 people, outnumbering the attendance of the 2016 event. We hope we will be able to work towards an even greater and longer lasting event for next year, offering more activities to reach a bigger and more diverse audience.The event was supported by SAN, the UNQ Department of Science and Technology, and SPU.

P4.-Analysis of NMDAR subunits expression after GluN2A knockdown in mature primary neuronal cultures

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For several years, NMDA receptors (NMDAR) have been investigated through different approaches because of their role in synaptic plasticity, learning processes and memory. NMDAR are composed by two GluN1 obligatory subunits and two regulatory subunits: GluN2 (A-D) or GluN3 (A-B). In hippocampus and other memory related brain structures GluN2A and GluN2B are the most expressed regulatory subunits, with different expression patterns. While GluN2B is expressed in immature synapses, GluN2A is characteristic of mature and stable synapses. In order to understand the role of GluN2A during memory acquisition and plasticity induction we built two AAV-eGFP vectors: one of them codifying a shRNA anti GluN2A (AAV-sh2A), and the other carrying a shRNA scramble as control (AAV-shSc). In this work we analyzed the specifity of GluN2A knockdown in primary neuronal cultures infected with AAV-sh2A or AAV-shSc. We observed a decrease in GluN2A mRNA by qPCR only in primary cultures infected with AAVsh2A, without changes in GluN1 or GluN2B expression. Interestingly in those cultures, GluN2A decreased expression was accompanied by a significant diminution on GluN1 protein level. On the other hand, GluN2B levels were similar to control cultures infected with the AAV-shSc. These results suggest that GluN2A decrease does not change NMDAR subunit expression at transcription level. However GluN2A decayed levels could activate some postranscriptional regulatory mechanisms that change GluN1 protein levels.

P5.-Cellular pathway through which Gpm6a functions in filopodium formation is dysregulated in the hippocampus of chronically stressed rats

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Chronic stress exposure modifies expression level of neuronal membrane glycoprotein M6a (Gpm6a) in a variety of animal models. Gpm6a functions in the processes of neuronal remodeling and plasticity. Recently, we have shown that in the formation of neuronal filopodia, Gpm6a acts through the actin regulator Coro1a and Rac1/Pak pathway. Lots of evidence exists for impairment of neuroplasticity after chronic stress exposure but intracellular mechanisms underlying these alterations are poorly understood. Previously, we have shown that in the hippocampus of chronically stressed rats, the exposure to restraint stress, apart from Gpm6a mRNA levels, decreases also Coro1a and Pak1 mRNA levels. To expand our analysis, we have performed qPCR and quantified mRNA levels of Rac1, Cdc42, Pak2, and Pak3. In addition, expression levels of miR-133b, miR-124a, and miR-9-5p, the epigenetic mechanisms described to regulate Gpm6a mRNA levels, have been analyzed. Decreased levels of these miRs in the hippocampus of stressed rats along with decreased levels of analyzed mRNAs suggest their mode of action through the common repressor and not directly through the decay or translational repression of Gpm6a mRNA. Moreover, we show that BDNF upregulates miR-133b, miR-124a, and miR-9-5p in primary hippocampal neurons, in agreement with reported findings that these miRs act downstream of BDNF and that BDNF expression is decreased in the hippocampus of stressed animals.

P6.-Effects of phytoestrogens on the expression of genes involved in serotonin, glutamate and GABA pathways in RNDA cells

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Phytoestrogens are plant-derived xenoestrogens that bind to estrogen receptor-β (ER-β) and are widely known due their potential use as therapeutic agents to overcome menopausal brain complications, which often reduce life quality in women. To elucidate their effect on neurotransmitters pathways we used RNDA cells, a cell line model consisting on serotonergic cells derived from embryonic day-13 rat raphe nuclei stably transduced with the human ER-β gene. RNDA cells were grown in proliferative conditions (37°C) until confluence and were then shifted to differentiation conditions (39°C). Different flasks were treated with the following ER-β ligands: Genistein (10 μM), Daidzein (10 μM), Equol (10 μM) and the soy isolate Novasoy (0.5 μg/ml). Estradiol (10 nM) was used as a positive control. RNA was purified from treated RNDA cells using TRIzol, retrotranscribed to cDNA and expression levels of several genes involved in the serotonergic, glutamatergic and GABAergic pathways cells were evaluated. Our results showed that phytoestrogens and estradiol increase the gene expression of glutamate decarboxylase 1, an enzyme involved in GABA synthesis, and slightly decrease the gene expression of tryptophan hydroxylase, a key enzyme in serotonin synthesis. The expression of genes related to glutamate synthesis and metabolism remained unchanged. These results indicate that phytoestrogens could promote a switch from the serotonin-producing phenotype of RNDA cells towards a GABAergic phenotype.

P7.-α1,2-AP2 EXPRESSION IN THE DEVELOPING BRAIN OF SPONTANEOUSLY HYPERTENSIVE RAT

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Offsprings of spontaneously hypertensive rats (SHR) suffer chronic hypoxia during gestation, they have low body weight at birth and impaired neurological development. Clathrin-mediated endocytosis is a mechanism involved in neuronal signaling, integrity and homeostasis. We aimed to assess changes in the expression of a member of the endocytic pathway, the adaptor protein AP2, in the developing brain of SHR. AP2 subunits (α1 and α2) expression were evaluated by western blot in cerebellum (CB), motor cortex (MC) and hippocampus (HIP) from P5 to P30 in SHR and WKY rat pups. Proteins levels were analyzed in postnuclear (PN), membrane (MB) and cytosol (CYT) subcellular fractions. Our results show that α2-AP2 expression increased gradually from P5 to P30 in PN and MB fractions of CB, MC and HIP in both groups of rats. On the contrary, α1-AP2 did not present significant changes during development. In the CYT of CB and MC, the expression of α1-AP2 increased gradually in both strains and α2-AP2 remained stable; interestingly, in the HIP α2 subunit increased with postnatal age. These results indicate that for both rat strains, the subcellular distribution of α2-AP2 is region specific and the pattern of the protein expression is equivalent in all brain areas studied, throughout postnatal development. We conclude that the delay in the neurological development observed in SHR might not be related to alterations in the neurotransmission mechanism, endocytosis-dependent.

P8.-Expression and function of KCNQ channels in Ciliary Body

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The ciliary epithelium (CE) consists of two layers of secretory cells which are responsible for aqueous humor formation. One strategy in the treatment of glaucoma is to reduce the inflow of aqueous humour, which relays on Cl- movement trough the epithelia. The rate of anion secretion depends on pumps, transporters, Na+ channels and still-unknown K+ channels, which aid the outflow of Cl- by increasing its driving force. KCNQ channels (Kv7) are voltage-gated K+ channels with 5 members in mammals (KCNQ1-5). Among some of their functions they participate in cell volume regulation and epithelial transport. We study the role of KCNQ channels in this process using KO mice for each channel. Whole-eye RT-PCR analysis showed expression of KCNQ3, 4 and 5. Total homogenates of CE exhibited immunoreactive bands for KCNQ4. Using KO controlled immunohistochemistry we found specific labeling for KCNQ4 on the membrane of the pigmented cells (PC) of the CE, while KCNQ3 and 5 were not present. KCNQ4 was confined to the basolateral as well as the apical membrane of PCs, co-localizing with Connexin-43. Preliminary patch-clamp studies of non-pigmented cells lacking KCNQ4 expression, showed no changes in potassium currents. We conclude that KCNQ4 is expressed in the pigmented cells of the CE. This channel could contribute to the Cl- movement from the ciliary body stroma to the aqueous humor, being responsible for the K+ current.

9.-The neddylation pathway regulates cytoskeletal dynamics in early neuronal stages

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Neuronal development is controlled by signaling cascades tightly controlled a myriad of post-translational modifications. The role of ubiquitin has been well stablished but the function of the family of ubiquitin-like proteins remains poorly understood. Nedd8 is the UBL with the highest homology to Ub and we recently demonstrate that is highly abundant in the brain and is critical for synapse formation and maintenance. Blocking Nedd8 conjugation with genetic and pharmacological tools reduced axonal and dendritic growth both in cell culture systems and in utero electroporation approaches. These effects were partially reverted by Cytochalasin D, and low doses of Taxol. These results suggest that cytoskeleton dynamics is involved in the effects of Nedd8 on axodendritic growth.

To identify the structural details underlying the effects of Nedd8 we employed superresolution and fluorescent microscopy. Neddylation blockade with the pharmacological inhibitor MLN4924 strongly reduced microtubular polymerization, induce ectopic lamellipodia formation and increase the growth cone size in early neurons. Finally in biochemical screenings we identified several neddylated targets related to the cytoskeleton structure and function. The potential effects of neddylation on some of these specific targets will be discussed.

10.-Medial ganglionic eminence restricted transcription factor expression and their relevance in cortical interneuron fate

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The human cerebral cortex is composed by two types of neurons: pyramidal projection neurons and interneurons. They use glutamate and GABA as their main neurotransmitter and are excitatory and inhibitory respectively. Parvalbumin and Somatostatin interneurons comprise 70% of the total cortical interneuron population. They are born from a transient embryonic region named medial ganglionic eminence, and have their peak of birth at different stages of development. Specification of both Parvalbumin and Somatostatin subtypes of interneurons is accomplished by the sequential expression of several known transcription factors. However, the molecular requirements for the specification of one type of interneuron from the other are currently unknown. The aim of our work is to identify the molecular pathway imposed by transcription factors or molecules that are involved in this process. Using Cre-lox technology, in situ hybridization, real time PCR, immunofluorescence and birthdating approaches we are in the way to elucidate the relevance of transcription factors with restricted expression in the medial ganglionic eminence in driving interneuron progenitors to a specific fate.

P11.-MURINE HIPPOCAMPAL ENCEPHALOPATHY DERIVED FROM HEMOLYTIC UREMIC SYNDROME (HUS) PRODUCED BY SHIGA TOXIN 2 (STX2) FROM ENTEROHEMORRHAGIC ESCHERICHIA COLI (EHEC)

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Stx2 from EHEC causes hemorrhagic colitis, HUS and neurological dysfunctions. In the hippocampus, Stx2 produces cognitive deficits in patients. EHEC not only secretes Stx2, but it also releases LPS. The aim of this study was to determine whether a sublethal dose of Stx2 or Stx2 with LPS altered the hippocampal neurovascular unit. Male NIH mice (n=4) were injected iv with either: control (C); 800ηg of LPS (L); 1ηg of Stx2 (S) or 1ηg of Stx2 with 800ηg of LPS (S+L). Fixed brains were subjected to immunofluorescence with lectins to determine the microvasculature profile, anti-GFAP and anti-NeuN to identify reactive astrocytes and neuronal damage respectively. Primary microglial cultures were incubated with either DMEM or 100ηg of Stx2 following immunofluorescence to identify Stx2 and microglial cells (anti-IBA1). The deepest hippocampal deterioration was observed after 2 days of S+L. S and S+L treatments resulted to increase fragmented immunopositive lectin particles (22 ±0.81 C; 29 ±0.8 L; 33 ±1.22 S; 40 ±1.57 S+L), expression levels of GFAP (0.19 ±0.02 C; 0.36 ±0.04 L; 0.52 ±0.02 S; 0.60 ±0.02 S+L) and decreased the thickness of pyramidal layer (59 ±1.3 C; 48 ±1.44 L; 42 ±1.15 S; 36 ±1.5 S+L) all in comparison to C group, $p<0.05$. Stx2 was found inside of activated microglia. Stx2 damaged the microvasculature, affected the astrocytic state and caused neurodegeneration. Also, LPS and activated microglia trigger an inflammatory reaction that may contribute to the observed damage.

P12.-GDNF/GFRα1 complex abrogates self-renewing activity of cortical neural precursors inducing their differentiation

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The balance between factors leading to proliferation and differentiation of cortical neural precursors (CNPs) determines the correct cortical development. In this work, we show that GDNF and its receptor GFRα1 are expressed in the neocortex during the period of cortical neurogenesis. We show that GDNF/GFRα1 complex inhibits selfrenewal capacity of mouse cortical neural precursor cells induced by FGF2, promoting neuronal differentiation. While GDNF leads to decreased proliferation of cultured cortical precursor cells, ablation of GFRα1 in glutamatergic cortical precursors enhances its proliferation. We show that GDNF treatment of CNPs promoted morphological differentiation even in the presence of the self-renewal-promoting factor, FGF2. Analysis of GFRα1 deficient mice shows an increase in the number of cycling cells during cortical development and a reduction in dendrite development of cortical GFRα1-expressing neurons. Together, these results indicate that GDNF/GFRα1 signaling plays an essential role in regulating the proliferative condition and the differentiation of cortical progenitors.

P13.-Role of CB1R in hippocampal dendritic arborization

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Endocannabinoid system (eCBs) regulates neurogenic processes (neuronal proliferation, specification and maturation). Cannabinoid receptor Type 1 (CB1R) is expressed in the progenitor cells of the subventricular zone and dentate gyrus (DG) in adult brain. In addition, intermediate progenitor cells are also targeted by eCBs. eCBs is involved in physiological processes such as memory, learning, motor coordination, anxiety and mood. CB1R deficient mice (CB1 - / -) is a genetic model of depression since it deregulates the serotoninergic system, producing mood alterations. The aim of this work was to evaluate the effect of genetic ablation of CB1R in hippocampal neuronal morphology in vitro and in vivo. Neuronal morphology was studied by MAP2 immnostaining in hippocampal area CA1 from CB1 - / - and their respective wild type (CB1 + / +) at postnatal day 0, and in primary cultures of hippocampal neurons of postnatal day 0, after 7 days of culture. In vitro observation shows that CB1-/- present a higher number of primary dendrites than CB1+/+, with a shorter length. In vivo the number of nucleus per area in pyramidal layer is lower in CB1 -/- mice as well as the relative area of dendritic profiles in the corresponding stratum radiatum. This result is in accord with the in vitro result. Conclusion: CB1R is implicated in the development of dendritic arborization of hippocampal neurons.

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P14.-Expression and function of the transcription factor Isl1 in the mammalian hypothalamus

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The hypothalamus is a brain region that regulates several basic homeostatic processes including reproduction, metabolism, energy balance, circadian rhythms, the response to stress and several behaviours. Its high anatomical complexity and location in the ventral forebrain has made it a difficult region to study, but the recent availability of gene expression atlases of the hypothalamus has helped the study of the generation of the different neuronal types in this structure. One transcription factor expressed during hypothalamic development is Islet-1 (Isl1), a member of the LIM-homeodomain family that regulates cell fate specification in multiple tissues. In the hypothalamus, Isl1 has a role in regulating gene expression of some neuronal populations of the arcuate nucleus, but its role in other areas has not been described. With this aim, we are creating a map of Isl1 expression at several timepoints in the developing mouse hypothalamus. In addition, with the purpose of elucidating the function that Isl1 exerts in the generation of hypothalamic neuronal diversity, we are employing a conditional knockout model which allows for the inactivation of the Isl1 gene at specific timepoints during embryonic development. Our research will shed light on the genetics of neuronal differentiation within the mammalian hypothalamus.

P15.-Analysis of cochlear outer hair cell degeneration in a mouse model of DFNA2 deafness

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DFNA2, a slowly progressive deafness, is characterized by sensorineural loss that starts affecting high frequencies and progresses across all frequencies. Mutations in KCNQ4 channel, the voltage-activated K+ channel expressed in outer hair cells (OHCs), are the main responsible factors for deafness, leading to cell death by unknown mechanisms. To analyze the role of KCNQ4 channel we used a mouse model that lacks its expression (KO mouse). Our aim is to determine OHCs degeneration over time analyzing cell death in different cochlear segments. We dissected cochleas from wild type (WT) and KO mice and analyzed by immunofluorescence the presence of OHCs in whole mount preparations. Our results indicated that at 4 weeks-old, the number of OHCs along the whole cochlear length decreased ~24% in KO compared to WT mice. The degenerative process progressed reaching 40% of cell loss at 8 weeks-old. OHCs loss was different depending on the cochlear turns: basal, middle and apical. We determined maximum degeneration of OHCs in the basal turn. In KO mice, at 8 weeks-old the number of OHCs in the basal fragment decreased 40% while it was ~25% in the other two fragments. Additionally, our preliminary analysis suggested that OHC loss was higher in the middle row than in the outer and inner rows. We concluded that cell death progresses at a rate of ~5% cell loss/week, starting at the basal turn, suggesting a higher expression or functionality of KNCQ4 channel in OHCs from the basal fragment.

P16.-ANALYSIS OF THE EXPRESSION PATTERNS OF ZEBRAFISH NICOTINIC ACETYLCHOLINE RECEPTOR SUBUNITS AT THE EFFERENT-LATERAL LINE SYNAPSE

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The alpha9 alpha10 (a9a10) nicotinic acetylcholine receptor mediates transmission at the synapse between efferent fibers and outer hair cells of the cochlea, controlling the activity of auditory afferent fibers. Fishes and amphibians have a superficial mechanosensory system, the lateral line (LL), which detects hydromechanical variations around their body. It comprises clusters of hair cells, called neuromasts, which share structural, functional and molecular similarities with hair cells of the cochlea. As in the cochlea, LL efferent innervation is mediated by acetylcholine and its stimulation leads to inhibition of afferent transmission. However the molecular actors at the LL efferent synapse remain unknown. The Genome Reference GRCz10 describes for Danio rerio (zebrafish) two CHRNA9, located in chromosomes 1 (a9-1) and 14 (a9-14), and two CHRNA10, located in chromosomes 15 (a10-15) and 21 (a10-21). To decipher the molecular identity at the LL efferent synapse we are studying the spatiotemporal expression pattern of alternative zebrafish a9 and a10 RNAs, performing RT-PCR and wholemount in situ hybridization. Our results show that all a9 and a10 subunits are expressed from early developmental stages up to 7 days post fertilization (dpf), and in adult tissues. Moreover, a9-1 and a10-15 expression is localized to neuromasts in 5 dpf embryos. We aim to extend the analysis to a9-14 and a10-21 subunits, performing wholemount in situ hybridization at different developmental stages.

P17.-Biochemical evidence for altered protein levels of plasticity-related genes in inducible TDP-43- **Δ**NLS transgenic mice

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Mislocalization and aggregation of the nuclear protein TDP-43 are hallmark features of the neurodegenerative diseases amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). We have shown in mice that inducible overexpression of a cytoplasmically-localized form of TDP-43 (TDP-43-ΔNLS) in forebrain neurons recapitulates several features of TDP-43 proteinopathies. Here, we focus on plasticity-related genes (PRGs) which are key for normal cognition, a function affected in both human disease and our mouse model. Using gene expression data from microarray studies in TDP-43-ΔNLS brain tissue as a springboard, we identified decreased mRNA levels of Zif268, c-fos and Arc, PRGs critically involved in cognitive function and neural plasticity. These changes were corroborated by immunofluorescence analysis of TDP-43-ΔNLS cortical and hippocampal tissue. Here, we complement this data using immunoblot analysis and investigate in TDP-43 mice the protein levels of BDNF, a neurotrophin with key functions in plasticity. We found that Zif268 protein levels are dramatically decreased in TDP-43-ΔNLS brain, while exposure to a behavioural challenge such as an open field does not elicit proper PRG induction in these mice. Remarkably, BDNF protein levels are increased in TDP-43-ΔNLS brain, suggesting a compensatory mechanism involving this neurotrophin. These results indicate that abnormal PRG protein levels may underlie the behavioural abnormalities in TDP-43 related pathologies.

P18.-Lrig2 promotes the development of hippocampal dendritic arbors and spines

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Dendrite size and morphology are key determinants of the functional properties of neurons, and many neurodevelopmental and psychiatric disorders are due primarily to structural abnormalities of dendrites and their connections. Dendritic development results from the interaction between extracellular signals, intrinsic modulators and electrical activity. Compared with the many identified factors that promote general dendritic growth and branching, little is known about the cell-type specific modulators that allow neurons to sculpt distinctive dendrite patterns. Here, we show that leucine-rich repeats and immunoglobulin-like domains-2 (Lrig2) is expressed in developing hippocampal pyramidal (CA1-CA3) neurons. Sholl analysis reveals that overexpression of lrig2 increases hippocampal dendrite complexity by promoting dendrite growth and branching. Gain and loss of function assays also reveals that Lrig2 affects dendritic spine density and the assembly of the presynaptic machinery to the synapses. Further behavioral and morphological analysis in Lrig2 mutant mice will be required to more fully characterize the effects of Lrig2 in hippocampal development and function.

P19.-Protein acetylation and synaptic composition during Inhibitory Avoidance Long-Term memory consolidation in mouse hippocampus.

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Protein acetylation affects synaptic plasticity and memory, but its effects on synapse composition “in vivo” during long term memory consolidation have not been addressed. Here we show that there is a correlation between the synaptic protein acetylation level and the synaptic protein composition at hippocampus during memory consolidation. We also show that altering the acetylation levels by administration of a Lysine deacetylase inhibitor specific for KDAC6 (mainly cytoplasmic) immediately after training facilitates retention at testing. These results suggest that the post translation modification, lysine acetylation, has a role regulating the synaptic changes that occur during memory consolidation.

P20.-Inmunological and behavioral modulation of Diazepam in a chronic model of Experimental autoimmune encephalomyelitis

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Experimental autoimmune encephalomyelitis (EAE) is an inflammatory demyelinating disease that mimics many of the clinical and pathological features of multiple sclerosis. The aim of the present study was to analyze the effects of diazepam on clinical signs and its neurobehavioral consequences in a monophasic model of the disease in mice. Female mice were immunized with MOG35-55 peptide or adjuvant alone and pertussis toxin. At first symptom, animals were injected with diazepam or saline alone every 48 hs. After recovery of clinical signs, animals went through a behavioral test battery in order to identify motor skills, anxiety, and cognitive deficits. mRNA expression of inflammatory and anti-inflammatory cytokines and BDNF were measured in hippocampus and spinal cord using Real-Time PCR. We found that 2 mg/kg diazepam reversed motor signs of the disease without affecting locomotor activity or anxiety. These results correlated with no differences of inflammatory cytokines at the spinal cord. However, EAE animals showed cognitive deficits in the T-maze test. Diazepam did not improve this symptom but EAE animals treated with this drug displayed a significant attenuation of inflammatory cytokines at hippoccampus. Future experiments are needed in order to understand the mechanisms by cognitive deficits persist in EAE animals.

P21.-Short-term selection for high and low ethanol intake yields differential baseline and ethanol-induced Fos immunoreactivity in the adolescent Wistar rat brain

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Adolescence is associated with the initiation and escalation of ethanol intake and is characterized by increased and reduced sensitivity to ethanol's appetitive and aversive effects, when compared to adulthood. It is unclear if this this differential sensitivity to ethanol's motivational effects has a casual role in the exacerbated ethanol intake pattern exhibited by adolescents. We performed, in Wistar rats, a short-term selective breeding program, as a function of low- or high-ethanol intake during adolescence. This work measured, in adolescent Wistar rats derived from parents that were selected for high (STDRHI) or low (STDRLO) ethanol consumption, baseline (0.0 g/kg) and ethanol-induced (1.25 or 2.5 g/kg ethanol) Fos immunoreactivity (ir) in central, basolateral and medial amygdaloid nucleus (Bla, Cem and Me, respectively); nucleus accumbens core (AcbC) and ventral tegmental area (VTA). Baseline (i.e., after 0.0 g/kg ethanol) neural activity was significantly greater in STDRHI than in STDRLO rats. STDRLO, but not STDRHI, rats exhibit ethanol-induced Fos-ir in Cem, yet the inverse pattern was found in Me. Moreover, STRDHI rats exhibited an ethanol-induced Fos-ir depression in AcbC. These results are consistent with the possibility of STDRHI rats exhibiting and anxiety-prone phenotype as well as an altered pattern of response to ethanol's pharmacological effects.

P22.-Tetraspanins as promoters of TrkA receptor tyrosine kinase activation, downstream signaling and biological responses to NGF

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Nerve growth factor (NGF) is a target-derived cue that controls many aspects of sensory neuronal development and plays a key role in pain sensation. The identification of signaling molecules that regulate TrkA activation and mediate NGF-dependent axonal growth and target tissue innervation currently represents a major challenge. Here, we identify an essential role of Tetraspanins (TSPANs) in the control of NGF/TrkA activation. In PC12 cells, TSPANs overexpression accelerated neurite outgrowth and promoted TrkA activation by NGF, while TSPAN knockdown inhibited both TrkA activation and neuronal differentiation in response to this neurotrophin. Furthermore, we show that TSPAN is expressed by developing TrkA-positive dorsal root ganglion (DRG) neurons and that downregulation of TSPAN in these sensory neurons inhibits axonal growth in response to NGF. Additionally, We also provide a mechanism by which TSPNs may be regulating the activity of TrkA. Together, these results provide an insight into TSPAN function and establish a new endogenous mechanism to modulate signaling and biological responses induced by NGF and TrkA in neuronal cells.

P23.-The membrane glycoprotein M6a endocytic/recycling pathway involves clathrin-mediated endocytosis and affects neuronal synapses

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SNPs or variations in the expression of the gene encoding the neuronal glycoprotein M6a have been associated with psychiatric disorders such as Alzheimer´s disease, depression and schizophrenia. In cultured neurons, M6a positively contributes to neurite extension, axon guidance, filopodia/spine outgrowth, and synapse formation. The endocytic processes of neuronal membrane proteins are linked to the differentiation, growth, signalling and plasticity of neurons. However, the roles of M6a and the precise mechanisms through which M6a internalizes and recycles back to the neuronal membrane are unknown. Here, by in vitro assay, we showed that if 30-40% of M6a is endocytosed, the number of synapses in hippocampal neurons decreases. When re-establishing the levels of M6a at the cell surface, the number of synapses returned to its normal values. M6a internalization involves clathrin-coated pits, AP2 and the 251YEDI254 motif located within the C-tail of M6a. Upon endocytosis, M6a is sorted to EEA 1- and Rab5-positive endosomes and, then sorted back to the cell surface via Rab11- or to degradation via Rab7 and, finally LAMP-1-positive endosomes. Our results demonstrated that the levels of M6a at the cell surface modified the formation/maintenance of synapses, without altering the protein levels of synaptophysin or NMDA-R1. This novel mechanism might be relevant during neuronal development, pruning and/or many of the mental disorders in which the number of synapses is affected.

P24.-Altered gene expression in the hippocampus of young adult female mice by early protein malnutrition

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Early life nutrition plays a key role in central nervous system development. An adequate dietary protein content appears to be critical for the development of neurological functions. To study the impact of perinatal protein restriction, we fed mice with a low protein diet (LP, 8% casein) or a control diet (NP, 20% casein) during pregnancy and lactation. These mice constituted the F0 and were the only ones exposed to the treatment diet, their offspring after weaning (F1) was fed with standard diet. Previous work in this model has shown a detrimental effect on maternal behavior of F0 and F1 LP mice and spatial and working memory deficits in LP offspring. In consequence, we have focused on studying the expression of genes related to memory formation, such as immediate-early genes; and genes relevant for the adaptation to environmental stress, for example the glucocorticoid receptor gene. In this work, we show that in 8-week-old female offspring hippocampus there is a significant decrease in Egr1, Arc, Fos, Nr3c1 and Ppp1r3c mRNA levels, as well as a strong tendency for Bdnf transcript variant 4 and Fosb expression decrease. This set of genes has been shown to be affected in several models where deficits in memory tasks and maternal behavior are observed, suggesting that the altered expression profile that is present in our model might be mediating the behavioral effects observed in previous studies.

P25.-CIRCADIAN CONTROL OF LIPID AND REDOX METABOLISMS IN PROLIFERATIVE GLIOBLASTOMA CANCER CELLS

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Immortalized cell lines contain circadian clocks conducting transcriptional/translational rhythms in gene expression whereas metabolic rhythms can persist without transcription. Circadian rhythm disruption by modern life may cause higher cancer risk; however, little is known about clock functioning in tumor cells. Here we evaluated glycerophospholipid (GPL) and redox metabolisms in cultures of glioblastoma T98G cells under proliferation (P) or partial arrest (A), synchronized with dexamethasone (100 nM) (time 0) and collected at different times. In arrested cultures, mRNAs for clock- (Bmal1, Per1, Rev-erbα) and GPL enzyme genes, and 32P-GPL labeling exhibited circadian rhythmicity; oscillations were also found in the redox state/peroxiredoxin oxidation cycles. In proliferating cells, circadian rhythms of gene expression were lost or their periodicity shortened whereas the metabolic rhythms persist with a similar or longer period to that observed under A. Also, cell viability significantly changed over time after bortezomib (500 nM) treatment. Nevertheless, cell viability and redox state rhythms were altered when Bmal1 expression was knocked down by CRISPR/Cas 9 genomic editing technology. Results support that a metabolic clock operates in proliferative tumor cells regardless the molecular clock; property that may confer tumor susceptibility for a time-dependent chemotherapy.

P26.-Regulation of gene expression by neuronal activity patterns

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Activity-driven transcription is an integral part of the neuronal response to environmental stimulation and it is crucial for different molecular mechanisms underlying synaptic plasticity (LTP/ LTD), learning and memory, behavioral responses and neuronal survival. The way in which gene expression is regulated by neuronal activity patterns has been broadly studied during the last few years and different studies have shown that neuronal activity stimulates the expression of a wide variety of Immediate Early Genes (IEG). Previous approaches studied the induction of IEG by applying different protocols of chemical neuronal deporalization that are quite robust, but highly artificial and far from any physiological condition. In this work, we compared the expression of IEG by using chemical, optogenetics and electrical stimulations on primary neuronal cultures and using brain slices from mice previously injected with AAV-ChR2 virus. Neurons were stimulated with different patterns of activity. Both, experiments performed in slices and in cultured neurons, showed an increase in the expression of particular IEG in response to stimulation at different frequencies or to chemical stimulations. The results indicate that activity patterns can determine the temporal dynamics of activation of IEG.

P27.-Neuronal maturation and synaptic function is affected by glyphosate exposure

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The right functioning of the brain relies on the precise connectivity of neuronal networks. Nowadays there is growing evidence of the high vulnerability of developing nervous system to environmental contaminants. Glyphosate-containing herbicides are the most used agrochemicals around the world, particularly on genetically modified cultures. Our previous studies have demonstrated that glyphosate affects the initial neuronal development in hippocampal neurons. Therefore, in this work, we study the potential effect of the herbicide on the nervous system during maturation through in vivo and in vitro assays. We found that rats exposed to glyphosate during a critical period of synaptogenesis (first three postnatal weeks) showed different signs of neurotoxicity, such as lower body weight, decreased motor activity and memory impairment. To go further, we analyse the effect of glyphosate on synaptic function on 14 DIV-hippocampal cultured neurons. We observed that glyphosate exposure markedly decreased the number of clusters of the pre-synaptic marker, synapsin I. After that, we analyzed whether the herbicide affects the formation and maturation of dendritic spines in 20 DIV pyramidal neurons. Our results evidenced that glyphosate induces a significant decreased in the spines density after 1 week of treatment. In conclusion these findings suggest that subletal doses of glyphosate alter nervous system functionality both in vivo and in vitro impairing synaptic activity.

P28.-Expansion Microscopy Allows for The Detection And Characterization of the Diffraction-limited Actin/Spectrin Membrane-associated Periodic Skeleton of Axons

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Expansion Microscopy was recently developed to decrease the limit of resolution of conventional fluorescence microscopy. Fixed biological specimen are embedded in a polymer network, which is then expanded up to ~4-fold in linear dimension (specimen-gel) and maintains the structure of the specimen and its labeling. In this work, we show the expansion of neuronal cells to identify the Actin/Spectrin membrane-associated periodic axonal cytoskeleton (MPS), previously characterized using super-resolution nanoscopy (STED and STORM). We first show that the adaptation of the technique in cell lines stained for microtubules, obtaining a consistent expansion of 3.5-fold. Hippocampal and sensory neurons in culture were successfully expanded and the MPS was characterized, with a structure indistinguishable from descriptions using superresolution microscopy. This is of interest for future investigations in our laboratory and we show preliminary results assessing MPS structure during axonal degeneration.

P29.-Co-expression of D1R increases GHSR1a constitutive inhibition of CaV2.2 calcium currents

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Voltage-gated calcium channels (Cav) respond to depolarizations of the axon terminal, allowing calcium influx and the following release of neurotransmitters to the synaptic cleft. They are highly regulated points of neurotransmission. G protein coupled receptors (GPCR) signaling pathways are efficient Cav control mechanisms. The ghrelin receptor GHSR (growth hormone secretagogue receptor) is a GPCR that modulates presynaptic Cav (Cav2), constitutively reducing channel density and through agonist-evoked inhibition. Among GPCRs, GHSR has the highest known constitutive activity and the ability to heterodimerize with other GPCRs. It heterodimerizes with dopamine D1 receptor (D1R), another GPCR with agonist-evoked inhibition on Cav2. This interaction modifies their signaling pathways and physiological aspects, as GHSR alters D1R's effects on memory processes. We investigated how GHSR/D1R co-expression modifies Cav2 regulation. Through patch clamp recordings on heterologous expression systems, we found that D1R expression increases Cav2.2 currents, whereas GHSR/D1R co-expression drastically reduces them. Cav2.2 current levels were same as control when D1R co-expressed with GHSR-A204E, a mutant lacking constitutive activity, suggesting current decrease is due to a raise in GHSR's constitutive activity. Co-expression and individual expression of these receptors would have different effects on Cav channels, resulting in a wider range of action of these GPCRs over synapsis regulation.

P30.-Implications of Wnt/Fz signaling pathways on axonal development

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Neuronal morphogenesis is crucial on brain development and requires complex signaling carried out by several molecules, such as Wnts. These ligands bind to receptors of the Frizzled (Fz) family, activating 3 pathways: Wnt/B-catenin, planar cell polarity (PCP) and Calcium. Our research focused on Wnt7b and its participation on neuronal development. Initially, we identified Fz7 as Wnt7b receptor and characterized its temporal and spatial expression in neurons. We found that Fz7 expression increased over time and is located on the cell body, dendrites and spines. According to this, we then evaluate the role of Wnt7b-Fz7 on dendritogenesis and observed that neurons exposed to Wnt7b or those overexpressing Fz7 developed more complex dendritic arbours. That effect was blocked when Fz7 is suppressed. To go further, we examined the intracellular signaling triggered by Wnt7b-Fz7 interaction and found that both CaMKII (Wnt/Ca2+pathway) and JNK (PCP pathway) are involved on its effects over dendritic architecture. Based on these previous results, we decided to evaluate the contribution of Wnt7b-Fz7 during earlier periods, particularly on axonal growth. We analyzed pyramidal neurons at early stages of development and observed that Fz7 is present along neurites and mainly at the growth cones. Furthermore, through Fz7 overexpression in neurons we noted it had an effect on axonal outgrowth. More analyses are yet to be performed in order to fully evaluate Wnt7b-Fz7 role on axon development.

P31.-Early microgliosis in a conditional mouse model of TDP-43 proteinopathies.

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Microglia-driven neuroinflammation can play an important role in the pathophysiology of neurodegenerative disorders. Frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are two neurodegenerative diseases associated to mislocalization and aggregation of TAR DNA-binding protein 43 (TDP-43). We developed transgenic mice conditionally overexpressing human wild-type TDP-43 protein (hTDP-43-WT) in forebrain neurons, a model that recapitulate key features of FTD/ALS. After post-weaning transgene induction during 1 month, these mice display impairment in cognitive and social domains in the absence of motor abnormalities. In order to determine whether there is an inflammatory signature when the early behavioral phenotypes are established, we used immunofluorescence analysis of Iba1 staining to characterize the regional microglial cell activation after short-term (1 month) expression of the transgene. hTDP-43-WT mice showed significantly higher levels of microglial activation in hippocampal CA1 region respect to controls. Somatosensory cortex of hTDP-43-WT mice displayed higher Iba1 staining than controls, while there were no significant differences in motor and prefrontal cortices. In sum, these results expand our understanding of the relationship between early-stage neuroinflammatory processes and behavioral deficits in TDP-43 animal models of FTD/ALS. This in turn will help elucidate the underlying mechanisms of these and other TDP-43 proteinopathies.

P32.-MOLECULAR AND FUNCTIONAL CHARACTERIZATION OF THE NICOTINIC CHOLINERGIC RECEPTOR AT THE EFFERENT SYNAPSE OF ZEBRAFISH LATERAL LINE

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Zebrafish (z) lateral line (LL) is a mechanosensory system that detects water movements and pressure changes. It consists of hair cells innervated by afferent neurons that transmit information to the CNS and by efferent neurons that contact directly to hair cells. LL hair cells share structural, functional and molecular characteristics with those in vertebrate inner ear. Efferent stimulation to the LL and the inner ear leads to similar effects suggesting the existence of similar synaptic mechanisms. It is known that the alpha9 alpha10 (a9 a10) nicotinic receptor (nAChR) mediates efferent transmission in the cochlea, however this information is lacking for zLL. Zebrafish has two a9 genes, located in chromosomes 1 (a9-1) and 14 (a9-14) and two a10 genes in chromosomes 15 (a10-15) and 21 (a10-21). To characterize the nAChRs at the efferent synapse in zLL, we have cloned all za9 and za10 subunits, expressed them in X. laevis oocytes and performed electrophysiological recordings under two-electrode voltage-clamp. Whereas ACh activates za9-1 homomeric nAChRs (EC50=11.71 uM), zα10-15 are only functional when co-expressed with zα9-1 (ACh EC50=437 uM). Moreover, zα9-1 nAChRs are blocked reversibly by strychnine with an IC50 of 0.12 uM. Both za9-1 and za9-1 za10-15 nAChRs exhibit high Ca2+ permeability and large desensitization rates. To study the properties of native nAChR at zLL, we are setting up procedures to perform whole cell patch clamp in zLL hair cells

P33.-Mice presenting a schizophrenia-like phenotype show alterations in maturation of perineuronal nets.

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Although the etiology of schizophrenia is not known, cortical GABAergic interneurons expressing the calcium-binding protein parvalbumin (PVs) have been implicated in its pathophysiology: levels of GAD67 and PV have consistently been found to be decreased in human postmortem brain studies. Furthermore, perineuronal nets (PNNs) have also been shown to be diminished in brain tissue from schizophrenic patients especially in PVs. PNNs – reticular structures of extracellular matrix that surround the soma and proximal dendrites of many neurons in the CNS, including PVs – are reportedly involved in synapse formation and stabilization.

Given that normal wiring of cortical circuits relies on the proper maturation of PVs during the postnatal period, and considering the neurodevelopmental aspect of schizophrenia, we hypothesized that an unsatisfactory formation of PNNs in early adulthood could be related to the onset of the disease. In order to address this, we resorted to an NMDA receptor knockout mouse model of schizophrenia and performed immunofluorescent stainings against PV and PNNs in young and adult mice, focusing in the medial prefrontal cortex. We found no differences in PNNs among asyntomatic pre-adolescent animals, but adult KO mice showed a greater percentage of PVs not enwrapped by PNNs when compared to adult controls. Thus, we conclude that the unsatisfactory maturation of PNNs during adolescence could be pathogenetically relevant for the emergence of the altered state.

P34.-The transcription factor Etv5 in adult neurogenesis

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The subgranular zone (SGZ) of the mammalian hippocampal dentate gyrus (DG) generates new neurons during adulthood. These adult-born neurons become functionally active and contribute to memory formation. The neurotrophin BDNF has been implicated in the regulation of adult hippocampal neurogenesis at different levels.

Based on our previous results indicating that the transcription factors Etv4 and Etv5 mediates the effects of BDNF in hippocampal pyramidal neurons, we analyzed the potential role of these transcription factors in adult-born neuron development. We observed that Etv4 and Etv5 are expressed in the majority of mature neurons from the adult DG. However, Etv5 but not Etv4 are expressed in the immature adult-born granule cells (GCs). Animals deficient in Etv5 (NestinCre:Etv5 f/f) showed an increased in the number of immature adult-born GCs. Moreover, our data indicates that proliferation of these cells is not affected in Etv5 deficient mice. The evidence obtained from our work indicates that Etv5 may play a relevant role in adult-born GC maturation.

P35.-Light-induction of the enzyme Aralkylamine N-acetyltransferase (AANAT) in the chicken inner retina and its potential physiological role

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The neurohormone melatonin is synthesized from serotonin through two steps of which serotonin is converted first to N-acetyl-serotonin (NAS) by the enzyme Aralkylamine N-Acetyltransferase (AANAT). AANAT is present mainly in the pineal gland, retina and other regions while NAS can activate the TrkB receptor to generate neuroprotective effects and neurogenesis. Melatonin synthesis is controlled by light (L) and the circadian clock. In photoreceptor cells, AANAT activity peaks during the dark and at subjective night while activity is significantly decreased by L exposure. By contrast, melatonin synthesis, AANAT expression and activity are high during the subjective day or L phase in chicken retinal ganglion cells (RGCs) (Garbarino et al 2004). Here we investigate the expression of AANAT and of nonvisual opsins in highly enriched RGC cultures obtained from embryos by a discontinuous BSA gradient, and exposure to different L conditions. Cultures expressed melanopsins, Opn3 and Opn5 which may confer intrinsic photosensitivity. In fact, cultures exhibited blue L induction of AANAT immunoreactivity as compared with dark or red L treated cells. In addition, expression of this enzyme was significantly increased by forskolin (10 uM), an adenylate cyclase activator, in the dark. Results suggest that AANAT is a blue L-induced enzyme in RGCs controlled by cAMP. Further studies will investigate the cascade controlling AANAT expression in RGCs and its effects on retinal cells.

P36.-Charged amino acid residues K250, D253, K255, E258 and E259A within the C-terminal cytoplasmic tail of Gpm6a mediate its function in filopodium formation

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Neuronal filopodia underlie many major morphogenetic events ranging from the initiation, extension, guidance and branching of neuronal processes to the formation of synapsis. A conserved cellular function in filopodium formation has been described for a neuronal membrane glycoprotein Gpm6a. It displays structural similarity to tetraspanins with four transmembrane domains, a small extracellular loop (EC1), a short intracellular loop, and a large extracellular loop (EC2), flanked by N- and C-terminal cytoplasmic tails. In our previous study we have showed that Gpm6a lacking C- but not N-terminal cytoplasmic tail fails to induce filopodium formation in hippocampal neurons. Here we used charged-to-alanine scanning mutagenesis to identify functionally critical residues within the C-terminus of Gpm6a. We show that neurons expressing K250A, D253A/K255A or E258A/E259A mutants display decreased filopodium number. Their recognition by a function-blocking monoclonal antibody directed to the EC2 and the accessibility to digestion with the extracellular proteinase K demonstrate surface exposure of these mutant proteins. When D253, K255, E258 and E259 were mutated individually, the effect on filopodium formation was lost suggesting that these residues function in synergy. Subsequent bioinformatic analysis revealed that the residues D253, E258 and E259 form a part of the internalization motifs pointing to the functional significance of the active membrane turnover in filopodial dynamics.

P37.-Brain-derived neurotrophic factor (BDNF) prevents 3-nitropropionic acid-induced death in Huntington's disease neuronal striatal cell model

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Huntington disease (HD) is an autosomal dominant disease caused by mutation of the huntingtin (Htt) gene leading to expanded polyglutamine repeats in mutant Htt (mHtt) that promotes oxidative stress, mitochondrial dysfunction, neurotoxicity, and motor and behavioral changes. Also, impairment in BDNF synthesis is considered determinant in the pathogenesis of HD. We have previously shown that BDNF prevents astrocyte apoptosis induced by 3-nitropropionic acid (3-NP), a toxin that causes mitochondrial dysfunction and oxidative stress as it occurs in HD. Now, we studied BDNF effects on HD neuronal striatal cell model ST14a-Q120 (Q120), which express human mHtt with 120 glutamine repeats and ST14a-Q15 (Q15) which express normal human Htt with 15 glutamine repeats. We detected mHtt aggregates in Q120 cells treated with 3-NP which were undetectable by coincubation with BDNF. Q120 cells were more susceptible to 3-NP-induced cell death than Q15. BDNF had a significant protective effect on 3-NP-induced death of Q120 cells while it was ineffective on Q15 cells. Finally, in agreement with this latest result, we found that ACM from 24h BDNF-treated astrocytes, reduced the decrease in viability induced by 3-NP in Q120 but not in Q15 cells. Altogether data suggest that BDNF protects Q120 cells but not Q15 cells from 3-NP actions, and that astrocytes may contribute to neuroprotection by BDNF. Understanding BDNF protective mechanisms may help find new targets for treating neurodegeneration.

P38.-Regional and temporal assessment of neurodegeneration in inducible TDP-43-WT transgenic mice

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Neurodegenerative diseases such as frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are characterized by neuronal inclusions mainly composed of insoluble Transactive Response DNA-binding Protein 43 (TDP-43). We developed a transgenic mice model with inducible overexpression of human wild-type TDP 43 protein (hTDP-43-WT) in forebrain neurons, which recapitulate several features of TDP-43 proteinopathies. These animals develop time-dependent brain weight loss and dentate gyrus (DG) neurodegeneration. In the present study we analyzed in detail the region-specific neuronal loss, at early (1 month) and late (6 months) time points of transgene (TG) induction. Using immunofluorescence against NeuN (a marker of mature neurons), we measured the total width and NeuN-positive cell count in three cortical regions (motor, somatosensorial and prefrontal) and in two hippocampal structures (CA1 and DG). The results show mild neurodegeneration on prefontal cortex, CA1 and DG with absence of neuronal loss on both motor and somatosensorial cortices after 1 month of TG induction. These results are consistent with the early behavioral phenotype observed in hTDP-43-WT mice, displaying spatial and work memory deficits but normal motor performance. Preliminary results of the late time point in the same structures indicates more extensive neurodegeneration. Ours findings contribute to our understanding of the pathological mechanisms underlying these TDP-43 proteinopathies.

P39.-Removal of Rab11 endosomes affects spines morphology and dendritic arbor development

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The neuronal dendritic arbor development requires a proper spatiotemporal distribution of the elements of the secretory and endocytic pathways, as well as a dynamic and regulated communication between them. Accordingly, our work has focused on characterizing the role of the recycling endosome (RE) during the development of the dendritic arbor in primary embryonic hippocampal neurons. We first determined the endogenous localization of the RE at different times in culture from day 1 to 21. In the first 24 hours the RE shows a juxtanuclear distribution and on the process tips. After 24 hours the RE, changes its localization to a more broad distribution throughout the neurites until the day 14 where it mainly concentrate on the processes tips.
Upon using a shRNA-Rab11 we observed morphological changes of the normal development of dendritic arborization. In addition, we observed a shortening of the main neurite and a concomitant increase in number of dendritic branches. Moreover, suppression of Rab11 resulting a significant change in distribution of two membrane receptors protein (TfR and GluRI). Taken together, our experimental results suggest that the temporal and spatial localization of Rab11 endosomes have a distribution dependent on the stage of neuronal development. This localization could be a possible requirement for the elongation of dendritic processes.

P40.-Lidocaine does not modify GFAP and NF expression in an excitotoxic spinal cord injury model

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Lidocaine has some neuroprotective and anti-neuroinflammatory effects when administered at certain concentrations. After a spinal cord injury (SCI), astrocytes may contribute either to the formation of an inhibitory glial scar or can participate in neural repair. Increased expression of GFAP is one of the hallmarks of their activation while neurofilament (NF) expression is an indicator of neuronal integrity. The goal of the present work was to determine the effect of an intraparenchymal injection of lidocaine on GFAP and NF expression in a rat spinal cord kainic acid (KA) excitotoxic model. Male Sprague-Dawley rats were injected either with 1mM KA (KA1), 0.5% lidocaine (L05), 1 mM KA + 0.5% lidocaine (KA1-L05) or saline (sham) at the C5 segment. Intact rats were used as controls. Rats were euthanized either at 1, 2, 3, 7 or 14 post-injection days and their spinal cord was extracted, segmented and immunohistochemically processed. Besides KA1-L05 protocol has previously shown that neuronal cell counting was not significantly reduced as it occurs with the KA1 group, in this work we showed that lidocaine alone or simultaneously injected with KA significantly avoids the GFAP+ astrocytes increase observed for the KA1 and the sham groups. In addition, KA1-L05 did not reduced NF expression as observed for the KA1 group, along the experiment. These results suggest that lidocaine might be preventing neuronal damage and astrocytes reactivity in the KA-excitotoxic SCI process.

P41.-SUMO-E3 ligase PIAS4 regulates tau stability and promotes its phosphorylation

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Tau is a microtubule-associated protein expressed mainly in neurons which plays a key role in regulating tubulin dynamics, axonal transport and axonal growth. Tau deregulation leads to neurodegenerative diseases known as tauopathies which are characterized by the formation of intracellular deposits of hyperphosphorylated tau. Hsp90 is a major cellular chaperone which assembles large complexes with a variety of co-chaperones like the immunophilin FKBP51. The Hsp90/FKBP51 complex has been described as a potential enhancer of abnormal tau stability, by inhibiting its proteosomal degradation. Our group has recently demonstrated that FKBP51 SUMOylation is necessary in order to form this complex, and that PIAS4 is its specific SUMO E3 ligase. Taking this into consideration we propose to study the role of PIAS4 on tau's function. Our preliminary results suggest that PIAS4 promotes tau and phospho-tau accumulation, increasing tau stability probably by inhibiting it´s degradation by the ubiquitin-proteasome system. PIAS4 effect over tau protein is dependent on PIAS4 E3 ligase activity and FKBP51 SUMOylation.

P42.-α5β1 integrin and Cdc 42 participate in axon growth promoted by urokinase plasminogen activator

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Axon growth requires control of mechanisms that include the activation of kinases, and small GTPases and the subsequent reorganization of the actin cytoskeleton. The complex formed by urokinase plasminogen activator (uPA) and its receptor (uPAR) promotes neural migration and neuritogenesis and is closely related to the phosphorylation of the focal adhesion kinase (FAK). The aim of this work was to investigate the role of α5β1 integrin and the small GTPase Cdc42 in uPA:uPAR mediated-axon growth. For this purpose we employed the chicken optic tectum (OT) at 7 days of development (E7). In order to explore whether α5β1 is necessary for uPA:uPAR-mediated axon growth and signaling, we performed explants cultures and evaluated the axon growth with uPA, echistatin (integrin inhibitor) or with both molecules. The level of FAK phosphorylation was evaluated by Western blot in similar experimental conditions. To evaluate whether Cdc42 activity is necessary for uPA:uPAR-mediated axon growth, we compared the axon growth between control and transfected explants with a plasmid coding for an inactive variant of Cdc42, with or without uPA. The results showed that α5β1 integrin is a necessary participant in the intracellular signaling processes activated by uPA:uPAR complex and Cdc42 GTPase is part of the signaling pathways activated after that uPA binds with its receptor and would be responsible for assembly-disassembly of the actin filaments responsible for axonal growth.

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P43.-The role of the inward rectifier potassium current IKir in the intrinsic pacemaker activity of thalamocortical neurons

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Repetitive burst firing of thalamocortical (TC) neurons has been linked to the expression of the rhythms that characterize slow wave sleep and the pathological spike and wave discharges (SWDs) of absence epilepsy. Oscillatory activity in the thalamocortical system is produced by the interaction between the membrane properties of TC neurons (i.e. intrinsic pacemaker activity that results from the interaction of sub-threshold operating ion conductances), and the synaptic inputs from reticular thalamic nucleus (nRT, recurrent inhibition) and the cerebral cortex (recurrent excitation). By combining electrophysiological techniques and dynamical systems analysis we show that the inward rectifier potassium current IKir promotes repetitive burst firing. The unique biophysical properties of IKir – specifically the existence of a negative slope region of membrane potential in the current/voltage relationship–induce bistability of the membrane potential which, in combination with the hyperpolarization activated cationic current Ih, induces oscillations at physiologically relevant frequencies. The troughs of these IKir-Ih mediated oscillations engage, in turn, the low threshold calcium current IT, resulting in repetitive low threshold spikes and repetitive bursting. We discuss the physiological and pathophysiological implications of this novel mechanism of amplification of the oscillatory activity of TC neurons.

P44.-High plasticity of new granule cells in the aging hippocampus

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The aging brain displays a generalized decline in cognitive capacity and circuit plasticity, including a marked decrease in production of adult-born hippocampal neurons. It is unclear whether development and integration of those new neurons are also affected by age. We have found that adult-born granule cells (GCs) in aging mice are scarce and exhibit slow development, but they display a remarkable potential for structural plasticity. Retrovirally labeled three-week-old GCs in middle-aged mice were small, underdeveloped and disconnected. Voluntary exercise induced substantial dendritic growth and the formation of functional glutamatergic inputs. The effects of aging were also attenuated by knockdown of Lrig1, an endogenous negative modulator of neurotrophin receptor signaling. Moreover the acceleration of neuronal development exerted by running was blocked by overexpression of Lrig1 highlighting neurotrophin signaling as a key player in the mechanism of neuronal plasticity in the aging brain.

P45.-Identification of a subpopulation of proopiomelanocortin neurons with a major role in energy balance and glucose homeostasis

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The hypothalamus is a main regulator of energy balance and glucose homeostasis. In particular, proopiomelanocortin (POMC) neurons in the arcuate nucleus of the hypothalamus sense the energy status of the organism by the integration of peripheral signals. In turn, POMC neurons coordinate energy balance by decreasing food intake and promoting energy expenditure, and facilitate glucose utilization. Some studies demonstrated the existence of two subpopulations of POMC neurons expressing GABA or glutamate. Considering the opposite responses elicited by these neurotransmitters, we hypothesize that both subpopulations have different physiological roles. In order to prove this hypothesis, we first characterized GABAergic-POMC neurons by using obese and diabetic mice bearing a reversible mutation that prevents arcuate POMC expression. Interestingly, specific Pomc re-expression only in GABAergic neurons, significantly decreased body weight and completely restored food intake, metabolic efficiency and glucose intolerance. Surprisingly, these improvements were achieved by rescuing only 25% of total arcuate POMC neurons. Finally, immunohistochemical analysis showed that GABAergic-POMC neurons preferentially project to the dorsolateral hypothalamus (DMH), a nucleus that induces food intake by releasing NPY. Altogether, these results suggest that GABAergic Pomc neurons participate in an arcuate-DMH circuit with a major role in the regulation of energy balance and glucose metabolism.

P46.-Microglia and astrocyte reactivity in a rat spinal cord excitotoxic model

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Different glial responses have been reported in kainic acid (KA)-induced excitotoxic models at the Central Nervous System. Our goal was to evaluate microglia and astrocyte number and morphological changes in an experimental excitotoxic model induced by the intraparenchymal injection of KA in the spinal cord. Male rats were injected either with 1 mM of KA (KA group) or saline (sham group) at the C5 segment and euthanized at days 1, 2, 3 or 7 post-injection (pi). Non-operated rats were used as intact controls. Total number of cells, morphological phenotype (microglia types I-V) and branches length (astrocytes) were evaluated. Immunohistochemistry/fluorescence using anti-IBA-1 and anti-GFAP antibodies were used to identify microglia and astrocytes, respectively. In the KA group, total microglia number significantly increased in comparison to controls along the experiment, and by day 3 pi in comparison to sham group. Types IV and V microglia increased by days 2 and 3 pi while types I and II did it by day 7. Astrocyte number was significantly higher at day 3 pi in sham and KA groups in comparison to controls, and their global branch length was longer in KA group than that of sham rats at days 2 and 3 pi. We found that microglia and astrocytes are morphologically reactive in the spinal cord under the KA-excitotoxicity model. Further molecular studies may define whether the glia is involved in the progression or the resolution of the neurodegenerative process in the present model.

P47.-Circadian modulation of motivational behavior in mice

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The striatal dopaminergic system is particularly important in the regulation of two key behaviors: temporal processing in the seconds-to-minutes range (interval timing) and motivation. In addition, evidence suggests that the dopamine D2 receptor (DRD2) plays a main role in this regulation. We have previously reported that interval timing, as well as striatal dopamine content, is subjected to modulation of the circadian system. In the present work we present evidence of circadian modulation of motivation for food reward in young (4-months old) but not in old-aged (over 1.5 years old) C57BL/6 mice. Motivation was assayed through the progressive ratio (PR) schedule. Young mice under a 12:12 light/dark (LD) cycle exhibited a significant reduction (almost 4-fold) in motivation during the daytime. Indeed, motivation during the nighttime was increased compared to both the daytime and to constant light (LL) conditions. Aged mice, however, did not display any differences in motivation. Moreover, young mice under a normal 12:12 LD cycle exhibited a daily oscillation in the striatal DRD2 content, both at mRNA and protein level, which was coincident with the observed variation in motivation. DRD2 daily oscillation did not persist under LL conditions. Taken together, our results may contribute to improve treatment related to psychiatric disorders or drugs of abuse. This knowledge would also be of great importance when planning behavioral experiments in animal models.

P48.-Photic synchronization of the circadian clock: Role of phosphatase 2A in the NO-cGMP-PKG pathway

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Circadian rhythms are 24-hour oscillations at the physiological and behavioral levels. In mammals, they are generated and synchronized to the light-dark cycle by a master clock located in the suprachiasmatic nucleus (SCN) of the hypothalamus. It has been demonstrated that a light pulse delivered during circadian night activates the ON-cGMP-GC-PKG signaling pathway in the SCN. Little is known about the molecular components downstream PKG activation leading to necessary changes in the activity of circadian core clock genes (i.e: Per1). Previous studies have identified specific PKG activity on G substrate (GS) peptide, which is found in different areas of the brain like cerebellum, retina, and olfactory bulb. It has also been reported that phosphorylated GS inhibits the phosphatase 2A (PP2A) activity, one of the most versatile and important phosphatases of the cell. In this work, we studied the putative role of PP2A in the pathway transmitting photic signals to the SCN. We show that PP2A activity is decreased at SCN homogenates after a light pulse delivered at the circadian night. In behavioral experiments, we found that intracerebroventricular administration of okadaic acid, a specific inhibitor of PP2A, potentiates the light-induced phase shifts of circadian locomotor rhythms, correlating with an increased number of PER1 positive cells in the SCN. These results indicate a possible role of PKG-pGS-PP2A as a positive branch in the photic pathway of the circadian rhythms.

P491.-Photic and thermic synchronization of Caernorhabditis elegans

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Circadian rhythms are driven by endogenous clocks and are synchronized by environmental cues. Although circadian responses of C. elegans have been extensively reported, the mechanism and pathways of synchronization of the nematode are still unknown. Here we present a novel behavioral approach to study entrainment to two of the most studied zeitgeiber: light and temperature, as well as the interaction between them and their possible pathways of actions. We show that the wild-type strain is able to synchronize to both stimuli, with a better performance when assessed under an optimal combination of light and temperature. Significantly lower performances of the mutant strain MT21793 (lite1-gur3 ko) and IK597 (gcy 8, 18 and 23 ko) were found in response to light and temperature, respectively; however, when both zeitgeiber were present and coordinated the mutants were able to entrain. Our results shed light on the C. elegans' response to different zeitgeiber as well as their possible synchronization pathways, the genes involved in this pathway and their relative strength. E are also presenting a mathematical model to approach the population dynamics, with a Kuramoto Model of coupled phases. With this method, we obtained a coupling value for the nematode of each strain and zeitgeiber.

P50.-The surprising effects of acute downregulation of a GABA receptor in Drosophila sleep behavior

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Sleep is a complex and vital behavior regulated by both, circadian and homeostatic mechanisms. The so called sleep homeostat is responsible for sensing the sleep debt that is accumulated during wake. The neural circuits involved in sleep homeostasis are not well described yet, but it has been suggested that GABAergic inputs to the large lateral ventral neurons (lLNvs) of the adult brain of Drosophila melanogaster may have the role of informing those arousal neurons about the sleep homeostat status.
Starting from this point, our aim was to analyze the mechanisms of GABAergic inhibition on those neurons, their influence on sleep behavior and their role on the sleep homeostat. For this, we quantified sleep behavior by inferring it from locomotor activity. In addition, we studied the circadian neuropeptide PDF (pigment dispersing factor) levels in the axonal projections of the lLNvs in order to evidence the effect over neuronal outputs under those circumstances.

Our findings indicate that downregulation of the GABAA receptor Rdl in the LNvs affects sleep behavior in the way it was previously reported. Moreover, we have now confirmed its previously suggested role on the sleep homeostat. However, we have surprisingly found that sleep can be differentially affected by the downregulation of Rdl in the LNvs when the genetic manipulation is performed in a constitutive or an acute way, opening unexpected possibilities of their mechanism of action.

P51.-Cell autonomous and non-autonomous mechanisms underlying axonal terminal remodeling of pacemaker neurons in Drosophila

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A number of years ago we reported that pigment dispersing factor (PDF) neurons, which are essential in the control of rest-activity cycles in Drosophila, undergo circadian remodeling of their axonal projections. We then proposed that such adult-specific remodeling could provide a means of transmitting time-of-day information complementary to differential neurotransmitter release (i.e., PDF). In terms of clock- dependent mechanisms, several neuronal types undergoing circadian remodeling hinted to a differential effect of clock genes; suggesting these genes could be playing additional roles to those ascribed to core clock function. To shed light onto this possibility we altered clock gene levels through RNAi-mediated downregulation and expression of dominant negative forms exclusively in the adult. These experiments confirmed that a cell-autonomous circadian clock is sufficient to drive the remodeling process independently of the clock protein affected. Interestingly, affecting the positive and negative elements of the feedback loop associated to distinctive configurations. Given the extent of the structural changes involved, glia would be expected to play a role to balance changes in neuronal volume and structure. Thus, we explored the contribution of glia to the remodeling of PDF neurons through disruption of their internal clock. Our results reveal the complexity of the mechanisms underlying structural remodeling taking place daily in taking place daily in the adult brain.

P52.-Differential thermoregulatory pattern in the circadian response to LPS-induced septic shock

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Bidirectional interactions between the immune and the circadian systems have been under intensive study under physiological or pathological conditions. Septic shock is a lethal condition caused by a pathogen-induced chain of events. In 1960, Halberg et al, reported a susceptibility rhythm to lipopolysaccharide (LPS) - induced septic shock, which showed that the same dose of LPS which is compatible with survival at the middle of the night (ZT19) can be lethal at the end of the day (ZT11). Also, mice that lack the clock gene Per2 are more resistant to LPS-induced septic shock (Liu, et al. 2006). In this study, we aim to further characterize the circadian response to high doses of LPS in mice. First, we measured skin temperature of animals injected with LPS at both times and we found that there was a higher decrease in mice injected at ZT11 than at ZT19. Moreover, in mice which survived the decrease was smaller. We analyzed neuronal activation by cFos immunoreactivity in the preoptic nucleus (PON) and paraventricular nucleus (PVN) of the hypothalamus, brain regions associated with thermoregulation and neuroendocrine/autonomic control, respectively. We found that both at the medial and the lateral PON, as well as in the PVN, cFos immunoreactivity was significantly higher after LPS administration at ZT11 than at ZT19. Also, we found differences in immune peripheral cellular activation. These results suggest a central thermoregulatory dependency of circadian response to LPS.

P53.-Sleep quality of a sample of the adolescent population in Bariloche, Argentina

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Sleep disorders can be a negative factor both for learning as for the mental and physical development of adolescents. Thus, it is important for Public Health to assess the quality of adolescent sleep. We have conducted a study in the city of Bariloche, aimed at measuring the sleep quality of an adolescent population, as part of the activities of the Semana del Cerebro (March, 2017), the local version of the Brain Awareness Week. We used the Pittsburgh Sleep Quality Index (PSQI), obtained from a questionnaire administered individually to groups of secondary students. Some adults (visitors and teachers) were also given the questionnaire, thus providing a small adult sample. Participants were 523 adolescents (age 15–19) and 204 adults (age 20-69). The results show that sleep quality is consistently worse for women than for men, in all age groups, and is worse for adolescents than for adults. The most important component to explain this is sleep dysfunction (i.e. daytime sleepiness). As there is no significant difference between the number of hours slept, this shows that adolescents should sleep more than adults (on average). In men, there is also a significant difference in sleep latency, which measures how fast the individual gets asleep. The difference between adolescent men and women is mainly due to greater sleep dysfunctions in women. We also found that sleep disturbances ("bad dreams") are more frequently reported by women and have a negative correlation with PSQI.

P54.-A novel treatment for glioblastoma: a chronopharmacological approach of the novel drug 1A and Temozolomide

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Glioblastoma, the primary brain tumor with highest incidence in the adult population, has a 90% mortality rate (five-year), a 14 month average survival time and had no therapeutical improvements in the last 30 years. Research for novel drugs and treatment strategies becomes critical. It was reported that the efficacy of several drugs is modulated by the circadian system leading us to hypothesize that a chronopharmacological approach (i.e., to study the effect of the drug as a function of the circadian time) would improve the efficacy of glioma treatment. We studied the effects of 1A (a Rac1 inhibitor), a novel candidate drug to glioblastoma treatments and Temozolomide (current treatment of choice) when applied at different circadian times to LN229 glioma cells.

Because two of the main roles of Rac1 are related to cell proliferation and migration, we studied the effects of 1A and TMZ over these processes when applied at different circadian times. We found that the effectivity of 1A is rhythmic and depends on the administration time showing a minimum of 15% inhibition of proliferation when applied 28 hs after a serum shock and a maximum of 60% inhibition when applied at 43 hs. A similar result was obtained for TMZ, the current drug of choice. Migration assays were performed at 28 hs and 43 hs with no significant effects at 28hs and over 50% inhibition of migration observed at 43 hs. Our results suggest that effects of this drugs are modulated by the circadian system.

P55.-Preliminary Data On Brain Representation Of Emotional Prosody (EP) In Patients With Mesial Temporal Epilepsy (MTLE) Resistant To Medication: Insights On Plasticity

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Lateralized epileptic seizures let us disentangle functional hemispheric differences. EP, a key social skill, depends mainly on a right temporofrontal circuit, and it is often affected in MTLE. We aim to reveal EP brain representation in right and left MTLE compared to controls (CTRL). 24 CTRL, 8 right-sided MTLE and 4 left-sided MTLE patients did an EP event related fMRI task by classifying utterances with different emotional tones. We acquired 165 volumes with a 2´ RT on a 3T Siemens Trio scanner. We applied random effects analysis with SPM12, computing a BOLD contrast image for each subject. Patient groups were compared to CTRL by t-tests. We compared EP (joy, fear and anger) Vs. baseline (neutral & silence). All groups activated the posterior superior temporal gyrus (STG) bilaterally; and also the bilateral precentral gyrus, right (R) frontal operculum, pallidum and cerebellum, and left (L) hippocampus. Right MTLE patients activated L pars triangularis and precentral gyrus, and R medial cingulate compared to CTRL. Instead, left MTLE patients activated R parahippocampal gyrus compared to CTRL. Our preliminary data replicates previous findings on EP representation in the STG and its associated components (frontal operculum, R pallidum, cerebellum, and hippocampus). Additionally, it suggests EP cerebral reorganization in right MTLE, as they recruited contralateral nodes (L pars triangularis); and in left MTLE, as they recruited right nodes (R parahippocampal gyrus).

P56.-Exploratory activity, habituation and object recognition memory in *Drosophila*

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Spontaneous recognition of novel objects is commonly used to examine exploratory behavior and recognition memory in vertebrates. In this assay, animals are exposed to two identical objects (where objects became familiar for the animal). Next, animals are tested with one of those familiar objects and a novel object. The natural tendency to explore novelty makes evident the memory of the familiar object. This behavioral paradigm does not require the use of unpleasant stimuli (e.g. electric shock) and make use of the natural tendency of animals to explore; seeking for food and other needs essential for survival. However, the neurophysiological mechanisms of these behaviors are largely unknown. Motivation is the driving force that prompts individuals to perform specific behaviors. Motivational states are essential determinants for innate and learned behaviors.
In this study we characterized in fruit flies the behavioral performance for exploratory activity, the subsequent habituation in distinct contexts and motivational states and finally novel object recognition memory. Our investigation showed that fruit flies have some behavioral properties similar to vertebrate, including the initial exploratory activity, the subsequent decay of such activity and habituation memory to the context. We expect that this behavioral assay in fruit flies contribute to determine genetic and neuronal components involved in motivation and its effects on learning and memory.

P57.-A combination of novel and familiar information is required to trigger Novel Object Recognition Memory Reconsolidation

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Memory reconsolidation is a process by which new information can be integrated into a previously consolidated memory. Following reactivation, the memory trace is destabilized and requires a new wave of de novo protein-synthesis to re-stabilize. NF-kappa B is a transcription factor that, when active, is involved in regulating memory-related gene expression. Several studies in different memory tasks show the requirement for a mismatch between the training and the re-exposure sessions in order to trigger the reconsolidation process. However, this had not yet been established in Novel Object Recognition (NOR) hippocampus-dependent reconsolidation. Here, we use sulfasalazine, a specific inhibitor of the NF-kappa B pathway, as a reconsolidation-blockade treatment, to study whether different re-exposure session protocols are effective in triggering memory reconsolidation. Trained animals exposed to a combination of novel and familiar objects underwent memory reconsolidation, while those exposed eiter only to familiar objects or only to novel objects, did not. These results show the requirement for novel as well as familiar information during the re-exposure session in order to trigger NOR memory reconsolidation.

P58.-Subjective Rather Than Absolute Reward Value Determines Long-Term Memory Formation In Honey Bees

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The honey bee is a classical model for studying the neural bases of associative learning. The establishment of a protocol in which bees learn the association between an odor and a reward while they provide access for neural recordings has been critical to elucidate many of the neural pathways involved in olfactory learning. The training protocol is based on the proboscis extension response which at the beginning of training is elicited by touching the antennae with sucrose solution. During conditioning an odor is presented few seconds before the sucrose solution. After few paired trials, the bees extend the proboscis toward the odor anticipating the reward. Several works have shown that increasing sucrose concentration, reward volume, or the number trials, have a positive impact on learning and memory. Here we studied if the effectiveness of reward to elicit memory formation does depend on the absolute value of the reward or if it is affected by its subjective value, which can be manipulated based on the animal's expectations. We found that positive and negative changes in the sucrose concentration of the reward used during the training, do have positive and negative consequences on long-term memory formation. In addition, we found that bees form short and long-term reward expectations that modulate how training induces long - term memory. The results are consistent with previous studies that analyzed the effect that different rewards have in memory in free flying bees.

P59.-Switching strategies to solve spatial navigation tasks requires striatal cholinergic interneurons

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Basal ganglia are classically related to motor function, including command of voluntary movements and motor skill learning. They are also involved in cognitive processes as decision making and balance between goal-directed and habitual behaviors. The striatum is the mayor input nuclei of basal ganglia and is strongly modulated by interneurons, in particular by cholinergic interneurons (SCIN). SCIN encode salient environmental events and contribute to context-dependent action selection. For that reason, SCIN are perceived as crucial elements for flexible switching of behaviors under changing environmental conditions. We have previously shown that SCIN ablation leads to exacerbated spontaneous emission of repetitive behaviors, including social interaction. Here we ask if perseverative behavior induced by SCIN ablation relates to an inability to switch from strategies while solving spatial navigation tasks. We selectively ablate SCIN using a Cre/loxP transgenic system combined with intrastriatal diphtheria toxin administration. Mice were repeatedly exposed to Barnes and cross mazes. We did not find differences in learning curves between groups. In both tests, control mice change their task-resolution strategy across days. However, lesioned mice fail to adapt their solving strategy. This result suggests that SCIN are necessary to switch between solving-problem strategies to optimize cost benefit ratios.

P60.-Dopamine responses to reward and reward-related cues are altered in a mouse that overexpresses dopamine D2 receptors in the striatum

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Dopamine (DA) hypothesis has been the leading pathoetiologic theory of schizophrenia (SZ) for many decades. Striatal DA hyperfunction has been consistently linked to psychosis. However, more recent studies show a generalized DA deficit including cortical areas and extrastriatal regions not previously considered to be hypodopaminergic in SZ such as the ventral striatum, with increase presynaptic DA activity restricted to the associative striatum. DA neurons compute reward prediction errors proposed to serve as the basic process underlying associative learning in classical and instrumental conditioning procedures. Patients show deficits in reinforcement learning including reward anticipation, reversal learning, probabilistic learning and reward representation. Such deficits, part of the cognitive and negative symptoms, do not improve with antipsychotic medication and their severity determines patient´s prognosis. To understand DA dysregulation in SZ, we use fast-scan cyclic votammetry to monitor DA release in the nucleus accumbens of a mouse model for cognitive and negative symptoms of SZ that presents a 15% increase in striatal D2 receptor levels as has been observed in patients with SZ. We hypothesize that striatal D2R overexpression induces changes in DA release that are responsible for the behavioral deficits observed in the mice. We show DA release to be altered and to correlate to altered behavior in order to explain the observed SZ-like phenotype.

P61.-Acute stress facilitates the generalization of contextual fear memory

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The generalization of fear is an adaptive function that allows an organism to respond quickly to new stimuli/contexts that resemble a previously acquired fear experience. However, it may be maladaptive when stimuli/contexts that do not represent a real threat are inappropriately treated as dangerous, as it occurs in patients with anxiety disorders. Exposure to stress is a major risk factor in this type of disorders and it is a modulator of fear learning; however, its impact on the generalization of contextual fear memory has been barely studied. To test the generalization of fear in a context (cxt-B) which is different to the original conditioning context (cxt-A) we used a 2 x 2 design, with stress and conditioning as factors. The restraint stress session (1 hr) was performed one day before the fear conditioning (2 shocks 1mA/3s, after 3 minutes of exploration of the conditioning box). The tests were performed at 24 and 48 h after conditioning in the cxt-B and cxt-A, respectively. The index of fear used was the percentage of freezing time. Conditioned animals that were previously stressed showed an increase of fear behavior in the cxt-B compared to non-stressed animals, which presented similar levels of freezing to those observed in the non-conditioned groups. In conclusion, a stress session prior to the contextual fear learning promoted the generalization of fear memory and it could be prevented by previous exposure to the conditioned context.

P62.-Pattern of ictal intracerebral EEG at the start of alteration of consciousness (AOC)

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Objective= AOC during seizures is one of the most striking features in patients with focal epilepsy and the subjacent mechanisms are incompletely known. Methodology= 9 patients (45 seizures) with drug resistant epilepsy were included. We analysed the patterns and localization of seizure onset and propagation, beginning and degree of AOC. Results= In mesial temporal epilepsy, the seizures with AOC were longer, the most commonly pattern of seizure-onset was sharp activity at ≤ 13Hz and the AOC occurred with the propagation of activity to contralateral hippocampus. In frontal seizures, the AOC occurred when is compromised more adjacent contacts in frontal lateral cortex. Meanwhile in insular seizures the AOC occurred when both part of insula were compromised. The hippocampi were never involved. Most common patterns at AOC were sharp activity high-amplitude at 10Hz, low-voltage fast activity and rhythmic slow waves at 4-5Hz. Conclusion= In our work, the AOC were mostly with of after the propagation of the seizure-onset activity. In mesial temporal seizures, the most of the AOC seizures were with contralateral hippocampus compromised. Meanwhile in frontal and insular seizures the AOC occurred when the area of discharged is enlarged without hippocampus compromised. Future works that apply different techniques for signal analysis are necessary to characterize functional connectivity between spatially distributed regions and pathophysiological mechanisms during AOC.

P63.-Tolerance and sensitization induced by ethanol in preweanling rats: effects of the administration of a sequestering agent of acetaldehyde

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Preweanling rats consistently display a locomotor stimulating effect in response to medium-to-high ethanol doses, and we have recently reported that chronic ethanol exposure during the second postnatal week results in tolerance or sensitization to this effect of the drug. The locomotor stimulating effect of ethanol and sensitization of this effect has not been frequently reported in adult rats. One possible explanation to this ontogenetic difference in the sensitivity to ethanol is the difference in central and peripheral ethanol metabolism observed at each age. Our goal was to explore the effect of the administration of d-penicillamine (dp), a sequestering agent of acetaldehyde, over the stimulating effect of ethanol after acute or chronic exposure to the drug in two-week-old rats. Firstly, we administrated rats (PD 12) with 2.5 g/kg ethanol, 25 min after being treated with saline or dp (50 or 75 mg/kg). Both dp doses reduced the acute stimulating effect of ethanol. Then we evaluated whether dp administration at training reduced tolerance and sensitization. Our results revealed that dp did not block these ethanol effects. These data suggests that acetaldehyde metabolism is involved in the acute locomotor response of ethanol, but not in the development of tolerance and sensitization in infant rats.

P64.-Blockade of D1/D5 dopaminergic receptors in the VTA promotes the persistence of weak appetitive memories

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Ventral tegmental area (VTA) dopaminergic neurons innervate the hippocampus and DA neurotransmission has been shown to modulate synaptic plasticity and memory. Dopaminergic inputs to the dorsal hippocampus are involved in the persistence of cocaine-associated memory 12 h after a single dose of cocaine. In this study we use a conditioned place preference (CPP) paradigm in rats using cocaine as a positive reward to analyze which are the structures involved in the persistence of this memory from the first exposure to the drug. Behavioral experiments were carried out with dopaminergic receptor agonists (SKF 38393) and antagonists (SCH 23390) infusions into the VTA, nucleus accumbens (NAcc) or medial prefrontal cortex (mPFC). We found that the blockade of the D1/D5 dopamine receptors in the VTA promotes the durability of a weak memory when it is infused at 12 h or immediately after conditioning. We also found that the neural activity in the NAcc is necessary for the formation of the memory from the beginning. In addition, mPFC may not be involved in this type of appetitive memory. Lastly, we wanted to test whether the VTA is involved in the maintenance of other types of appetitive memories. To do that we developed a food-CPP protocol in which animals were conditioned with food instead of drug. Same results as with cocaine were obtained showing that the memory persistence of appetitive tasks is due to the activation of neural circuits involving VTA.

P65.-Impact of NMDAR ablation in dorsomedial striatum on behavior

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Goal directed behavior and habit formation depend on corticostriatal circuit operation. It is assumed that alterations in these circuits are related to neuropsychiatric conditions like obsessive compulsive disorder, attention deficit and hyperactivity disorder and Tourette syndrome. In a previous study we found a decrease in prefrontostriatal connectivity in mice with neonatal dopamine (DA) depletion that emerge in parallel with deficits in exploration of novel environments, social behavior and exploitation of nutritional resources and shelter. Here we specifically study whether a decrease in prefrontostriatal connectivity in adult mice could be related to some behavioral features observed in DA depleted mice. Since blockade of NMDA receptor (NMDAR) decreases the response of striatal neurons to cortical inputs, to mimic a prefrontostriatal disconnection we have ablated the NMDAR in dorsomedial striatum by injecting a GAD-Cre virus in loxP-flanked NR1 adult mice. Preliminar results show that NMDAR ablation produces a decrease in exploration in a task dependent manner. This reduction seems not to be due to a general decrease in locomotion because in some settings we did not observed differences. Mice with NMDAR ablation also showed deficits in nesting and marble burying behavior but not in social exploration. In summary, NMDAR ablation in dorsomedial striatum produced deficits in exploration but does not fully reproduce the behavioral phenotype of DA depleted mice.

P66.-Influence of the fear memory labilization/reconsolidation process on the hippocampal structural plasticity.

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Under certain conditions, the reactivation of a consolidated fear memory induces a labile state followed by a stabilization process (reconsolidation). During destabilization, the memory trace is vulnerable to interfering agents such as propranolol (PROP). We evaluated whether the reactivation of a fear memory impact on the dendritic spines remodeling in CA1 dorsal Hipocampus (DH) associated with contextual fear memory. Stressed and control animals were fear conditioned and 24hs post conditioning or post retrieval, were sacrificed. Additionally, animals were Basolateral Amygdala complex (BLA) cannulated and PROP administered after fear reactivation. One day later the animals were sacrificed. Independently from the reactivation session, conditioned animals -but not stressed- exhibited a higher number of dendritic spines in comparison to non-conditioned animals. Prior stress exposure prevented such increase; even the behavioral freezing response was similar. Likewise, the intra-BLA PROP administration prevented the increase in the number of dendritic spines in comparison to SAL administration.
Fear conditioning induced structural remodeling in DH is not affected by memory reactivation. However, stress-induced resistance to memory reconsolidation or the blockade of this process prevented the structural plasticity suggesting that destabilization/reconsolidation following reactivation is a critical step to induce spines remodeling after reactivation in fear conditioned animals.

P67.-Insight into the amphibian brain: the amphibian medial pallium as a model of an ancestral hippocampus?

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We are interested in the evolution of neural mechanisms that rule spatial learning. Our group is looking for learning patterns potentially present in a common ancestor to several vertebrates using as model the terrestrial toad, Rhinella arenarum. It is known that mammalian hippocampus is a critical brain structure involved in spatial learning and amphibians have a homologous area to this hippocampal formation, the medial pallium. The analysis of how involved this structure is in spatial orientation tasks will help us to infer potential ancestral spatial abilities and its neural basis. We conducted medial pallium lesion studies with toads daily trained in a plus maze for the acquisition of two basic spatial orientation strategies: a visual cue guided response and a turn response to reach a goal. In addition, spatial learning and memory related morphological changes in the argyrophilic nucleolar organizer region (AgNOR) of medial pallium neurons were quantitatively evaluated by means of AgNOR neurohistochemical stain in other set of experiments. Altogether, our results suggest that medial pallium is involved in basic spatial orientation strategies in amphibians, supporting thus the idea that hippocampus and medial pallium are partially functional equivalents. Furthermore, these results telling us that this ability is evolutionary conserved.

P68.-Differential role of retrosplenial cortex in object recognition memory

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Several studies had demonstrated that the retrosplenial cortex (RSC) is strongly implicated on navigation and contextual memory. Furthermore, lesions in animal models show that RSC shares functional similarities with the hippocampus (Hp), suggesting that RSC has a supporting role to the hippocampal function. In this study we contrasted the role of RSC and Hp on recognition memory, particularly on the "what" and "where" components of this memory, using three variants of the object recognition task: two of them focused on objects themselves (the non-spatial Y-shaped maze object recognition, Y-OR, and the spontaneous object recognition, SOR, which includes spatial cues) and the third focused on the position of the objects in the context (object location, OL). Our behavioral and molecular results demonstrate functional differences between RSC and Hp on recognition memory. When we tested the "what" component of memory (Y-OR and SOR) the inactivation of RSC, but not Hp, impaired memory formation and expression. Moreover, there was an increase in RSC, but not hippocampal, c-Fos level one hour after the animals were exposed to Y-OR sample phase. In contrast, the inactivation of both structures decreased memory index on OL task, indicating the requirement of RSC and Hp for the "where" component of recognition memory. Our current findings suggest a novel role of the RSC in recognition memory, processing not only the "where", but also the "what" component of this memory.

P69.-A massive experiment on choice blindness in political decisions

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We implemented a Choice Blindness Paradigm containing political statements in Argentina, Brazil and the USA to reveal the existence of categorical ranges of introspective reports, identified by confidence and agreement levels, separating easy from very hard to manipulate decisions. CBP was implemented in both live and web-based forms. Importantly, and contrary to what was observed in Sweden, we did not observe changes in voting intentions. Also, confidence levels in the manipulated replies where significantly lower than in non-manipulated cases even in undetected manipulations. We name this phenomenon unconscious detection of self-deception. Results in argentina have also shown that females are more difficult to manipulate than men. This difference was not significant in our Brazilian sample. Additionally, participants closer to the conservative axis were easier to decieve compared to their progressive counterparts. This result was consisten through all three countries.

P70.-Contribution of ERK/MAPK activation to the formation of a two trial long term memory in the crab Neohelice granulata

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Long term memory (LTM) model of the crab Neohelice granulata has been extensively studied from different points of view (e.g. behavioural, pharmacological, molecular and electophysiological). For context-specific LTM to be successfully expressed in a 24h-postraining testing session, the training protocol typically used consists of 15 trials with a 3-min intertrial interval. We study a long-term memory induced by two-trial training with an intertrial interval of 45 min. This type of training represents an attractive model for studying individual trials and intertrial interval contribution to the activation of putative molecular pathways involved in memory formation during training. It has been proposed that in two-trial training protocols the first trial induces a specific molecular context mediated by the activation of the ERK/MAPK pathway, which enables the formation of a long term memory only after a 45 min intertrial interval training. Here, we present preliminary results regarding context-specificity of this type of memory as well as synaptic ERK/MAPK pathway's activation dynamics and dependence.

P71.-Understanding memory loss: Development of a retrieval-induced forgetting paradigm in rodents

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In the last two decades there´s been a growing human literature on a phenomenon called retrieval-induced forgetting (RIF). RIF has pointed to inhibitory control processes that resolve retrieval competition as a cause of adaptive forgetting. Using spontaneous recognition memory in rats, we have developed a rodent paradigm for RIF. We were able to show that forgetting of an item associated with a particular context happens under conditions that cause competition between memory traces for two items that share a particular retrieval cue. Under these conditions, forgetting is long lasting and independent of the selected retrieval cue. We used local pharmacological inactivation to show that this kind of forgetting requires the activity of the medial prefrontal cortex (mPFC). With pharmacological inactivation, we showed that the Ventral Tegmental Area (VTA) is necessary for the forgetting to occur and that the infusion of a D1/5 agonist in the mPFC is sufficient to rescue the expression of the RIF phenomenon impelled by the inactivation of the VTA. These results are consistent with the idea that the RIF occurs via a top-down inhibitory control mechanism exerted by the mPFC on structures linked by hypothesized memory traces. With the latter results, we bring new evidence supporting the role of dopamine in the resolution of interference via mPFC inhibitory control.

P72.-The spectral signatures of serotonergic and dissociative psychedelics in the human brain

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Recent findings in psychedelic research have highlighted the need for a deeper understanding of how these drugs affect brain activity. Several psychedelic drugs have proven to be useful for the study of consciousness (Schartner et al, 2017), and for a wide range of psychiatric therapies (Vollenweider and Kometer, 2010). Yet, their applications are hard to exploit since the neural mechanisms behind their actions are still on debate. It has well been established that subjective psychedelic-like effects can be produced by two kinds of substances with partially overlapping molecular actions: serotonergic psychedelics (SP) and dissociative drugs in sub-anesthetic doses (DP). No study has quantitatively compared their effects on brain activity. The present work analyzed magnetoencephalography recordings after the administration of two SP (LSD and psilocybin) and one DP (ketamine). For quantifying the similarities and divergences, machine learning algorithms were implemented. Classifiers were trained using power spectrum and connectivity values obtained for one drug, and tested on another drug dataset. It was found that, in some spectral bands, the generalization capacity of the classifiers extended only to SP. However, in other frequency bands, DP can be used to efficiently decode the effects of SP, and vice versa. Results might then support the hypothesis that the similarities and differences in the molecular underpinning of both drugs are also expressed at a system's level.

P73.-Single Neuron Recordings In The Human Medial Temporal Lobe

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Surgical treatment is indicated for some patients with pharmacologically intractable epilepsy. In these cases, depth electrodes were implanted to localize the epileptic focus to be surgically removed. This offers an exceptional opportunity to record directly the single neuron (SN) activity in the human brain while patients perform different types of cognitive tasks. The aim of this work is to assess the response of SN in the medial temporal lobe to visual stimuli. The electrical activity of multiple SN and local field potentials (LFP) from the hippocampus and amygdala of 5 patients (males, 19-49 y/o) during the presentation of pictures through a laptop monitor (persons, landmarks, objects and animals) was recorded. Then, 3 different pics, text and audio were presented corresponding to the concept whose picture triggers a response in previous session. The recorded activity from depth electrodes were processed using "spike sorting" algorithms. The activity of dozens SNs were identify, many of which selectively responded to specific concepts. It were recorded 33 SNs (22 hippocampus and 11 amygdala) that responded in an invariant way to 44 concepts (famous characters, landmarks, animals, family and medical members). The implantation of depth electrodes in epileptic patients allows us to observe SN responses to different concepts in brain areas related with memory, which provides unique information on the neural mechanisms involved in the formation and coding of memories.

P74.-Early Cognitive Impairment associated with a parkinsonian animal model: synaptic plasticity and initial approaches with IGF-1 gene therapy

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Parkinson´s disease (PD) is a neurodegenerative disorder with a progressive dopaminergic (DA) neuronal loss and a variety of non-motor symptoms such as cognitive dysfunctions Growth factors as IGF-1 could be neuroprotective in PD models by improve changes in neuronal activity. 1) To determine the early cognitive decline and the correlation of hippocampal changes in 6OHDA model 2) to carry out therapeutic approaches with IGF-1 to understand plasticity processes associated with cognitive decline. Male Wistar rats were CPu bilaterally injected with 6OHDA or vehicle (SHAM). Independent groups were tested after 7, 14, 20 and 28 days for Y-maze and locomotor activity. Another set of rats were divided into 6 groups according the adenoviral therapy in hippocampus: SHAM, 6OHDA, SHAM-RAd-DS-Red, SHAM-RAd-IGF-1, 6OHDA-RAd-DS-Red and 6OHDA-RAd-IGF-1. At 20 days post lesion, were tested for behavioral tasks. Then rats were perfused, the brains fixed and IHQ performed for TH and IGF-1R and hippocampal synaptic plasticity. At 20 post-lesion, memory deficits, changes in dendritic spines were observed in 6OHDA rats compared to SHAM rats. This behavioral cognitive decline was partially modified with IGF-1 overexpression in 6OHDA-RAd-IGF-1 rats. 6-OHDA was sufficient to cause memory impairments. Knowledge of this neurodegenerative progression could result in potential therapeutic strategies as IGF-1 gene therapy which motivates us to further studies under this experimental model

P75.-Memory updating in crabs: adding opposite information during reconsolidation

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Reconsolidation theory postulates that, once reactivated, a stable memory becomes labile and goes through a process of stabilization, enabling memories to be modified or updated depending on new information acquired during retrieval and allowing animals to adapt their behavior to a changing world. Although memory updating has been studied in diverse species and several memory paradigms, it is not yet clear what would happen if during reconsolidation animals receive information that contradicts the prediction generated by a previous experience. A recent work performed in rats, has shown that contextual fear memory is weakened if animals receive a positive stimulus during retrieval in a previously learned aversive context. In this study we trained crabs in either aversive or appetitive paradigms and, once memories were consolidated, animals were re-exposed to the training context and received a training session with opposite valence to the previous one. We demonstrated that, despite the strength of protocol, the original memory is not occluded by the new one and the memory associated with the new stimulus can be revealed, together with the original trace. Considering previous results showing that two parallel memories are built when crabs receive two training paradigms with opposite valence at the same time, we wonder if under these conditions animals are forming two memories or, on the contrary, new information is added to the original trace.

P76.-STRESS EFFECTS ON STUDENTS LONG TERM MEMORY

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Long-term memory (LTM) formation requires protein synthesis. We have demonstrated in rodents that a weak learning task (spatial object recognition-SOR) which only induces short-term memory (STM) can be stabilized into LTM if an event of acute stress is experienced 1 hour after. It was postulated that stress provides the necessary proteins, which could be captured at tagged sites induced by the weak learning task, process referred as behavioral tagging. However it was observed that if stress occurs 1 hour before learning is not able to promote a LTM and results suggest an effect of stress on the tag. Surprisingly, when the rats are exposed to a stress 1 hour after strong SOR the promoting effect does not occur and we postulated that could be due to competition for resources necessary for memory consolidation. In the present work we want to assess if an acute stress could induce similar effects in humans. We made activities using a modification of the Rey-Osterrieth's complex figure task to test graphic memory in students and analyze the effects of exams on the promotion of LTM and its temporal course. The behavioral results are similar to those found in rodents: when students have a programmed exam before learning they do not show LTM promotion, while students who have an exam 60 min after learning show positive or negative effects on figure retention depending of the learning strength.

P77.-Effect of stevia sweeteners consumption on the expression of **Δ**-FosB in nucleus accumbens and striatum in adolescent rats

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Stevia sweeteners (steviosides) are natural non-caloric sweeteners 100–300 times sweeter than sucrose which are obtained from the leaves of Stevia rebaudiana Bertoni (family Asteraceae) and contain a complex mixture of sweet diterpene glycosides. Little is known about the effect that NNS could cause on the reward system and their potential addictive properties. On the other hand, sugar has been demonstrated to activate the mesolimbic reward pathway the same way drugs as nicotine, alcohol, and other recreational drugs do, for instance, increasing the expression of the transcription factor Δ-FosB, a transcription factor member of the Fos family, which plays a role in the addiction process. Thus, the aim of this study is to evaluate the effect of stevia sweeteners on relevant areas of the mesolimbic reward system. Adolescent rats had continuous access to 0.2% stevia extract solution for 20 days (from postnatal day 30-50) using a two-bottle free choice test, at the end of the treatment were sacrifice and serial coronal sections (40 µm) of the nucleus accumbens and striatum (from bregma +2.16) were obtain and immunohistochemistry to Δ-FosB was performed. Images were obtained using a digital camera. Quantification of the Δ-FosB positive nuclei was performed. Results compared with a control group with only access to water show not just preference for stevia extract solution but also an increment in chow consumption, besides a tendency in overexpression of Δ-FosB in nucleus accumben

P78.-Words, hands or looks? Understanding teaching strategies in children with cochlear implants

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Some aspects of human communication rely on an implicit communication protocol. Previous studies (Csibra & Gergely, 2009) demonstrated that learning in children changes when demonstrations are accompanied by ostensive behavior. Ostensive cues (OC), which are signaled by a broad set of non-verbal behavior, act as prosodic markers providing emphasis to relevant items of the discourse. At the lab, Calero et al observed that preschool children can not only detect, recognize and react to OC, but furthermore, they are capable of generating them when teaching. Also, there are other non-verbal behaviors that are not ostensive but nonetheless have clear pedagogical importance. The clearest examples are gestures. Children spontaneously produce gestures early in life and it has been shown that encouraging them to use gestures brings out implicit knowledge and leads to learning. However, we wonder whether non-verbal language will have the same impact on all populations. Previous studies have shown that deaf children use their gaze more and develop more gestures as iconic symbols to communicate, even without being exposed to sign language. With that in mind, we performed an study in collaboration with Oral Model Institution, a school of children with cochlear implants. We are trying to understand if they are able to receive and emit the same OC in pedagogical events described in children with expected development, or, as an alternative, they develop other strategies with the same goal.

P79.-Analysis of the complexity of electrophysiological recordings acquired during three different meditation traditions

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A wealth of experimental studies suggests that different meditation practices can modify global brain activity parameters such as connectivity and the power of spectral oscillations (Cahn and Polich, 2006). These studies, in combination with the phenomenomenological experience of meditation, suggest that meditation is capable of inducing a distinct brain state that can be characterized by idiosincratic modes of information processing. Recently, Carhart-Harris and colleagues (Carhart-Harris et al., 2014) proposed that global brain states can be characterized as a continuum parametrized by the level of entropy/complexity of brain activity. For instance, it has been shown that states of reduced awareness correlate with reduced levels of complexity (Schartner et al., 2015), whereas serotonergic psychodelics increase complexity (Schartner et al., 2017).
In this work, we attempt to place the brain states induced by three different meditation traditions (Vipassana, Himalayan Yoga and Isha Shoony) in the aforementioned continuum of brain states. By analyzing high-density EEG data acquired from 67 expert meditators and 32 controls, we explored a wide array of complexity metrics including temporal correlations, information integration, algorithmic complexity and sampling entropy. Our results indicate that meditation can increase the complexity of brain activity, resulting in a “scrambling” effect that could underlie some of its reported physical and psychological health benefits.

P80.-Electrophysiological correlates of encoding faces in different emotional contexts

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It has been well established that emotion enhances memory; however, it is still unclear if experiencing a non-emotional event in positive or negative emotional contexts affected recognition. The aim of the present study was to investigate the effects of encoding faces with neutral expressions under different emotional contexts (positive, negative or non-emotional) on the subsequent memory effect (SME). Event related potentials, heart rate (HR) and skin conductance response (SCR) were also examined. Twenty-eight adults participated in a betting-game task in which they could win (positive context) or lose (negative context) money. The participants also completed a non-betting task (non-emotional context). Afterward, the participants completed an old/new recognition task for the faces. The recognition was superior for the faces encoded under positive emotional contexts than for those encoded in the non-emotional ones. The SCR amplitude was equivalent for both of the emotional contexts and greater than for the non-emotional contexts. Electrophysiological findings showed that the N170 and P300 components at occipital sites and the frontal slow wave manifested SME that were modulated by positive contexts; neither negative nor non-emotional contexts influenced these effects. The behavioral and neurophysiological data demonstrated that positive contexts are stronger predictors of episodic memory than negative or non-emotional contexts.

P81.-Role of dorso-medial telencephalic adult-born neurons on Active Avoidance learning in a teleost fish model

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Teleosts exhibit adult neurogenesis throughout their brain, making them an excellent model to study the way in which network remodeling by adult neurogenesis shapes brain function. Cognitive ability was assessed by Active Avoidance (AA) paradigm in adult rainbow trout (Oncorhynchus mykiss). Learning performance correlated with neuronal activity in dorso-medial (Dm) telencephalic region. To investigate the relationship between Dm neuronal addition and cognitive performance we attempted to behaviorally modulate adult neurogenesis. For this purpose, adult trouts were injected intraperitoneally with bromodeoxyuridine (BrdU), and then housed either in an Enriched Environment (EE) or in Social Restriction (SR) for 4 weeks. In order to avoid treatment-related stress on learning tasks, individuals from both groups were transferred to a common barren tank for 2 more weeks, until sacrifice. On week 6, AA learning, short and long-term memory performance were assessed (STM & LTM: 1h and 24h post-training, respectively). Fish reared in EE showed a better learning, STM and LTM performance, in terms of latency and % of avoidance, in contrast to SR fish. Proliferation, cell survival and neuronal activity analysis are currently being assessed.

P82.-Actin cytoskeleton: the backbone of memory trace?

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Long-term memory has been associated with morphological changes in the brain, in strict correlation with changes in synaptic efficacy. Such plasticity is proposed to rely on dendritic spines as a sort of neuronal canvas on which these changes can take place. Given its key role on spine morphology, actin cytoskeleton dynamics and its major regulating factors (such as ADF/Cofilin) become an attractive target to study processes underlying dendritic plasticity.

Using a contextual fear conditioning paradigm in mice, we found that pharmacological induction of depolymerization of actin filaments through an intra-hippocampal injection of BMS-5 –a potent inhibitor of LIM kinase, which is in turn an inhibitor of ADF/Cofilin activity– causes an impairment in memory consolidation and reconsolidation. On the other hand, when favoring stabilization of actin filaments by intra-hippocampal injection of Jasplakinolide immediately before a short reminder session that usually elicits memory reconsolidation, the formation of an extinction memory was facilitated. On top of that, we found an increase in P-Cofilin/Cofilin ratio in synaptoneurosome-enriched hippocampal extracts obtained after a reconsolidation eliciting reminder, implying a diminished depolymerization activity by this factor, therefore favoring stabilization of actin filaments when this phase of memory is taking place. Our results support the importance of actin cytoskeleton dynamics underlying the memory trace.

P83.-Effect of emotional states upon risky decisión making in youngs Argentines: preliminary results

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The main goal of this study was the evaluation of the effect of positive, negative and neutral emotional states upon risky decision making in young Argentines. 91 undergraduate students (18-27 years old) were assessed (M(Age)=21,92; SD±2,09). For emotional induction film clips were used and to assess emotional experience, Self Assessment Manikin (SAM) and Visual Analogue Scale (VAS) were reported before, during and after induction. To evaluate risky decision making, Balloon Analogue Risk Task (BART) was administered. Repeated measures ANOVA showed an interaction effect of time and type of induction on VAS scores [F(4, 90)=2.89; p.05; ŋ2p =.14]. Post hoc analysis indicated that participants under a positive emotion won more points in BART than participants under neutral or negative emotion. Scores in BART are considered as a measure of risk because indicate larger pumpings in every balloon. This result is coherent with several studies that indicated that youngs under positive events and with a positive urgency trait shows more risky behaviors.

P84.-Activity regulated cytoskeleton-associated protein is required for consolidation of overlapping object, but not spatial memories in the Perirhinal cortex

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Successful memory involves not only remembering information over time but also keeping memories distinct and less confusable. The ability to separate the components of memories into distinct memory representations relies on pattern separation, a computational process by which differences are amplified. Pattern separation has been investigated in the dentate gyrus of the hippocampus and shown to occur in a spatial domain (DG), but little is known about this process in other brain regions like the perirhinal cortex (Prh) that process a different type of information (ie. non-spatial object memories). In this work, we used a PRH-dependent task and manipulated the load of pattern separation during information encoding. We showed in male rats that consolidation of pattern-separated object memories (and not spatial memories) depends on the expression of the gene Arc is required in the PRH for separable storage of overlapping, but not distinct, object representations, and also the neurotrophin BDNF is required for this pattern separation process, which is identical to its role in the DG., and that interaction between Arc and the neurotrophin BDNF is necessary for successful pattern separation. We provide novel evidence regarding the proteins involved in pattern separation outside the DG and suggest that, despite the anatomical differences, similar mechanisms underlie pattern separation in the DG and Prh that are engaged depending exclusively on the similarity of the stimuli.

P85.-Novelty improves LTM after reconsolidation through a behavioral tagging process.

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Last year we introduced that memory reconsolidation occurs through a behavioral tagging process. We demonstrated this showing that reconsolidation blockade, induced by the infusion of the protein synthesis inhibitor emetine (EME) after retrieval, in either the spatial object recognition (SOR) and the inhibitory avoidance (IA) tasks, can be rescued by previous exploration to a novel open field (OF) that provides the proteins required for the process to occur. Here we stepped forward by studying how does the novel experience, in the context of memory reactivation, affects LTM performance after reconsolidation. We observed that SOR reconsolidation established a different memory with the new position of the object during the reactivation session. Also, EME infusion after memory reactivation blocked the reconsolidation inducing amnesia for the original and the new memory. Interestingly, the exploration of a novel OF 1h before memory reactivation rescued the LTM for both the original and the new position of the object. Besides, the same exploration performed before a reactivation session in normal conditions (without EME) improved the LTM after the reconsolidation. Moreover, this effect depended on protein synthesis induced by the novel experience. Similar effects were observed in the IA task. As whole, our results show that experiences close to memory reactivation can improve LTM performance, by taking advantage of the behavioral tagging process underlying the reconsolidation.

P86.-5-HT2a receptor in mPFC controls context-guided reconsolidation of long- term object memory in perirhinal cortex

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The object recognition memory retrieval is a complex process that required the interaction of multiples structures. It has been proposed that mPFC interacts with the hippocampus (HIP) during contextual-guided versions of the spontaneous object recognition paradigm. Using a pharmacological disconnection experiment, we have shown that mPFC 5-HT2aR modulation and HIP interacts in an ipsilateral way during the resolution of an object-in-context recognition memory task. Since the information regarding the identity of the object could be stored in other structures such as the perirhinal cortex (PRH) then, the mPFC-HIP interaction could control the reactivation/reconsolidation in the PRH. To test this idea, we infused a 5-Ht2aR antagonist (MDL) in mPFC before the reactivation phase and immediately after a protein synthesis inhibitor (EME) in the PRH or dorsal dHIP. We also evaluate the interaction between the ventral hippocampus (vHIP) and the mPFC using a disconnection approach. We infused MDL in mPFC and muscimol in the vHIP before the retrieval and EME in the PRH after the reactivation session. We found that blocking 5-HT2aR signaling in the mPFC affects the reconsolidation in the PRH but not in the dHIP. In the disconnection experiment, only contralateral infusions made memories for both objects susceptible to the action of EME. Our results suggest that the interaction between mPFC 5-HT2a modulation and HIP activity controls the reconsolidation of object memory traces in PRH.

P87.-Sleep Accelerates Memory Re-Stabilization

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Consolidated memories can be reactivated by the presentation of a memory-cue (reminder) returning to a labile state followed by a process of re-stabilization known as reconsolidation. Thus, if amnesic agents are presented inside the reconsolidation time window (when the memory is still labile) the memory is impaired. However, if they are presented outside (~6 hours after reminder presentation), it has no effect on re-stabilization. Sleep is known to support the consolidation of newly encoded memories and it is also suggested that sleep has a beneficial effect on reconsolidation. Here we ask whether sleep accelerates re-stabilization of consolidated memories protecting reactivated memories from interferences. Participants learned a list of non-sense syllable pairs on Day 1. On Day 2, they received a reminder and they were allowed to sleep a 90 min diurnal-nap or they stayed awake for the same period of time or for 10 hours. After that, they received an interference task (new list of syllables). We found that the memory performance was impaired only when the interference task was given 90 min after the reminder (inside the time window of reconsolidation). There was no impairment when it was given after 90 min sleep or 10 hours after the reminder presentation (outside the reconsolidation time window). This finding suggests that a short-nap after reactivation during wakefulness accelerates memory re-stabilization.

P88.-mTOR controls hippocampal long-term inhibitory avoidance memory retrieval

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Understanding how stored memories emerge is a central question in the study of memory that is just beginning to be addressed. Although controversy concerning molecular events required for memory retrieval, protein synthesis has been recently investigated during this memory stage. Mammalian target of rapamycin (mTOR), a central regulator of protein synthesis in neurons, has been implicated in synaptic plasticity and memory. Using inhibitory avoidance (IA), a fear-motivated and hippocampus-dependent task, we evaluate the role of mTOR in memory retrieval. Infusion of a selective mTOR inhibitor,rapamycin, into the dorsal hippocampus 15min but not 3h before a test session carried out 24h post training impaired memory expression in a reversible way. We observed the same result using emetine, a general protein synthesis inhibitor. Then, we analyze if the effect depends on the age of the memory studied. mTOR inhibition 15min before test at 7 or 14 days, but not at 2h impaired memory retrieval. As previously seen in our laboratory with pretest hippocampal inactivation induced by muscimol, infusion of rapamycin 15min before test at 28 days did not cause temporal amnesia. Rapamycin infused in retrosplenial cortex, another structure required for IA memory retrieval, also impaired memory retention. Our results support the idea that ongoing protein synthesis mediated by mTOR pathway is necessary for long but not for short term memory retrieval when memory still depends on the hippocampus.

P89.-Becoming Anxious: How Threat Conditioning Affects Negative Valenced, Positive Valenced And Cognitive Systems

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Classical conditioning is the process by which the representation of two stimulus become associated and then, one of them (CS) is capable of predicting the occurrence of the other (US).Neurobiological basis of anxiety disorders were studied in laboratory settings using threat conditioning (TC). Although, little is known about how the formation of a fear memory affects other cognitive and behavioral systems associated with these type of mental disorders. Anxiety manifest as a persistent and generalized defensive system, activated when predicted aversive events are perceived as a threat and uncertain. Here we aim to study how an aversive implicit memory (TC) in humans could affect other valenced and cognitive systems such as those mentioned. To reach such goal, we used different anxiety inventories (BAI and STAI) to discard potential symptoms, electrodermal activity as our implicit memory measure, after that conditioning groups were evaluated on negative valence, positive valence systems and cognitive systems using several different tasks. In Experiment 1 we compared trained and untrained groups which underwent TC followed by the valenced and cognitive tasks in the same day. In Experiment 2, we used the same design evaluating the different cognitive systems 48 hs later. We revealed that the formation of a fear memory affects some cognitive and behavioral systems which are involved in the etiology and maintenance of anxiety disorders.

P90.-Stiatal role in the exploration/explotation balance

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Little is known about the subjacent mechanisms regulating the balance between exploitation and exploration. It is presumed that the striatum is implicated in the action selection process by integrating information coming from different cortices like prefrontal, orbitofrontal and anterior cingulated cortex. Our aim is to analyze striatal neural activity during a virtual foraging task where animals must decide between exploiting a depleting water patch and search for another, richer one. The task consists of a virtual linear track with short rewarded areas followed by longer unrewarded corridors. Two visually distinct rewarded areas are associated with different reward probabilities. Mice are implanted with tetrodes in the dorsal striatum and a metal plaque used to restrain the animal's head. Mice run on a cylinder and their movement is detected and translated into its position in the virtual corridor. Water deprived mice virtually navigate the track until the rewarded zone is reached, where the animal needs to lick a port a certain number of times to obtain a drop of water. Currently, we trained 7 mice to run on a virtual corridor and to stop in the rewarded areas and lick for a drop of water. We recorded striatal single units and local field potential as well as the position of the mice and relevant events during the task. Our results also reveal that mice are able to learn the task in hand by running towards the rewarded area and licking the port to obtain the reward.

P91.-Pattern Separation in humans in a virtual reality environment

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The mechanism by which the ability to separate the components of memories into distinct complex memory representations that are unique and less easily confused is called ‘‘pattern separation”. The objective of this work is to study this mechanism in humans in a virtual reality environment, which allows us to develop a task similar to that studied in rodents in our laboratory. The task consists of collecting separate flags from different angles and then recognize the middle flag. Preliminary results show that in sedentary people there is an angle at which it is not possible to differentiate the memories of the location of the flags (since they are too similar) whereas for another angle this does not happen. In this way, the results of the experiments in humans will benefit from those that occur in parallel in rodents and vice versa. It is a translational proposal that can undoubtedly have an impact on the knowledge of the biological bases of human cognition, mental health and cognitive improvement policies.

P92.-Modulatory effect of novelty on episodic memory and creativity tasks

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Recent studies in neuroimaging show that imagination, creativity, and episodic memory share neural networks. Motivated by this and based on previous results from our laboratory, we decided to study the effect of novelty in memory and imagination. For this we used a declarative memory task (Rey-Osterrieth complex figure), a convergent thinking task (Remote Association Test), a divergent thinking task (Uses Alternative Test) and an imagination of scenes task. The latter is evaluated across different age ranges from 6 to 90 years. Preliminary results show an enhancing effect of novelty on both retrieval of declarative memory and on divergent thinking. On the other hand, in the convergent thinking task, a positive effect was only observed in the more difficult items, but not in the easier ones. In the task of imagination of scenes, children (5-6 years) and elderly people (70-90 years) obtained similar scores, smaller than those found in adolescents (13-14 years) and young adults (20-30 years). Interestingly, novelty increased the number of reported entities by children to values that matched the ones observed in the rest of the groups. In conclusion, novelty enhanced retrieval of a declarative memory, divergent thinking and also convergent thinking, but only for the more difficult items. Surprisingly, novelty was able to increase imagination of scenes in children. These results could point at new strategies to improve memory and imagination in humans.

P93.-Contextual learning and the development of memory systems in the infant rat

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It's common to think about development as a period of immaturity. It doesn't mean that infants are immature but as a society, we consider that there's only one stage of maturity (the adulthood). We can find this social conception of development into neurocognitive theories. In cognitive neuroscience it's common to assume different memory systems and to describe their development through the study of contextual learning and the functional development of the hippocampus. For instance, the absence of recovery-from-extinction effects in preweanling rats has been related to the immaturity of the hippocampus, which in turn is linked to a simple memory system. This relationship has been confirmed in an experiment designed to show up that the administration of MK-801 (that blocks extinction learning in adult rats) does not affect extinction in infant rats (Langton, et al 2007). In the present study, we analyzed the relationship between MK-801 and extinction learning in infant rats, from an ecological model. Given that immaturity isn't a valid explanation in this model, our experimental designs were different to the one used by Langton et al., and they allowed us observing that MK-801 doesn't block extinction learning, but it produces conditioned motor responses interfering with the behavioral index of memory. These results are analyzed in the framework of the discussion between the ecological and the neuromaturational model of development and in terms of the construction of meanings.

P94.-Influence of The Words of Action in the Consolidation Processes in Different Memory Tests

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Consolidation is a process whereby a certain episode is labile during a limited time window after coding, which over time becomes an increasingly resistant memory to interference (McGaugh, 2000). In contrast to consolidation, it is believed that the reactivation returns the memory to a new labile state which will allow that episode to be susceptible to change. These memories are retained in memory through a process similar to the initial consolidation of the episode, that is, they are reconsolidated (Nader & Hardt, 2009; Stickgold & Walker, 2005). Research indicates that in order for this new memory footprint to be reconsolidated, time is needed; Therefore, studies on the process of reconsolidation in episodic memory carry an experimental design that is developed over three days. On the first day coding takes place. The second day, the memory is reactivated and manipulated. Finally, the third day a memory test is performed. The purpose of the present study was to investigate the impact of motor activity on the consolidation / reconsolidation process of movement related information and to see its effects on a free recall test and on another recognition test.

P95.-The influence of stress on fear memory extinction is not associated with dendritic spines remodeling in the ventral hippocampus.

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Fear extinction results in the suppression of the fear response once the conditioned stimulus does not predict the threatening event anymore. Different anxiety disorders have typical deficits in both extinction memory formation and expression. Ventral Hippocampus (VH) is critically involved in the processing of the aversive information as well as in the expression fear extinction memory. The aim of the present work was to evaluate whether the structural plasticity of CA1 VH accompanied the characteristic extinction memory formation and the influence of stress on the extinction memory. Stressed animals were fear conditioned to context and later trained in an extinction paradigm (repeated context re-exposures without foot-shock). Animals were sacrificed for preparation 1 day after conditioning (before extinction) or 1 day after extinction. Prior stress exposure induced a deficit in the formation of the extinction fear memory. With respect to structural plasticity, and on the contrary to the higher density of dendritic spines observed in CA1 Dorsal Hippocampus after fear conditioning, returning to basal levels after extinction training, CA1 VH presented no changes in the number or the morphology of dendritic spines, regardless of the fear conditioning, extinction training or stress condition. Thus, changes in the dynamic of the extinction fear memory might not be supported by synaptic structural remodeling in VH.

P96.-Cognitive Enhancer effects of chronic administration of fluoxetine are mediated by 5-HT2aR in mice

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In recent years, a body of studies have shown that some serotoninergic drugs have a role as cognitive enhancers. It has been proposed that, like in the case of LSD, this effect could be mediated by the serotonin type 2a receptor (5-HT2aR),. However, little is known about the possible cognitive enhancer effect of other serotoninergic drugs used in medical practice. Fluoxetine (FLX) is a selective serotonin reuptake inhibitor, well known for its antidepressant effects and for being widely prescribed in the treatment of different psychiatric disorders. We intended to analyze if chronic administration of FLX presented cognitive enhancer effects and the role of 5-HT2aR in this effect. For this purpose, we administrated a chronic oral dose of fluoxetine (10mg/kg) to Wild Type (WT) and 5-HT2aR knockout. mice (KO). After 4 weeks of FLX administration, we performed a novel object recognition task. The results showed that a 3 min training session is not enough to generate a long term NOR memory (24 h delayed) independently of the genotype. Interestingly, FLX treatment allowed WT mice to solve the NOR test. However, we didn't see this effect in KO mice. This result suggests that fluoxetine might have a role as a memory enhancer and that requires 5HT2A signaling.

P97.-Evaluation of Dopaminergic System Activity In Rats Treated With Cannabinoids and Consume of Artificial Sweeteners

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Nonnutritive sweeteners are sweet substances that no offer energy input to consumers. Sucralose is a nonnutritive artificial sweetener, sweetening food products and beverage. It is known that sweet foods have been implicated in the activation of mesolimbic reward pathway due to strong hedonic components, in fact many researchers have found sucrose has the same impact in dopaminergic system as some drugs of abuse like cocaine, this activation can be detected trough the accumulation of ΔFosB. To sense sweetness is necessary the activation of the heterodimer taste receptor T1R2-T1R3, in last years has been discovered that cannabinoids enhance the preference to sweet. Having this as a reference we hypothesize, that animals treated chronically with cannabinoids alter sucralose intake and modify their dopaminergic system. Whereby our aim is evaluate the sucralose consume of Wistar male rats treated chronically with cannabinoids and assess activity in dopaminergic areas like prefrontal cortex, amygdala and accumbens nucleus trough immunodetection of ΔFosB. Animals are being treated for 20 days with an intraperitoneal injection of anandamide (1mg/kg bw), vehicle injection (DMSO 95% and tween 5%), or without injection, sucralose consume or only water consume. Daily consume of food, water, sucralose solution (0.02%) and weight are measure in each group. The preliminary results suggest that an activation of dopaminergic system exists for the differential expression of DFosB.

P98.-Acute Ethanol Exposure Induces Anxiety Like-Behaviors In Infant Rats: Omega 3 As A Protective Factor

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Introduction: Literature shows that prenatal alcohol exposure can have teratogenic effects on brain structure and function as well as long lasting neuro-behavioral effects including enhanced anxiety-like responses. Omega-3 polyunsaturated fatty acids, the essential fatty acids found in fish oil, have protective effects against ethanol-induced neurotoxicity. Objective: the aim of this study was to explore the potential protective effects of Omega 3 against the increased anxiety-like behavior induced by acute ethanol exposure in infant rats. Method: A 20% solution of ethanol in saline was administered to postnatal day 7 (PND) Wistar rats in two separate treatments, 2 hours apart, each treatment delivering 2.5 g/kg (sc); control rats were treated with saline only. Another group was administered with one dose of Omega3 (720mg/kg, i.g) 15' after the last alcohol injection. Control Omega3 group was considered. Behaviors related to anxiety were analyzed in the open-field task at PND 14. Results: acute ethanol exposure at PND 7 leads an increase in anxiety-like behaviors. Omega3 administration, a single dose, ameliorates the acute alcohol effects. Discussion: This is the first study to demonstrate that an acute ethanol exposure occasioned behavioral alterations that persist in the offspring. Furthermore, Omega3 ameliorated the ethanol-induced effects in rats. Omega3 administration may have therapeutic effects to reverse or mitigate some of ethanol´s damaging consequences.

P99.-Fight outcome modulates an associative memory in the crab Neohelice granulata

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A new area of study has emerged with the aim of studying the effects induced by social relations in processes such as learning and memory. Cognitive abilities of an animal can not be studied and understood if it is not in function of the ecological pressures that mold its behavior. In this sense, several studies have demonstrated that aversive social events can modulate memory. Recently, we studied the influence of an agonistic encounter on an aversive learning paradigm based on a Contextual Pavlovian Conditioning (CPC) that occurs immediately after a paired fight. Results revealed a differential modulation, losers showed significantly higher memory retention than the respective winners. Thus, we propose that the agonistic experience differently modulated the crab's memory consolidation. Taking this together a new question arises in terms of the physiological mechanisms that are involved. A prior hypothesis is that differential stress levels as a consequence of the fight outcome could be implicated. To address this issue we measured glucose levels, after the fight. We found glucose increase between animals that were involved in an agonistic encounter and control animals. No differences between losers and winners were found. Our ongoing research combines the agonistic encounter with an appetitive paradigm. We expect to determine whether their different memory abilities extend to other types of protocols or are only noticeable feature in the aversive memory.

P100.-Effects of handling during a critical period on an animal model of autism

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Autism spectrum disorders (ASD) are characterized by reduced sociability, diminished communicative skills and repetitive behaviors. To identify the physiological mechanisms that underlie this disorder, we used a mouse model of ASD: the prenatal exposure to valproic acid (VPA).

Previous results from our group show that weaning VPA mice at postnatal day 21 (PD21) with control mice reverts the reduction in sociability observed in adult VPA mice reared with other VPA peers. These evidences suggested that there is a critical period between PD21 and PD60, when sociability can be determined. To narrow this critical window, we aimed to study the physiological and behavioral consequences of a procedure called handling (H) and carried it out between PD21 and PD34. H was reported to produce long-term behavioral and immune alterations, and can even counteract the effects of prenatal infections.
We observed that H reverts some of the behavioral alterations observed in our model: increases sociability and diminishes self-grooming. It also reverts the effects of VPA observed in the forced swimming test and open field test. We will evaluate neuroinflammation and alterations in the piriform cortex, as they were identified previously as candidates in our VPA model. We hope that this study will help us identify a possible physiological mechanism underlying the effects of prenatal VPA exposure on behavior and their rescue by handling.

P101.-Waiting for reward: An animal model for studying binge like behavior

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Increasing the intake of highly palatable food in a short time is one of the most important features of binge eating episodes. These are usually related to the previous experimentation of negative emotions. The objective of this study was to explore some aspects of binge eating behavior in a new animal model that involve exposure to frustrating events due to the delay of an expected reinforcement. Adult male Wistar rats were used. In Experiment 1 it was observed that animals trained to receive a highly palatable reinforcer (32% sucrose solution) express a significant intake increase if they are re-exposed to the reward after a 2 min delay, as compared to a control group without delay. In Experiment 2 we explored whether the magnitude of the intake increase is dependent on the state of frustration. Specifically, a group of animals were evaluated upon re-finding a 16% sucrose solution after a delay, which represents a less stressful condition since the discrepancy between the obtained and expected reward is lower. The effect of increased intake by delayed reinforcement was replicated in animals trained with 32%, while no increase intake was observed in animals trained with 16%. These data suggest that the state of frustration produced by delayed reward would involve an increase in the motivational value of the expected reward. This could be one of the behavioral mechanisms underlying the intake increase after frustrating situations.

P102.-Layer IV-Va neurons of the granular retrosplenial cortex (A29) project and control the activity of layers II-IV neurons of dysgranular retrosplenial cortex (A30) during contextual fear memory processing

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Retrosplenial cortex (RSC) is connected with the hippocampal formation and neocortical areas, and has a role in cognition and spatial navigation. It is subdivided in two main regions, A29 and A30, according to their cytoarchitectural organization and connections. It is unknown how these subdivisions are functionally integrated. MK801-treatment was used as a non-invasive method for selective elimination of layers IV-Va neurons of A29 (A29MK801). Immunolabeling of GABA-associated proteins parvalbumin and calretinin revealed that MK801-treatment does not affect these neuronal populations in A29. This suggest that A29MK801 are not GABAergic neurons. Microinjections of the retrograde tracer Fluoro-Gold (FG) in superficial layers of A30 showed FG positive neurons (FG+) exclusively in layers IV-Va of A29 distributed similarly to A29MK801 neurons. MK801 treatment dramatically reduced the number of FG+ in layers IV-Va of A29. These data indicate that A29MK801 neurons establish efferent projection to layers I-IV of A30. cFos and EGR-1 expression during contextual fear memory (CFM) encoding and retrieval indicate A29 and A30 involvement during memory processing with a different activation pattern. Ablation of A29MK801 neurons after consolidation of CFM reduces freezing and IEGs expression in A30, without affecting A29 and other related areas. Together, our results indicate A29MK801 neurons involvement in fear memory processing and their relevance in the interaction between A29 and A30.

P103.-Evaluation of behavioral phenotypes before and after transgene suppression in a conditional TDP-43 mouse model of Frontotemporal dementia /Amyotrophic lateral sclerosis

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Mislocalization and aggregation of TDP-43 are two common features of frontotemporal dementia (FTD) as well as amyotrophic lateral sclerosis (ALS). We developed transgenic mice conditionally overexpressing human wild-type TDP-43 protein (hTDP-43- WT) in forebrain neurons, a model that recapitulate key features of FTD/ALS. After post-weaning transgene (TG) induction during 1 month, these mice display an early behavioral phenotype, including impaired cognitive and social function with no substantial motor abnormalities. In this study we evaluated the behavior before and after 2 weeks of TG suppression. hTDP-43-WT mice evaluated in the Y-maze test displayed normal spatial and working memory both before and after the suppression protocol. This indicates that TG suppression prevents the installment of early cognitive deficits. TG suppression also prevented the development of the mild spasticity observed in mice expressing the TG for 1 month. Both locomotion and exploratory behavior (open field test) and motor coordination (rotarod test) were indistinguishable from controls before and after TG suppression. Since the results of these tests were consistent with the ones seen after 1 month of TG expression, the suppression protocol had no unspecific effects on motor behavior. No social deficits were found before TG suppression. These results contribute to our understanding of FTD/ALS and provide valuable information for susceptibility windows in therapeutic strategies.

P104.-Are CB1R and CB2R interacting in the regulation of anxiety?

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The neuromodulatory role of the endocannabinoid system contributes on maintaining the homeostasis of physiological states including mood and emotion. Changes in the expression of the CB1 receptor (CB1R) gene have been related to depressive effects. Mice lacking CB1R exhibited a behavioral state analogous to depression in experimental animals. Previous results, showed that CB1R knock-out mice (CB1-/-) presents an increase in CB2 receptor (CB2R) expression and altered neuronal plasticity. The aim of the study is to evaluate the effect of CB2R agonist (JWH015) and antagonist (AM630) in behavioral paradigms of anxiety and depression in CB1 receptor wild-type mice (CB1+/+) and CB1-/-. CB1+/+ and CB1-/- mice were divided into four groups and were injected with Vehicle, JWH015, AM630 or JWH015+AM630. Open field test (OF) and forced swimming test (FST) were performed 30 minutes and 2hours after injection, respectively. In OF test, time spent in periphery was decreased by JWH015 and increased by AM630 in CB1+/+ meanwhile time spent in central zone was increased by JWH015 and decreased by AM630 in CB1+/+. No differences were observed in CB1-/-. In FST, time of immobilization was increased in CB1-/- respect to CB1+/+. Treatment with agonists or antagonist did not show any differences in CB1-/- or CB1+/+. Since CB2 agonist, JWH015 has an anxiolytic effect in CB1+/+ but has no effect on CB1-/-, we proposed that CB1R and CB2R could be interacting in the regulation of anxiety.

P105.-c-Fos immunoreactivity in hypothalamus and reward system of young rats after social novelty exposure

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Enriched environments are benefical during youth, since they help to develop cerebral plasticity and decrease the chances to suffer certain diseases. This environments are compose of various types of stimuli that can be classified, in a rough way, in social and non-social, and in turn, in novel and familiar. Doing an analysis of the changes that social novelty causes over c-Fos production (a neural activity marker protein) in the brain, in comparission with other type of socio-ambiental stimuli, we observed that, during novel social encounters between young rats, there is a significant increase of c-Fos expression in the hypotalamus PVN, principal producer of pro-social hormones, oxytocin and vasopressin, and also, in the hedonic hotspots of the reward system, the Nacc and the VP. Our results agree with previous behavioral and physiological observations, wich show preference for social novelty, and participation of the hypotalamus and reward system diuring socialization in adult rodents and humans. This work could be a precedent to new enriched environment studies, manipulating the social variable, aiming to observe its effects over some deseases asociated to the reward system, such as addictions.

P106.-Role of the serotonergic receptor 2a (5-HT2a) in Cognitive Flexibility

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Living organisms inhabit environments that are being permanently modified, so adapting their behavior to such changes could determine their survival. The concept of "cognitive flexibility" refers to this ability, and the processes that mediate it involve cortical regions of the brain such as the prefrontal and the orbitofrontal cortex.
Given that serotonin (5-HT) has been identified as an important player in decision making, it would be reasonable to assign the serotonergic system a major role in processes of cognitive flexibility. Pharmacological experiments support this statement. However, it is still a question which are the receptors that mediate these processes.
One of the most important post-synaptic receptors of the serotonergic system is the type 2A receptor (5-HT2aR). This receptor is highly expressed in the limbic system as well as frontal regions of the cortex and has been associated with various psychiatric disorders. The lack of specific antagonists makes complex the identification of its function. Then, we would assess the role of the 5-HT2aR using protocols of extinction and reversal learning as measures of cognitive flexibility in genetically modified mice. Since cognitive rigidity is a common behavior symptom of many psychiatric disorders, it has clinical relevance to identified its underlying neurobiological substrate in order to generate new and specific pharmacological tools.

P107.-Neuroprotective potential of Insulin-like Growth Factor 1 (IGF1) in a rat model of sporadic Alzheimer's disease

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Alzheimer's disease (AD) is the most prevalent neurodegenerative pathology with no efficient therapy. Our objective is to develop biotechnological therapeutic strategies for preventing and/or overcoming the degenerative changes in the brain with experimental AD. In this context, we implemented gene therapy for Insulin-like Growth Factor 1 (IGF1), a potent neuroprotective molecule, in rats. We evaluated the effectiveness of IGF1 gene transfer to reverse or at least attenuate the deleterious effects caused by the intracerebroventricular (icv) injection of streptozotocin (STZ), an experimental model of sporadic AD. Animals were submitted into three experimental groups: Sham, STZ and STZ+IGF1. STZ and STZ+IGF1 groups received 3 mg/kg STZ-icv and, 7 days later, the STZ+IGF1 group received an adenovirus vector-expressing IGF1 icv. During the last two weeks until the end of the study (day 24 post-STZ-icv) we performed different behavioral tests. STZ treated rats were deficient in all tests. Interestingly, STZ+IGF1 group improved their hippocampus-dependent learning and spatial memory performance in the Barnes Maze. Anxiety-like and depression-like behaviour were also attenuated in the Marble Burying and Forced Swimming test, respectively, by exposure to IGF1. In this study, we concluded that brain over-expression of IGF1 protected against behavioral impairment in our AD rat model. Thus, IGF1 emerge as promising therapeutic molecule for AD treatment.

P108.-An hypothesis-driven analysis of brain functional connectivity during the acute effects of 3,4-Methylenedioxymethamphetamine (MDMA)

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In spite of its discovery during the early 20th century, the notable psychoactive properties of the substituted amphetamine 3,4-Methylenedioxymethamphetamine (MDMA, also known as "ecstasy") were first discovered and documented in the 1970's by the pioneering work of the american chemist Alexander Shulgin (Shulgin, 1986). These psychoactive effects include strong feelings of well-being and empathy along with mild to moderate stimulation and occasional perceptual distortions (Peroutka et al., 1988). The classification of MDMA as a Schedule 1 substance in 1970 halted ongoing investigations on its effects on brain activity and on its promising use as an adjoint for psychotherapy. Recently, the first contemporary neuroimaging study of MDMA performed by the Imperial College Group (Carhart-Harris et al., 2015) adopted an exploratory approach to reveal the alterations in global brain activity produced by the the substance (using a sample group of 25 individuals in combination with a double-blind placebo comdition). Here, we adopt a hypothesis driven approach based on the selection of regions of interest from the Neurosynth database (http://neurosynth.org/), corresponding to terms related to the subjective effects of MDMA (e.g. "empathy", "love", "emotion", "peace", "serotonin", etc). Using these regions as centers of coordinates for seed functional connectivity analysis, we revealed a core set of functional changes that could underlie the subjective acute effects of MDMA.

P109.-A novel and fully automatic spike sorting implementation with variable number of features

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The most widely used spike sorting algorithms are semiautomatic in practice, requiring manual tuning of the automatic solution to achieve a good performance. In this work, we propose a new fully automatic spike sorting algorithm that is able to match, or even improve, the performance of semiautomatic solutions with supervised intervention from expert users. We achieved this by incorporating: 1) a set of heuristic criteria inspired by the expert actions following the solution from semiautomatic algorithms, and 2) an improved feature selection method that increases the number of units that can be isolated from a single electrode recording. We evaluated the performance of the proposed method with real and simulated data. With the real data, the algorithm retrieved, in a fully unsupervised way, nearly 95% of the clusters isolated by the sorting experts while keeping a low number of false positives. With the simulated data, the algorithm managed to correctly isolate up to 18 neurons from a single channel, where 20 neurons were simulated. The new implementation presented here significantly outperformed the experts' sorting considering the number of hits obtained, while reducing the number of false positives by 40%.

P110.-Sturmian -Wavelets: an effective tool to analyze eye tracking data

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Eye tracking people while performing cognitive tasks allows one to gain novel insights regarding the brain structure and operation. However, movements associated with cognitive tasks are entangled with the mobility information related to the dynamics of the eye as a rigid body [1], the movement of the different parts of the internal eye structure, and also the noise produced by the eye tracker itself. In this contribution we present a novel Sturmian-Wavelets model which mathematically is able to separate out the cognitive information. Priorly used in physics [2], the Sturmian functions are chosen here to form a basis to represent the information associated to the eye dynamics. With kernel polynomials associated to these functions we define a Wavelet basis and use them to analyze time series, finally extracting the relevant cognitive information.

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P111.-An explanation for post saccadic oscillations on eye tracking data

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The analysis of the data obtained from eye tracking experiments during the performance of a cognitive task requires the knowledge of a wide variety of phenomena. The information associated to the cognitive task is entangled with many other phenomena. Commercial eye trackers, as the EyeLink 1000, obtain the position of the eye by registering the border of the pupil. The dynamics of the eyeball [1] and their internal structures, such as the iris and crystalline, influence the data obtained. The relevant cognitive information is also mixed with the noise produced by the eye tracker itself.

In this contribution we present a model which explains the post saccadic oscillations appearing on the EyeLink type eye trackers. The model describes, first, the dynamics of the eyeball, while the iris is represented as a driven damped harmonic oscillator mounted on it. The results allows to describe all the characteristics of the saccadic movements: the relation between the peak velocity and the saccadic size, the shape and size of the overshoot, the amplitude and period of the oscillations, among others.

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P112.-The analysis of a large-scale database of neuroimaging activation maps reveals a hierarchical correspondence between spontaneous and evoked brain activity patterns

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Since the seminal work by Biswal et al. (Biswal et al., 1995) - later expanded using multivariate methods by Beckmann and colleagues (Beckmann et al., 2005) - it is known that spontaneous brain activity recorded using fMRI presents a spatio-temporal organization consistent with well-defined neural systems. This correspondence was revealed for the first time by Smith and colleagues (Smith et al., 2009), who compared the independent components obtained from a database of fMRI task activation maps (http://www.brainmap.org/) with those obtained from resting state fMRI data. The striking correspondence between both sets of components suggested that spontaneous brain activity recapitulates spatio-temporal patterns that might be required for the rapid reaction to environmental demands. Here we investigate a database (http://neurosynth.org/) comprising 413429 maps obtained from 11406 studies. Combining graph-theoretical tools with modularization optimization algorithms, we performed a hierarchical clustering of these maps and observed task-positive and negative clusters at a coarse-level, which were then subdivided into maps associated with well-defined functions. In contrast with the work by Smith et al., the correspondence between task-derived maps and resting state networks was only manifest at an intermediate resolution. This result suggests that the wandering of brain activity around a hypothetical landscape of attractor states can only occur at a certain spatio-temporal grain

P113.-Towards a new protocol for study pattern separation in humans within virtual reality enviroment

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We present a computational kit to create neuroscience experiments in virtual immersive environment like a CAVE (Computer Assisted Virtual Environment). The virtual scenarios should be as similar to the real ones as possible, to improve experiences. The purpose of this work is to study the response of the human central nervous system in similar situations avoiding external factors (such as weather) or distraction. Protocols about perception, attention, cognition and memory is designed and implemented in CAVE. To examine pattern separation, the participant searches and collects objects inside CAVE using spatial strategies. All information about each participant trajectory, virtual scene configuration, location of objects indoors, and answers to particular questions regarding the experience is automatically collected.

P114.-Metric on the color space mediated by adaptation process

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In spatially uniform and temporally stationary conditions of luminosity, the ability of discrimination for trichromat humans depends on the compared colours. For example, it is pretty much easier to discriminate two orange chromas whose wavelengths differ in a quantity $\delta \lambda$, that two green chromas with the same difference. In previous work, we developed a theoretical model which explains this inhomogeneities in term of the physiological properties of the retinal cones. The absorption of photons is a stochastic process which variability depends on the wavelength. This variability puts a limit to the discrimination of the electrical signals that represent the two compared colours. There are recent experiments that extends the previous studies to the situation where illumination is not spatially uniform (the colour of the sorround is controlled in the experiment) , neither temporally stationary (the stimulus are shows for a brief period). The results show that the capacity of discriminating colour depends strongly on these conditions. On this work, we extend the previous theoretical models by including the spatial and temporal structure of the stimulis used in the more recent experiments. We show that, as response to the chroma of the surround, the visual system generates a representation such that the test colour moves away from the colour of the surround, distorting in this way the directions in colour space where it is easier or harder to make discriminations.

P115.-Testing the spacing effect on Mate Marote: a cognitive training software designed for large-scale educational interventions

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Mate Marote is an open source cognitive-training software aimed at children between 4 and 8 years old. It consists of a set of computerized games specifically tailored to train executive functions (EF): a class of processes critical for purposeful, goal-directed behavior, including working memory, planning, flexibility, and cognitive control. In previous studies we showed that (1) less than 7 hours of training elicited transfer to some (but not all) facets of EF, (2) the academic performance of children living at risk was boosted by the intervention, and (3) the quality of play and behavioural patterns in unsupervised interventions are comparable to the data collected in one-to-one supervised designs. The spacing effect in learning is well known. However, the effect of distributed practice on cognitive training has never been tested. In the present study we show that children performance in the EF tests obtained in controlled school environments with their own teacher are enhanced when children had played spaced versus massive designs, one session a week. In this unsupervised experiment, the gameflow, the instructions and the feedback were entirely provided by the platform and teachers only had to ensure the correct login of each children. This results represent an important step towards the ultimate goal of the investigation: the implementation of the platform in large-scale educational interventions as an online free resource which improves cognitive functioning.

P116.-AN INTEGRATED MODEL FOR MOTOR CONTROL OF SONG IN CANARIES

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Birdsong is a learned motor behavior that emerges from the interaction between a nervous system with a peripheral vocal device. The neural substrate that controls song production is known as the song system and consists of an interconnected structure of neural nuclei that is bilaterally organized, with anatomically indistinguishable structures in each hemisphere. These nuclei ultimately project to the periphery, (i.e. expiratory and inspiratory muscles and syringeal muscles) and therefore oversee the generation of complex motor gestures necessary for phonation. The vocal organ, or syrinx, is a bipartite structure that contains two pairs of phonatory membranes (labia) that can be controlled independently to produce complex sounds. Then, to vocalize, a bird must coordinate these motor gestures that regulates the tension of the labia, the airflow, and the gating patterns. In this work, we present a computational model that puts together the neuronal substrate with the biomechanics into an integrated model for birdsong production: First, we propose a computational model whose variables are the average activities of different neural nuclei of the song system of oscine birds. As an output of this model, two variables represent the air sac pressure and the tension of the labia during canary song production. Then, we show that these time dependent gestures can drive a biomechanical model of the vocal organ into synthesizing realistic canary like songs.

P117.-Modulation of glial cells activation in Parkinson's Disease induced by Lipopolysaccharide (LPS)

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Parkinson's Disease (PD) is a progressive neurodegenerative disorder which manifests as a motor disorder, characterized by slowness of movements, rigidity and tremor. Motor dysfunction of PD is due to dopamine loss in the neostriatum and due to the neurodegeneration of dopaminergic neuron's cell bodies of the Substantia Nigra pars Compacta (SNPC). Evidence suggests that chronic neuroinflammation, mediated by activated microglial and astroglial cells in the SNPC, could be essential for the degenerative process. It has been shown that intranigral LPS injection in rodents induces activation of glial cells, which release neurotoxic and pro-inflammatory factors that damage nigral dopaminergic neurons. Based on this evidence, our objectives were the following: *Generate a PD in vivo model by injecting LPS unilaterally in SNPC in order to characterize its impact on the motor function. *Implement gene therapy for IGF1 in order to evaluate its neurorestorative effect on rats' motor performance, on glial activation and on inflammatory response. Our results show that IGF1 gene therapy is capable of restoring motor deficit present on a PD model induced by LPS. Moreover, we observed a significant increment of both GFAP+ (astrocytes) and Iba1+ (microglia) cells on the ipsilateral hemisphere of rats injected with LPS. In conclusion, IGF1 gene therapy can modulate glial activation and improve motor impairment caused by LPS injection.

P118.-Synchronized HVC activity in auditory perception in canaries

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Songbirds have been the focus of neuroethological research of the principles underlying vocal production, perception and learning. A birdsong's brain presents specialized neural nuclei dedicated to these tasks (the 'song system'). Telencephalic nucleus HVC is sensorimotor: it is required for song production and its neurons present a highly selective response to auditory presentations of the bird's own song (BOS). Previous works showed that in zebra finches (Taeniopygia guttata), the elicited auditory response presents a similar firing pattern to the one measured while the bird is singing, suggesting a shared coding mechanism for the motor production and sensory perception of song.
With the advent of multielectrode arrays, it is possible to obtain high-quality neural data across many recording sites simultaneously. In this work, we studied HVC activity using a 32-channel silicon probe by measuring the auditory response to BOS in head-fixed, urethane-anaesthetized canaries (Serinus canaria). Spike sorting allowed us to isolate many single units from each protocol and we found that population firing patterns tend to be highly correlated, even among cerebral hemispheres. Since auditory responses to BOS could be used as a proxy for neural activity during singing, these results may also inform the neural code for song production. Finally, we studied the relation between local field potentials (LFPs) peaks and bursts of activity of single units at HVC.

P119.-Modelling temperature manipulations in the brain during birdsong production

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The neural mechanisms in the birdsong motor pathway that lead to the generation of respiratory patterns are a matter of extensive debate. In a top-down control paradigm, vocal gestures emerge from a unique timescale ruled by the telencephalic nucleus HVC, which engages other brain regions downstream. Another possibility is that the generation of motor instructions is distributed throughout the neural network, flowing both upstream and downstream. In this circular architecture, the song results from the integration of more than one timescale. In order to disambiguate these views, we used local focal cooling of HVC in canaries to manipulate the timescale present there. Within the frame of the circular model, we fitted the experimental pressure patterns of four recurring types of syllables, which form a full song. We show that at least two separate timescales must be taken into account to reproduce them, as one timescale is manipulated and the other remains unchanged. The modifications -stretching and breaking- of the syllables were quantitatively reproduced in this frame.

P120.-From EMG to frequency modulation in the zebra finch song

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Behavior requires the central nervous system (CNS) to control a set of biomechanical devices. The instructions from the CNS are electrical in nature, and need to be translated by these devices. In the case of birdsong, a delicate and fast control of a set of muscles is required to control the configuration of the syrinx (the avian vocal organ), and the respiratory system. In particular, the syringealis ventralis muscle (vS), controls the tension of the vibrating labia, which modulate the airflow to produce sound. However, the translation of the instructions into acoustical features is complex and species specific. In the case of zebra finch, although the mean fundamental frequency in a syllable is correlated to the mean electromyographic (EMG) activity of vS, it is not trivial to account for the fast frequency modulations, or to interpret bursts of activity between syllables.
In this work we present a biomechanical model of the dynamics of the vS muscle and the labia. The model is driven by the EMG activity of the vS muscle and allows to calculate the frequency modulation produced by the stretching of the labia.
We show that even using small segments of data, the parameters of the model can be fitted, and the predicted frequency for different types of syllables and frequency ranges is in agreement with the measured sound.

P121.-Development of a low cost eye tracker

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The registration of the eye movements is turning into common practice in games, business, marketing, science, and other areas. It is also turning into an important tool for diagnosis of diverse medical or psychological conditions like AAD, Autism, Alzheimer desease, etc. Among the various types of eye movements, the most important ones for the diagnosis are the saccadic. Most of the commercial eye trackers like those produced by EyeLink and Tobii are expensive and even prohibitive for most of the health institutions. This make difficult the use of these equipments widely on clinical and health institutions.
In this contribution we present a low cost eye tracker developed to be accurate enough to make a precise registration of the saccadic movements with the only requirement of essentially any common webcam. Possibilities in this direction has already been studied and reported [1]. We worked on a custom-made Javascript code that localize pupils positions in real time, with a featured-based method. Different type of information processing can be performed with a set of in-browser tools on the web page front-end. Some preliminary results are presented using the eye-tracker in an experiment consisting of fixating gaze on a grid of equispaced points over a large screen.

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P122.-HVC neural activity supports a circular model for birdsong production

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Songbirds are a well-established animal model for the study of vocal production, perception and learning. During singing, the respiratory system and the vocal organ are driven by neural instructions from a set of nuclei dedicated to song production. Telencephalic nucleus HVC (used as a proper name) plays a key role in the production of motor commands that drive the periphery. In canaries (Serinus canaria), the interaction between air sac pressure and muscle tension necessary for song production has been previously studied in detail. Recently, these biomechanical motor gestures have been obtained as solutions to a neural population model of the song system. This model makes specific predictions about the timing of the sparse activity in the neural nucleus HVC during the production of motor gestures. We developed a tetrode array to chronically record extracellular activity in HVC of singing canaries. We were able to isolate single units from the recorded data and found a set of neurons locked to singing behavior for different phrases. We analyzed spike time delay with respect to syllable onset for specific phrases and found that neurons fire at a particular instance within a syllable and robustly for all syllables within a phrase across renditions. Spike times from different syllables from two birds occur at note transitions within the syllable. These findings support the predictions from the neural population model.

P123.-Modulation of glutamate release induced by GABAergic and glycinergic inhibitors during excitotoxic damage in a model of spinal injury

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In the spinal cord high extracellular glutamate concentration-evoked excitotoxic damage has large negative impact on loss of locomotor function and neuronal death. We have shown that the glutamate analogue kainate largely destroys neurons via excitotoxicity with a modest white matter damage (Mazzone et al, 2010). Our present objective was to determine the relative role of glutamate and GABA neurotransmission in the process of excitotoxicity. Using an in vitro model of excitotoxicity evoked by kainate on mouse organotypic spinal slice cultures, we investigated the timecourse and extent of endogenous glutamate release following 1 h application of kainate using a commercially available biosensor placed in the ventral horn area of such slices. We have analyzed the effect of different pharmacological inhibitors of glycinergic and GABAergic receptors, i.e. strychnine (0.4 µM), bicuculline (20 µM) and gabazine (20 µM) on this phenomenon. A strong release of endogenous glutamate induced by kainate to mimic spinal injury in vitro could be reliably monitored on a real-time basis. Our data indicate that blocking GABA receptors by bicuculline potentiated glutamate release, while no effect was observed with gabazine or strychnine. Thus, this method can offer an advantageous approach to explore the role of inhibition in controlling excitotoxicity and to test the mechanism of action and time-dependence of neuroprotective drugs aimed at blocking glutamate release. Supported by ICTP, CONICET.

P124.-Mesenchymal stem cell therapy improves motor performance in a rat excitotoxic spinal cord injury model

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Spinal cord injury (SCI) is a very common tissue destroying condition that leads to permanent or temporal loss of motor and autonomic functions as well as sensory capacity of the organs innervated by the injured spinal cord segment. In recent years, mesenchymal stem cells (MSC) therapy has generated promising results due to their anti-inflammatory, immunomodulatory and neuroprotective properties, although their ability to functionally replace neurons and glial cells remains highly discussed. The goal of the present work was to determine whether intracerebroventricular injection of MSC modifies the behavioural performance of rats affected by an excitotoxic SCI model. Male Sprague Dawley rats were intraparenchymally injected with 1mM KA at the C5 cervical segment. Three days later, 10 µl of either MSC (6x103 cells/µl) or saline were injected by intracerebroventricular via into the fourth ventricle. Motor and sensitive abilities were evaluated at days 3, 7 and 14, post KA injection (pi). We found that sensory evaluation showed no significant difference between both groups at any day pi. However, motor performance was significantly better in KA-MSC animals than in KA-injected animals. Intracerebroventricular injection of MSC showed a beneficial motor effect on KA- injected animals, thus indicating a potential use of the MSC therapy on the rat excitotoxic spinal cord model. Further studies are needed to correlate clinical with possible morphological changes.

P125.-Deep hypothermic shock reverses the damage caused by perinatal asphyxia in the rat's striatum

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The striatum is particularly vulnerable to perinatal asphyxia (PA). The main cells of this structure are the median spiny neurons, which are GABAergic calbindin (CB) positive neurons. At the time of delivery GABA has excitatory properties and the excitotoxicity process could be mediated through GABA-GABA synapses. The GFAP is an astrocyte protein that is overexpress after brain injury. The present work aims to quantify CB and GFAP after exposure to PA in the striatum and to evaluate the therapeutic effect of a short and deep hypothermic shock after asphyxia. The uterus was removed by caesarean section and the fetuses were exposed to hypoxia (19 min at 37 C˚) by immersion in water and, also, exposed to a temperature of 10 C˚for 30 min in case of the hypothermic group. Four experimental groups of 3-4 rats each were formed. The labeling of CB, GFAP, neuN, DAPI was measured in adult rats. In the PA group there was a significant decrease in CB positive neurons and an increase in GFAP expression compared to control. Treatment with post-asphyxia hypothermia prevented changes in CB and GFAP showing expression levels similar to control. The quantification of NeuN, DAPI did not show differences between groups. Perinatal asphyxia generates a decrease in the GABAergic cells of the striatum and increase a marker of brain insult as GFAP. Hypothermia seems to reverse this damage. Deep hypothermia could be a superlative option to reduce severe disability generated by the PA.

P126.-Neuroendocrine control of puparium morphogenesis

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Drosophila larvae undergo a dramatic change in body shape at the end of the larval growth period when the thin, flexible and transparent cuticle of the larvae is transformed into the puparium. This remodeling is achieved by a series of muscular contractions such as retraction of the anterior segments and body contraction, and accompanied by structural remodeling of the cuticle. Even though the onset of the metamorphosis is known to be under the control of ecdysone, other molecular players have been shown or hypothesized to act downstream of it to mediate different aspects of these behavioral and morphogenetic processes. Serendipitously, we observed that animals lacking the relaxin-receptor like G-protein coupled receptor Lgr3 produce a thin and elongated puparium, indicating that Lgr3 is required for proper puparium morphogenesis. This activity is separable from the previously described role for Lgr3 during larval development, where it has been shown to act in a subpopulation of CNS neurons to coordinate growth with developmental timing by inhibiting ecdysone biosynthesis, in a Drosophila insulin-like peptide 8 (Dilp8)-dependent fashion. Rather, our results are consistent with Lgr3 acting in a distinct population of neurons that respond to a developmentally-triggered surge of carcass-derived Dilp8 peptide that occurs at the onset of pupariation. Hence, the Dilp8 and Lgr3 constitute a new neuroendocrine pathway directly contributing to puparium morphogenesis.

P127.-Unbalanced Corticostriatal Connectivity in a Mouse Model of Neonatal Dopamine Dysfunction

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Neurodevelopmental psychiatric disorders as attention deficit hyperactivity disorder (ADHD) might stem from alterations of dopamine (DA) regulation of the corticostriatal system. Previously, we found that neonatal DA depleted mice (proposed as an ADHD mouse model) showed alterations in exploration of novel environments and deficits in the capacity to exploit opportunities and social behavior. These behavioral changes were accompanied by a reduction in corticostriatal connectivity and a contraction of medium spiny neuron (MSN) dendritic tree. In order to understand whether the neonatal DA lesion affects differentially the activity of the direct (dMSN) and the indirect MSN (iMSN), here we performed in vivo juxtacellular recordings of individual MSN in transgenic mice showing dMSN-type-specific expression of the fluorescent protein tomato allowing us to indentify the cellular identity of the recorded cell. We examined the in vivo MSN response to cortical inputs from prelimbic and M2 cortical areas. We found that the neonatal DA neuron lesion did not affect the response of dMSN and iMSN to prelimbic inputs. Interestingly, we also found that lesion mice dMSN were more responsive to M2 inputs with no changes in iMSN response. Together, our results suggest that DA is essential during postnatal development for the normal functional and structural maturation of the corticostriatal system, and the correct balance of corticostriatal inputs to the direct and indirect pathways.

P128.-Connexin switch in glial network maturation

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Olfactory bulb innervation by olfactory sensory neurons (OSNs) refines post-natally and is a sensory activity-dependent process. OSNs associate to olfactory ensheathing cells (OECs), specialized glia organized in connexin 43 gap junction mediated networks. We propose that glial networks refine simultaneously with neuronal circuits. Previous results showed that OEC networks exist at neonatal ages, and that OEC sensitivity to meclofenamic acid (MFA, gap junction blocker) is comparable at neonate and juvenile stages. MFA-sensitivity is absent in OECs with deletion of the gap junction protein Cx43 at juvenile and adult ages. Strikingly, OECs show minimal Cx43 expression at P0-3 and higher levels from P4-30, suggesting a connexin switch during circuit refinement. By means of dye-coupling experiments we show that OEC network size diminishes with age. Surprisingly, dye-coupling is affected at P7 but not at P3 Cx43 KO OECs, indicating Cx43 independence at P3. To assess the molecular bases of these results, we used mice expressing a fluorescent reporter in OECs. mRNA was extracted from OEC-enriched samples by laser microdissection microscopy. We were able to specifically detect OEC markers and avoid contamination with neuronal transcripts. Cx29, a putative candidate to mediate OEC networks in the absence of Cx43 was not detected. These results suggest that OECs mature with the neuronal circuit, reflected in network selectivity and the molecular bases for connectivity.

P129.-Voltage Activated Conductances in Motoneurons, and their Influence on Motor Circuits

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Motoneurons have been conceived as mere output units of networks that control motor behaviors; however, several evidences suggest that they play active roles in shaping motor patterns. In leeches the motoneurons responsible for the elongation of their body, CV (circular ventral) neurons, are linked to the crawling central pattern generator (CPG) via a positive feedback connection. Intrinsic properties of neurons can markedly shape the output of the circuits inwhich they participate. CV motoneurons exhibit a low threshold spike (LTS) on topof which a burst of action potentials is fired. In the present work we aim at analyzing the properties of the CV LTS, and develop tools to analyze the role of this phenomenon on crawling. The results suggest that the LTS of CV motoneurons exhibits a threshold close to the resting potential of the neurons, depends on Ca2+]o, and NNC 55-0396, a blocker of T-type Ca2+ channels, inhibits it.

P130.-Ghrelin Signaling Diferentially Activates Non-Dopaminergic Neurons of the Ventral Tegmental Area Subregions

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The ventral tegmental area (VTA) together with the nucleus accumbens (Acb) form the mesolimbic pathway, which is involved in the regulation and processing of the rewarding aspects of food consumption. The VTA comprises different neuronal populations, including dopaminergic, GABAergic and glutamatergic neurons. The VTA and Acb are both divided in three different sub-divisions with differential connectivity. Ghrelin is a peptidic orexigenic hormone secreted from stomach that binds to a G-protein coupled receptor, the growth hormone secretagogue receptor (GHSR). GHSR is expressed in several brain nuclei involved in food intake regulation, including the VTA. In this study, we investigated the ability of ghrelin to reach and activate VTA and Acb sub-divisions. We found that peripherally administered ghrelin fails to reach and increase the levels of the marker of neuronal activation c-Fos in both the VTA and the Acb. We also found that centrally administered ghrelin reaches VTA neurons and increases c-Fos in different sub-divisions of the VTA and Acb. Finally, we show that dopaminergic neurons of the VTA fail to increase c-Fos in response to centrally administered ghrelin. Thereby, we conclude that central ghrelin is able to reach the VTA and to activate VTA and Acb sub-divisions, and that VTA neurons activated by ghrelin are not dopaminergic neurons.

P131.-Neuronal projections from the lateral neocortex to the amygdala

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Cognitive function is a product of the concerted and synchronized activity of many brain areas with a proposed hierarchical relation. Previous results indicated that the lateral neocortex is necessary for contextual fear memory reconsolidation and suggested a functional connection with the amygdala, a key structure for processing emotional information. To further investigate the synaptic connections between these areas, we first used an optogenetic-based strategy in which we expressed the light-activated cation channel rhodopsin in the lateral neocortex on the left side of the brain and implanted an electrode array plus optic fiber in the amygdala in this hemisphere. We observed changes in amygdalar local field potential upon light stimulation in almost half of the electrodes. Furthermore, we performed paired-pulse stimulation and found a deflection of the paired pulse ratio when diminishing the pulse delay, indicating monosynaptic connectivity. To evaluate the possibility of a direct morphological connection between the areas we performed retrograde labeling studies. Overall, our results support a monosynaptic connection between the lateral neocortex and amygdala.

P132.-Experience-dependent retinal protection against acute ischemia

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Ischemia is a key component of several retinal diseases that are leading causes of irreversible blindness. At present, there are no effective strategies to prevent retinal ischemic damage (ID). Enriched environment (EE) is a paradigm that involves sensory, cognitive, motor, and social stimulation. The aim was to analyze whether the previous exposure to EE prevents acute retinal ID. Adult male Wistar rats were exposed to standard environment (SE) or EE for 1 or 3 weeks before ischemia. Retinal ischemia was induced by increasing intraocular pressure to 120 mm Hg for 40 min. After ischemia, both groups were housed in SE for 3 weeks, and subjected to functional (by electroretinogram (ERG) and anterograde transport to central visual areas) and histological analysis. The number of retinal ganglion cells (RGCs) was assessed by Brn3a-immunoreactivity. In animals housed in SE, ID induced a significant decrease in ERG a- and b- wave amplitude and oscillatory potentials and anterograde transport, whereas the previous exposure to EE prevented these alterations. Two weeks after ischemia, a significant decrease in the total retinal thickness, the number of RGCs as well as an increase in Iba1 and ED1 immunoreactivity were found in retinas from animals housed in SE, whereas in ischemic retinas from animals housed in EE, these parameters were significantly preserved. These results suggest that the exposure to EE decreases retinal vulnerability to ID.

P133.-Analysis of Single-Unit Activity and Local Field Potentials during the Progression of Epileptogenesis on an Experimental Epilepsy Model

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Epileptic seizures are sudden changes in neural activity that interfere with the normal functioning of the neural network, expressed through hypersynchronic discharges. The aim of this study is to analyze how single-unit activity (SUA) and local field potentials (LFP) would be affected during the progression of epileptogenesis. Male Wistar rats were implanted with a bipolar macroelectrode in the CA1 region of right ventral hippocampus, through which they were kindled, and eight microwires were placed in the CA1 region of right dorsal hippocampus (rdH). SUA and LFP were recorded continuously during the rapid kindling protocol. SUA and LFP ictal and interictal activity of rdH were analyzed. We found heterogeneous changes in neuronal firing rate during electrographic seizure activity. Different patterns of neuronal activity were observed. Some neurons increase and others decrease their firing rates, while many units did not change. The interictal firing rate becomes higher according as epileptogenesis progresses. These different degrees of stereotypical firing patterns during seizures might depend on whether or not neurons are actually being recruited by the propagating wave of seizure spread. The combined study of SUA and LFP can provide new insights into the process of transition to seizure, allowing us to assess precisely the dynamic changes involved in epileptogenesis. Future studies are needed to understand how these patterns would be involved in epileptogenic networks.

P134.-Reward-related signaling in the dorsal striatum

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The ability to predict rewarding outcomes is essential for learning and consolidating stimulus-reward associations. The striatum is part of the basal ganglia and it is involved not only in the motor control of a sequence of actions but also in coding other aspects related to a task such as cues that are associated to a reward, estimation of time, reward-prediction error, etc. Here we used tetrodes to record striatal activity in a self-initiated rewarded task. Briefly, after a minimum inter-trial interval of 2.5 s, water-deprived rats must enter a nosepoke and, following a visual cue, emit an eight-licks sequence onto a tube to receive water. Behavioral analysis shows that subjects quickly learn to perform lick sequences but have more difficulties in the control of their timely emission, as they prematurely enter the nosepoke. Premature entries reset the timer, reducing the reward rate, but with training animals learn the action-outcome association, improving their performance in the task. In electrophysiological records we found bracketing-like activity in beginning and the ending of the trials and also activity related to the visual cue and the delivery of the reward. Interestingly, we found neuronal activity modulation that correlates with the length of the ITI, both for correct trials and premature entries with sequences. These findings show that the striatum is coding multiple aspects of the task.

P135.-Influence of young vs. mature adult-born dentate granule cells on CA3 in vivo

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The hippocampal dentate gyrus is among the few areas of the adult mammalian brain that constantly incorporates new neurons. Ex vivo experiments revealed that young granule cells (GCs) are more excitable than mature GCs, while both populations evoke similar postsynaptic potentials on their main target neurons in CA3. However, the influence of young vs. mature GCs on CA3 in vivo remains unknown. Here we show CA3 neuronal activity recorded while mice explored different environments, with or without optogenetic stimulation of young and mature GCs of the same cohort (longitudinal analysis). Our preliminary data suggest that stimulation of mature GCs evokes greater local field potentials in CA3 than young GCs. Furthermore, only the mature population evokes greater responses at 1 Hz than 0.1 Hz, suggesting differential facilitation effects. Ongoing experiments explore this phenomenon at higher stimulating frequencies and varying intensities. On the other hand, we identified three frequency bands in the local field potential that coordinate their amplitude with theta oscillations. Preliminary analyses suggest that exposing mice to an enriched environment potentiates the coupling at high frequencies but reduces it at low frequencies. This effect is partially reverted upon stimulation of adult-born GCs. These results suggest that CA3 information processing is dissimilarly affected by adult born GCs at different maturational stages.

P136.-Neuromodulators in the processing of afferent inputs in the dentate gyrus

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Neurogenesis in the adulthood continuously provides the dentate gyrus (DG) of the hippocampus with pools of granule cells (GC) which integrate into the preexisting network. The maturation process of this newborn neurons is well characterized and is similar to the maturation of GC during development. It has been shown that newly born GC are necessary for many types of memory but how these neurons contribute to the hippocampal function is under intense investigation. As inputs arrive to DG, they activate both excitatory and inhibitory neurons, and the excitation to inhibition (E/I) balance results in a pattern of population activity. Immature 4 week old GC have specific processing features, as they exhibit a higher E/I balance compared to mature GC. Thus, even though this population of neurons represents only 3-6 % of the total GC, their contribution to processing could be important due to their higher activity, their higher spiking rate and their higher plasticity. Neuromodulatory circuits projecting to the DG could modulate E/I balance in GC, providing a new level of plasticity for information processing of afferent stimulation.

P137.-Effects of cortical parvalbumin positive neuron dysfunction on the physiological properties of prefrontal cortex pyramidal neurons

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The underlying circuit mechanisms involved in cognition require a balanced interplay of interneurons and pyramidal neurons (PN). In the PFC, executive control and cognition correlates with gamma oscillations and with membrane potential (mp) subthreshold oscillations. Importantly parvalbumin interneurons (PV) are required for the generation of gamma oscillations and the balance of excitatory and inhibitory (E/I) inputs producing mp subthreshold oscillations. Thus a dysfunction in the PV activity may alter the PN physiology and the E/I balance. Such dysfunction is believed to be present in neurodevelopmental illnesses like schizophrenia, thus the study of PV dysfunction in PFC circuits is highly relevant for the understanding of cognition in health and disease. We focused on the effects of PV dysfunction on the morphology, membrane properties and E/I balance of PNs in mouse mPFC using a mouse line where the NMDAR is eliminated from corticolimbical PV neurons early on, showing molecular and behavioral markers resembling schizophrenia. We found a reduced and less complex dendritic tree and an increased excitability in PNs of KO mice. Furthermore whereas the E/I balance was not altered in the spontaneous activity of acute slices, the miniature events displayed a reduced IPSC and normal EPSC frequencies, increasing the E/I balance. These results suggest that PV dysfunction early on, impacts the maturation of the circuit altering both functional and structural characteristics of PNs

P138.-Study of cortical oscillatory activity in the development of dyskinesias associated to L-Dopa treatment in a rodent model of Parkinson's disease

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Prolonged treatment with L-Dopa in Parkinson's disease (PD) often leads to the emergence of abnormal involuntary movements known as L-Dopa-induced dyskinesias (LIDs). Recent findings in a rodent model of PD have shown that dyskinetic symptoms are linked to the occurrence of a prominent 80Hz oscillatory local field potential (LFP) activity within the primary motor cortex. Additionally, L-Dopa treatment decreases exaggerated beta (13-30Hz) oscillatory activity, which is exacerbated in parkinsonian state and has been associated with rigidity and bradykinesia. Despite of this, the correlation between motor symptoms and oscillatory activity in the development of LIDs is not fully understood; mainly because the animal’s behavior in the "on" state is a major constraint for multi-electrode chronic recording studies. To solve this and with the purpose to characterize the relationship of beta and high gamma (70–110Hz) cortical activity with parkinsonian state and the development of LIDs, we design a new setup based on a mouse spherical treadmill where animals could walk freely but had the head restrained of movement. This system allowed us to record cortical LFP and spike signals by means of high density electrodes in hemiparkinsonian mice as well in animals with LIDs, both in “on” as in “off” states. Movements were also tracked in order to correlate them with brain activity. Preliminary results showing a characterization of the oscillatory activity in the beta range will be presented.

P139.-Design of an affordable and easy-to-implement one photon microscope for imaging of neural activity during behavior

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Fluorescence microscopy of proteins such as GCamp6 has made it possible to observe neural activity of large neural populations. In particular, recently developed miniaturized one-photon microscopes enable the simultaneous recording of hundreds of genetically targeted neurons in behaving animals, with stability of months. However, commercially available microscopes are prohibitively expensive, while Do It Yourself alternatives have two main drawbacks. On one hand, they require a complex logistics that makes difficult their implementation in developing or peripheral countries. On the other, the manufacturing process requires specialized skills, such as experience with soldering ultra-small surface-mount device components. Here we test an open source prototype and propose several improvements adapted to the needs of Latin American laboratories. As a proof of principle, fluorescence images of fixed YFP-expressing mouse brain slices taken with the miniaturized prototype are shown to match those obtained with standard bench fluorescence microscopes. Based on the experience of building this prototype, we discuss several improvements regarding the design of the microscope body, the optics and the imaging hardware. Together, these improvements will make this technology affordable to neuroscience laboratories with no previous knowledge in microscopy or specialized skills in the assembly of electronic components.

P140.-Analysis of the encoding properties of nucleus accumbens neurons during learning of a self-paced operant conditioning task

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The available behavioral and anatomical evidence points strongly toward a role of nucleus accumbens (NAc) in promoting behavioral responses associated with reward and it has been proposed to function as a limbic-motor interface. Recordings in NAc in animals performing operant conditioning tasks have revealed phasic responses, in partially overlapping subpopulations, correlated with different aspects of the task, including motor responses and reward associated cues. However, little is known about how this responses evolve place during learning of a behavioral task. To unveil the evolution of encoding properties of NAc neurons along the acquisition of an operant conditioning task we implanted Long-Evans male rats with a microelectrode array in the NAc. Rats were motivated by water restriction to obtain water droplets from a lick tube located within a recessed “nose-poke” in a standard behavioral chamber. Rats were daily trained using a protocol in which trials were self-paced by the animal. Animals were required to lick 8 times for a water reward to be presented. To differentiate reward receipt from expectancy, half of the total correct trials were rewarded, half unrewarded. We identified different subpopulations of units responding to environmental salient events and motor responses. Interestingly, signaling properties and population composition of the NAc responses evolved along the learning of the task, supporting the notion that NAc participates in the learning process.

P141.-Minocycline prevents chronic stress-induced vulnerability to cocaine self-administration

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Clinical evidence supports the idea of individuals that suffer stressing events along their lives are vulnerable to developing substance use disorders (SUDs). Here, we demonstrated how exposure to chronic stressful life events can facilitate the acquisition of cocaine self-administration (SA). We also attempted to prevent SA behavior by minocycline pre-treatment. Thus, rats were exposed to chronic restraint stress (2 hs daily) during seven days. A week after that, animals were implanted with indwelling jugular catheters. A week after surgery, rats began daily 2 hs cocaine SA sessions for ten days. Four days before the onset of SA paradigm, the minocycline (30 mg/kg/12hs) or vehicle (DMSO 5%) daily treatments started, which were carried out until the end of the SA behavior. SA consists of a fixed ratio 1 schedule (FR 1) in which one response on the active lever yielded one intravenous cocaine infusion (0.2 mg/infusion, followed by a 10 s timeout period), paired with a tone and a light cue. An inactive lever was also available each session. SA criterion was defined as the first day animals obtaining more than ten infusions of cocaine. Our results point out a facilitation of the acquisition of cocaine SA as well an augmented intake of cocaine induced by chronic stress, which was interestingly abolished by minocycline. These findings constitute a starting platform to study the mechanisms underpinning the comorbility between stress and SUDs.

P142.-Big data analysis of whole striatum transcriptome after L-DOPA or Pramipexole treatment in a rat model of Parkinson's disease

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L-DOPA is the most effective treatment of Parkinson's disease (PD), but it frequently produces response fluctuations and abnormal involuntary movements after long-term treatment. Pramipexole is a D2/D3 dopamine receptor agonist which has a lower efficacy but also a lower propensity to induce motor complications. Therefore, it is likely that different molecular changes underlie these specific pharmacological responses. Transcriptomic technologies have aided large-scale research to elucidate the link between a specific gene or a cluster of genes and a particular biological mechanism. We used DNA microarray technology to assess whether the striatal gene expression profiles of hemiparkinsonian rats treated with L-DOPA or Pramipexole show statistically significant differences. To produce a model of early PD, rats received a unilateral injection of 6-OHDA in the striatum and were treated with L-DOPA or Pramipexole for three weeks. Differences in gene expression were assessed using the empirical Bayes moderated t-statistic. Overall, more than a thousand of genes were differentially expressed. The PD map of the University of Luxembourg was used as an exploratory tool to point out the localization of differentially expressed genes within biological pathways and compartments refining gene selection. This analysis will reveal new genetic striatal networks possibly contributing to the therapeutic effects of the most common treatments for PD.

P143.-Understanding ADHD dopaminergic neurotransmission: the p35 KO mice have a preserved D1 but an altered D2 function

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Attention-deficit hyperactivity disorder (ADHD) is a behavioural condition characterized by atypical levels of inattention, hyperactivity and impulsivity. A recent study suggest a global prevalence of 3,4 % in children, being the most diagnosed psychiatry disorder at present. Previous studies from our lab have demonstrated that transgenic mice lacking p35 protein (p35KO), the specific activator of Cyclin dependent kinase 5 (Cdk5) exhibit behaviors resemble those described in animal models of ADHD. P35 KO mice display hyperactivity and less anxiety-like behaviors. Besides, these mice have an increased striatal dopamine (DA) level. These behavioral and biochemical phenotypes are reverted by Methylphenidate and d-Amphetamine, drugs used in ADHD treatment. Since locomotor activity is dependent on dopaminergic neurotransmission, we decided to study the function and expression levels of the two main DA receptor, D1 and D2, in the p35 KO mice. We found that striatal D1 and D2 contents are similar between p35 KO and Wild Type (WT). To test D1 and D2 function, we used pharmacologic agonist (SKF81297/Quinpirol respectively) and antagonists (SCH23390/Haloperidol respectively) drugs. We found that p35 KO mice have a preserved D1 but an altered D2 function, since a low dose of the antagonist Haloperidol (0,03 mg/kg) induces an increase in WT locomotor activity and a decrease in p35 KO. These results may help us to elucidate the mechanism underlying the hyperactivity of this ADHD model

P144.-High dose ketamine increases glutamatergic neurotransmission in the prelimbic cortex of female rats

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Ketamine, a noncompetitive NMDA receptor antagonist, has potent psychomimetic effects, being able to accentuate the psychotic state of schizophrenic patients. One of the brain areas affected by its use is the prefrontal cortex, as the performance on tasks dependent upon their activity is deeply influenced by administration of ketamine. As in schizophrenia, these changes may be modulated by hormonal factors, and can be explained by the influence of female sex hormones. Attentional disturbances can be analysed by prepulse inhibition (PPI), heavily regulated by cortical-limbic circuits in rats. In this study we examine the effects of chronic administration and withdrawal of ketamine on attentional processes of female Wistar rats, tested at different stages of the estrous cycle, as well as the effects of pharmacological modulation of glutamatergic systems of the prelimbic cortex (PL). We confirm the hypothesis that PPI varies throughout the estrous cycle in rodents and the menstrual cycle in women, and is increased by estrogen treatment. Our results also show that the NMDA agonist alone in PL has no effect on PPI, but in association with the high dose of systemic ketamine was able to reverse the PPI deficit, independent of the estrus cycle phase. In conclusion, high doses of ketamine are able to increase glutamatergic neurotransmission in the PL in female rats. Financial Support: FAPESP (2014/09685-9).

P145.-Oral administration and behavioral testing of an inhibitor of serotonin synthesis

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Adult hippocampal neurogenesis can be enhanced by factors like serotonin (5-HT) depletion. Indeed, chronic administration of para-chlorophenylalanine (PCPA), an inhibitor of the 5-HT rate-limiting enzyme, results in increased survival of hippocampal newborn neurons, without affecting proliferation. We thus aim to dissect the role of 5-HT in the neurogenic multistep process, and in order to avoid intraperitoneal injections, experimental conditions for PCPA oral administration were set up. C57Bl/6J, male, 6-week old mice received PCPA (aprox. 100 mg/kg) by means of palatable yeast and jelly cubes, during 5 or 8 weeks. Brain and plasma samples were recovered to analyze 5-HT level. Neurogenic parameters were studied by immunohistochemistry and determined by unbiased stereologically counting. To study the role of PCPA-enhanced neurogenesis in the ability for pattern separation, we have previously performed 2 approachs: the Contextual fear discrimination learning test and the Object location task (OL). No difference were found between control and treated mice in any of these 2 tests. We now set up the Object Pattern Separation task, a recently developed test similar to the OL, but with more resolution. We suspect that this test may allow us to find subtle differences. These results will prove useful for a future proposal of replacement in the way of administration of PCPA and to implement this new test when studying animal models of enhanced neurogenesis.

P146.-LiCl treatment during cocaine abstinence leads to modifications on Wnt/B-catenin pathway in mesocorticolimbic areas.

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Cocaine addiction is a chronic relapsing disorder characterized by the loss of control over drug-seeking and taking. Recently, we reported that Wnt/b-catenin pathway's activity, in the prefrontal cortex (PFC), is important in the early stages of cocaine-induced neuroadaptations. Also, we found that a cocaine challenge after a period of abstinence, increased the pathway activity in the in the nucleus accumbens (NAcc). Moreover, we have shown that LiCl administered before each cocaine injection prevented the development of sensitization by restoring b-catenin levels in the PFC, CPu, and Amygdala, and prevented the expression of sensitization keeping the levels of b-catenin increased in the NAcc.
Thus, to elucidate if LiCl treatment during abstinence in animal models may prevent the expression of cocaine induced sensitization, all animals received one injection of cocaine or saline per day for 7 days. Then, they were administered with LiCl or saline for 7 days and 2 weeks later received a final cocaine challenge on day 28. Locomotor activity was measured after cocaine injection on days 1, 7 and 28. Then animals were sacrificed and their brains removed to evaluate b-catenin levels in PFC and NAcc.
Our results showed that LiCl treatment during abstinence exacerbated the response to cocaine on day 28, while preliminary data indicate that b-catenin levels are decreased in PFC. Ongoing studies are aimed to evaluate if LiCl during abstinence also modifies b-catenin levels in NAcc.

P147.-Influence of chronic restraint stress on cocaine-induced glutamate release in the nucleus accumbens

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Cross-sensitization between stress and drugs of abuse may be explained by long-term neurobiological changes in the mesocorticolimbic dopamine (DA) and glutamate (GLU) transmissions; specifically, within Nucleus Accumbens (NAc), the major limbic-motor integration area. In this sense, previous results from our lab have demonstrated that after two weeks of a single exposure to restraint stress a challenge of cocaine induced locomotor sensitization and a parallel increase in extracellular DA levels in Core compartment of NAc, meanwhile GLU levels in this area were not modified. The present study attempted to determinate the long-term effect of chronic restraint stress pre-exposure in extracellular levels of GLU in NAc Core in response to cocaine. Wistar rats were exposed to repeated (2h for 7 days) restraint stress and two weeks after the last stress session, all animals were implanted with probes of microdialysis in NAc Core. The day after surgery, GLU dialysate samples were collected and quantified by HPLC. After cocaine administration (15 mg/kg, i.p.), animals pre-exposed to chronic stress did not show increased extracellular glutamate levels in NAc Core, similarly to our results obtained following pre-exposure to acute stress. These findings could be explained in the framework of a dysregulation of GLU homeostasis induced by stress. The current study provides neurochemical basis in order to investigate the mechanisms underpinning the comorbidity between stress and drug abuse.

P148.-The kinase Fyn has an important role in NMDA receptor regulation in L-DOPA induced dyskinesia in a mouse model of Parkinson's disease

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Levodopa (L-DOPA) induced dyskinesia (LID) is a side effect of Parkinson's disease (PD) treatment. A great challenge is to reduce the development of LID without affecting the restorative effect of dopamine stimulation. It has been established that DA stimulation increases the phosphorylation at tyrosine 1472 of NR2B, regulatory subunit of NMDAR, which is one target of the Src kinase Fyn. Our aim is to address the role of Fyn in the NMDAR activation under L-DOPA stimulation in a mouse model of PD and the role of Fyn in the genesis of LID. We developed a model of PD in Fyn-KO and WT mice by induction of dopaminergic death by means of unilateral injection of 6-OHDA, and mice induced to developed LID by daily treatment with L-DOPA. Dopaminergic denervation was confirmed by immunodetection of TH in the SN. ΔFosB, TH, pNR2B were determined in the striatum by WB. Fyn-KO mice show a significant reduction in NR2B phosphorylation concomitant with a LID reduction, as shown by behavioural tests and ΔFosB levels reduction. In an independent set of experiments, WT mice were injected with 6-OHDA and randomly assigned to receive Amantadine (NMDA receptor antagonist), Saracatinib (Src kinase inhibitor), both, or vehicle together with L-DOPA. The three groups were compared in their ability to develop LID and the expression of molecular markers of LID.

Neurochemistry and Neuropharmacology

P149.-Molecular Function of Heteromeric Nicotinic Receptors Containing the α7 Subunit and its Duplicated Form

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The α7 nicotinic receptor subunit gene, CHRNA7, codes for a subunit that forms the homomeric α7 receptor, which is involved in learning and memory. In humans, exons 5-10 of CHRNA7 were duplicated and fused to the FAM7A gene, given rise to the CHRFAM7A gene. The product of the resulting chimeric gene, dupα7, is a truncated subunit that lacks part of the ACh binding site. We here combined cell expression, confocal microscopy, western blot, and electrophysiological recordings in HEK cells to understand the functional role of the dupα7 subunit. We found that cells transfected with dupα7 cDNA express the dupα7 protein but show neither surface binding of an α7 specific antagonist nor agonist-elicited currents. To determine if dupα7 assembles with α7 into functional receptors, we used an α7 subunit carrying mutations in determinants of conductance (α7LC) as a reporter of receptor stoichiometry. Co-expression of α7LC with dupα7 or the reverse combination, α7 with dupα7LC, allowed detection of single-channel openings elicited by ACh, indicating that α7 and dupα7 subunits co-assemble into functional heteromeric receptors. The analysis revealed that a minimum of two α7 subunits is required for forming functional receptors and that activation of the heteromeric receptors occurs through the α7/α7 interface. Our results contribute to the understanding of the functional significance of the partial duplication of the α7 gene.

P150.-Enriched environment as a non-pharmacological tool to prevent changes in hippocampal oxidative state induced by different noise exposure schedules at an early developmental age

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Previous results showed different hippocampal (HC)-related behavioral alterations in noise-exposed rats. In addition, enriched environment (EE) housing was effective to prevent most of them. However, data of HC oxidative state after noise exposure have not been obtained yet. Thus, the aim of the present work was to test a potential noise effect on HC oxidative state through the measurement of endogenous antioxidant enzymes in rats exposed to different schedules as well as the possible prevention of these changes by rearing in an EE. 7-days-old rats were exposed to noise (95-97 dB, 2h) for one (N1) or five (N5) consecutive days. After weaning, groups of rats were transferred to EE or standard cages. One week later, levels of Trx1 and Trx2 -two antioxidant enzymes from the thioredoxin family- were tested. Results showed that Trx1 levels were increased in N1 and N5 rats. In contrast, rearing these animals in an EE was effective in preventing these changes. On the other hand, Trx2 levels were increased only in N5 animals and EE was successful in preventing these changes. These findings suggest that an oxidative imbalance might be triggered after noise exposure, being Trx1 more susceptible to noise impact since only one exposure was enough to alter its levels. Conversely, several consecutive noise exposures might be necessary to generate changes on Trx2 levels. Finally, EE seems to be an effective strategy to reverse noise-induced changes in HC oxidative state.

P151.-Rac1 is essential for the expression of behavioral sensitization induced by chronic stress in nucleus accumbens

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It is well known that there is a high rate of co-occurrence of substance abuse disorders and stressful life experiences. It has been shown that both drug administration and exposure to stress induce adaptations at the level of synapses involving modifications in the density and morphology of dendritic spines that are regulated, at least in part, by a small GTPase known as Rac1. Evidence from our laboratory revealed that repeated stress alters the capacity of a subsequent cocaine injection to modulate dendritic spine morphology and actin dynamics in the NA core. Moreover, the pharmacological inhibition of actin polymerization in the NA prevents stress cross-sensitization with cocaine. Thus, the main goal of this project is to evaluate whether changes in Rac1 signaling induced by chronic stress, facilitate the development of sensitization to cocaine. For this purpose, we have generated lentiviral particles containing a constitutive active form of Rac1 (CA-Rac1) to express in NA, and explore its function during cross-sensitization between stress and cocaine. Thus, Wistar rats will be exposed to chronic restraint stress two hours daily during 7 days. Stressed and control animals will be administered with an intra-accumbens injection of CA-Rac1 before a challenge with cocaine, when behavioral sensitization will be evaluated. Our data suggests that the expression of the active form of Rac1 is sufficient to prevent the expression of cross-sensitization between stress and cocaine.

P152.-Study of the role of yerba mate (Ilex paraguariensis) as a neuroprotective factor to dopaminergic neurons in a mouse model of Parkinson's disease

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The clinical signs of Parkinson's disease (PD) are a consequence of the degeneration of the dopaminergic neurons in the substantia nigra. Since the mechanisms that underlie this neuronal degeneration have not been fully clarified, currently there is no preventive therapy for PD. However, an inverse association was found between coffee intake or smoking and the occurrence of PD. Similarly, a case-control study conducted in Argentina in 2013 revealed that consumption of 'mate' also has an inverse association with the risk of developing PD. Mate is a drink widely consumed in several South American countries, made with yerba mate (YM), obtained from the plant Ilex paraguariensis. We propose to characterize the extract of YM by HPLC and to quantify the concentrations of the main bioactive components (caffeine, theobromine, chlorogenic acid and rutin), and to evaluate if the consumption of YM provides a benefit on the survival of dopaminergic neurons in a mouse model of PD. The extract of YM was obtained by 'cebada simulada' and the main bioactive components were quantified by HPLC. Wild type mice with a moderate lesion of the nigrostriatal system are currently under treatment, receiving water or 'mate' as their only source of fluid in their feeding bottle. These results could contribute to the development of novel therapeutic interventions, using YM in association with the frequently used antiparkinsonian drugs and to have thus a direct impact on the quality of life of patients.

P153.-Ghrelin Action in the Ventral Tegmental Area Increases Locomotor Activity Independently of Food Intake Regulation

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Ghrelin is a stomach-derived octanoylated peptide hormone that regulates a variety of central functions via its action on a specific ghrelin receptor that is highly expressed in the brain. Here, we investigated if ghrelin´s effects on food intake and locomotor activity in mice involve the action of the hormone on the ventral tegmental area (VTA), a midbrain area known to regulate both functions and express ghrelin receptor. We found that: 1) subcutaneously-injected ghrelin increases both food intake and the level of the marker of neuronal activation cFos in the hypothalamic arcuate nucleus (ARC) while it fails to increase cFos levels in the VTA. In addition, subcutaneously injected ghrelin fails to affect locomotor activity in mice without access to food; 2) centrally-injected ghrelin increases food intake as well as cFos levels in the ARC and the VTA. In addition, centrally-injected ghrelin increases locomotor activity in mice without access to food; 3) intra-VTA injected ghrelin fails to affect food intake and cFos levels in the ARC while it increases locomotor activity as well as the cFos levels in the VTA. Thus, our results show that ghrelin action at the ARC increases food intake without effects on the locomotor activity while ghrelin action at the VTA increases locomotor activity without effects on the food intake. We conclude that the ghrelin effects on food intake and locomotor activity are neuroanatomically dissociated.

P154.-Sex differences in X-linked gene expression in embryonic hypothalamic neurons

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Although sex hormones are usually considered the main architects of sexual dimorphisms, recent studies have demonstrated that sex chromosomes can also induce sex differences in somatic gene expression in the absence of hormonal differences. Ngn3 is a Notch regulated gene that, in developing neurons, is involved in neurite extension and remodeling. Previous results showed that hypothalamic neurons carrying the XX sex chromosomes present a higher expression of Ngn3 and a faster rate of development than XY neurons, irrespectively of gonadal hormones. Using the Four Core Genotypes (FCG) mouse model, here we analyzed the expression of X-linked genes involved in neuronal growth and differentiation which are probable candidates to regulate Ngn3 expression. By qPCR, we have evaluated the expression of Ddx3x, Eif2s3x, Kdm6a, Syp, Mecp2 and Usp9x in primary hypothalamic cultures from E15 FCG mice. Ddx3x, Eif2s3x and Kdm6a showed higher expression levels in XX neurons than in XY neurons, regardless of the embryo sex. Importantly, Kdm6a is an epigenetic regulator codifying for a histone demethylase, whereas Ddx3x and Eif2s3x codify translation regulators. Thereby, it is possible to hypothesize that some of these genes might be regulating Ngn3 expression and neuronal development. Further experiments blocking these X-linked genes are required to determine the effect of this specific down regulation over Ngn3 and neuronal development. Financial support: CONICET, ANPCyT and SECyT-UNC.

P155.-The neurohormone tyramine modulates the intestinal release of insulin like-peptides (ILPs) to coordinate systemic stress response in C.elegans.

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The nervous system plays a pivotal role in the coordination of systemic stress response. Our results demonstrated that in C.elegans the neuronal release of tyramine (TA) (the invertebrate counterpart of adrenaline) inhibits the systemic response to long-term stressors. We found that the intestinal adrenergic-like receptor TYRA-3 is involved in the tyraminergic control of stress response. We also observed that the insulin receptor DAF-2 is essential for this response, suggesting the compromise of the conserved insulin/insulin-like growth factor signaling (IIS) pathway. However, the identity of the signals that connect these pathways remains unknown. Our screening of the 40 insulin like-peptides (ILPs) revealed that null mutants of INS-3 and INS-7 are as resistant to thermal and oxidative stress as tdc-1 (incapable of synthetizing TA) and tyra-3 null mutants. We also found that INS-3 and INS-7 co-localize with TYRA-3 in intestine. Moreover, INS-3 is down-regulated upon oxidative and thermal stress. The analysis of double null mutants (tdc-1 or tyra-3 with ins-3 and/or -7) suggest that these genes acts in the same pathway to modulate stress response. Therefore, we propose that TA inhibits the systemic stress response by allowing the release of INS-3 and INS-7, which in turn activate DAF-2 in different worm cells. This study will contribute to understand molecular mechanisms involved in neuronal regulation of stress response in a multicellular organism.

Sensory Systems

P156.-Early and late onset of inflammation affects AT2R expression levels and subcellular localization in different subpopulations of nociceptors

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Pharmacological evidence suggests that the type 2 receptor for angiotensin II (AT2R) plays a role in relieving neuropathic pain, an effect that has been attributed to both inhibition (by EMA401) and activation (by mycolactone) of the receptor. Thus, more research is needed to uncover the underlying mechanisms. We injected Complete Freund's Adjuvant (CFA) into the hindpaw of female Wistar rats and analyzed the effect 1 (CFA1) and 4 (CFA4) days thereafter. We combined immunohistochemistry with a detailed quantification analysis to examine a) subcellular localization and b) relative levels of AT2R. We found that AT2R was restricted to both small and medium size dorsal root ganglion neurons that either bound IB4 or expressed TrkA or both. These markers indicated that AT2R expressing neurons were C and A-delta nociceptors. The intracellular localization of AT2R varied amongst the neurons. We observed two patterns: retracted to the peri-nuclear region or evenly distributed to the cell membrane. Membrane-associated staining is likely to reflect functional AT2R whereas cytoplasmic distribution reflects receptor synthesis and availability. Hence, we measured both signals and compare them across neuronal sizes. At CFA1 the receptor level increased significantly only at the cell edge of small neurons, whereas at CFA4 AT2R levels increased only at the edge of medium neurons. This pattern could partly explain the dual behavior observed for AT2R in pathological pain models.

P157.-Strength of the efferent olivocochlear system modifies the activity of a central auditory nuclei

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The auditory system in many mammals is immature at birth but precisely organized in adults. Spontaneous activity in the inner ear comes into play to guide this process. This spontaneous activity is modulated by an efferent pathway that descends from the brain. In this work, we used a mouse model with enhanced medial efferent activity (Chrna9L9'T, KI) to understand the role of the olivocochlear efferent system in the correct establishment of auditory circuits. Wave III of auditory brainstem responses (which represents synchronized activity of synapses within the Superior Olivary Complex) was smaller in the KI suggesting a central dysfunction. In order to analyze this functional observation, we studied the underlying mechanism on brain slices containing the medial nucleus of the trapezoid body (MNTB) where neurons are topographically organized along a medio-lateral axis. Various MNTB physiological properties with a tonotopic organization in WT mice were abolished in the KI. Additionally, slice recordings evidenced synaptic alterations on the MNTB in agreement with the ABR recordings. Our results suggest that medial efferent activity before hearing onset is involved in the refinement of the tonotopic map of the MNTB.

P158.-Visual stimuli induce retinal neuroprotection against acute retinal ischemia

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Enriched environment (EE) is a complex combination of inanimate and social interaction. EE boosts exploratory conduct, voluntary physical exercise, sensorial and cognitive functions, and social interaction. We have previously shown that EE induced neuroprotection against unilateral retinal ischemia in adult rats. However, the relative contribution of each component to the effects of EE is still controversial. Our aim was to dissect the individual contributions of the EE repertoire components in its protective effect against retinal ischemia. The social and exploratory components by themselves were unable to protect the retina against unilateral ischemia. However, when ischemia was bilaterally induced, regardless of motor activity, the protection triggered by EE was abolished, suggesting that the visual input within EE was necessary for retinal neuroprotection. To confirm this hypothesis we induced unilateral ischemia and housed animals in a standard laboratory cage surrounded by monitors showing black/white contrast or grey patterns during the 12 h light phase. Contrast patterns achieved retinal protection against unilateral ischemia. Finally, we administered a Trk-b receptor antagonist (ANA-12) to animals with unilateral retinal ischemia exposed to contrast patterns. ANA-12 prevented the retinal protection against ischemia, further suggesting that visual stimuli, likely in a BDNF dependent manner, could account for the retinal protection induced by EE.

P159.-Perception of relevant components in odor mixtures depends on experience

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In nature, olfactory stimuli are present as mixtures in which their elements differ in their meaning. This meaning may even change among individuals from the same species but with different experiences. We studied honey bees, as they are generalist foragers that depend on olfaction and on their own experience to find food sources.
In previous works we studied the neural representation of mixtures and pure components and found that the representation of a mixtures is shifted toward the representation of the learned components and away from components that have no predictive value. Here we asked if these changes do have a correlate at the behavioral level.
In a first experiment we trained bees using appetitive conditioning toward pure odors and after that we tested them using mixtures that contain that odor. We found that bees are highly efficient in detecting the rewarded component embedded in the mixture.
In a second experiment we trained the bees using pure odors, and then, we retrained them again but using as conditioned stimulus a mixture that contains the learned odor plus a novel odor. Finally, the bees were tested with the novel odor alone. A second group of bees underwent only the learning session with the mixture. We found that learning the novel odor was affected in animals that had a previous experience. These result are consistent with the hypothesis that odor and mixture perception is adjusted by experience.

P160.-DETECTING MINORITY COMPONENTS IN A BINARY MIXTURES: THE ROLE OF OLFACTORY SENSORY ADAPTATION

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The olfactory system is an excellent model system to study how contextual information is detected and processed by the nervous system. The coding of olfactory information undergoes multiple changes due to prolonged or repeated exposures to odorants. Sensory adaptation is defined as a phenomenon by which the sensitivity towards a stimulus is rapidly decreased after a prolonged exposure to it; it is followed by a complete recovery after the disappearance of the stimulus. Here, we use Apis mellifera to study the effect that the olfactory sensory adaptation has on the capability of animals to detect minor components embedded in binary mixtures. By means of behavioral experiments, we were able to show that olfactory sensory adaptation reduces the learning level of pre-exposed stimuli, while enhancing the learning of stimuli that would be normally overshadowed by the major component of the mixture. Additionally, by performing calcium imaging experiments to measure odor induced signals in the olfactory system, we were able to show that the glomerular activation patterns elicited by a binary mixture, changes after pre-exposure of the animal to one of the components, resulting in a representation that drastically favors the underrepresented (or minor) component of the mixture. These results suggest that olfactory sensory adaptation is critical to allow detection of minor components present in complex in mixtures, and that it increases the sensibility of the animal to certain stimuli.

P161.-CB1 Receptor Agonist Protects The Retina From Light Induced Retinal Degeneration

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Endocannabinoids are neuromodulators whose effects are mediated by G protein coupled receptors named CB1 and CB2. CB1 agonists play a neuroprotective role in glaucoma models of retinal injury. Light induced retinal degeneration (LIRD) is a model that resembles other human retinal degenerative diseases as AMD. The aim of this work was to evaluate the potential neuroprotective effect of the modulation of CB1 receptor in LIRD. The right eyes of Sprague Dawley rats were intravitreally injected either with ACEA (CB1 agonist), or AM251 (CB1 antagonist) while the left eyes received vehicle as controls. Later, rats were subjected to continuous illumination (12.000 lux) for 24 hs. Retinas were dissected out and processed by Western Blot (WB) using either antibodies to GFAP or to activated Caspase 3. The optical density data were statistically analysed using Student´s t-test and differences were considered significant when $p<0.05$. The eyes treated with ACEA showed retinas with significant lower levels of activated Caspase 3 and GFAP. Conversely, the eyes treated with AM251 showed retinas with significant higher levels of activated Caspase 3 and GFAP. The administration of ACEA previous to illumination stress was neuroprotective (decreased apoptosis and glial reactivity), while AM251 worsened retinal damage (increased apoptosis and glial reactivity) in LIRD. Although further work is needed, CB1 receptor agonism may be considered a potential neuroprotective strategy in AMD.

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P162.-Interaction between sensory feedback and attention in a finger tapping task

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In the present work we investigate the effects of attention and sensory feedback on finger tapping performance. Subjects must synchronize to an auditory metronome and, after an abrupt tempo change, must resynchronize to the new tempo. It is expected that both, an increased level of attention and the addition of sensory feedback, will improve task performance. Preliminary results (N = 4) show that under this paradigm of augmented attention the mean asynchrony decreases and the resynchronization velocity increases with respect to a basal/normal level of attention. On the other hand, the presence of additional auditory feedback also decreases the mean asynchrony, but contrary to what is expected diminishes the resynchronization velocity after a tempo change.

P163.-Activation of presynaptic GABAB receptors minimize depression and enables sustained transmission at high rate stimulation of cholinergic olivocochlear-hair cell synapses

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During development, medial olivocochlear (MOC) neurons transiently innervate cochlear inner hair cells (IHCs). Although acetylcholine (ACh) is the main neurotransmitter at this synapse, an abundant GABA innervation is also present. Electrical stimulation of MOC efferent fibers triggers the release of ACh, but also activates presynaptic GABAB receptors, that in turn reduce the amount of ACh released. GABA-mediated mechanism is through the inhibition of P/Q type Ca2+ channels. We are now studying the consequences of GABAB-mediated inhibition in the short-term plasticity of this synapse. Inhibitory synaptic currents (IPSC) were recorded in IHCs of acutely isolated organs of Corti at P9-P11, while MOC fibers were electrically stimulated. In control condition, 10 pulses applied at high frequency (50 Hz) resulted in a progressive decrease on IPSC amplitudes throughout the train (P10/P1= 0.54). On the contrary, the specific GABAB agonist baclofen, increased the facilitation rate and eliminated depression at the same frequency (P10/P1= 1). Moreover, application of CGP35348, a GABAB antagonist, produced a bigger depression even at low stimulation frequencies (10Hz). These results suggest that the activation of presynaptic GABAB receptor, minimizes depression and would enable sustained transmission during high-frequency stimulation at the MOC-inner hair cell synapse.

P164.-Kv7 channel openers and non-steroidal anti-inflammatory drugs decrease striatal cholinergic interneuron excitability

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Striatal cholinergic interneurons (SCIN) have emerged as key modulators of the striatal circuitry controlling voluntary movement. SCIN dysfunction has been involved in the genesis of movement disorders such as Parkinson's disease (PD) and L-DOPA-induced dyskinesia (LID). Therefore, a better understanding of SCIN physiology may provide new potential therapeutic targets for PD and LID. SCIN are autonomous pacemakers and display spike frequency accommodation in response to sustained current injection. Previous work found that blockade of Kv1 channels strongly increase SCIN excitability but the contribution of other voltage-dependent potassium channels has been less studied. Here we aim to disclose the role of Kv7 currents in SCIN excitability. Blockers of Kv7 channels had no effect on SCIN response to somatic current injection and spontaneous tonic firing but increased EPSP summation induced by intrastriatal electrical stimulation. Retigabine, a Kv7 channel opener, markedly decreased SCIN excitability, which was restored by subsequent addition of XE991. Non-steroidal anti-inflamatory drugs (NSAIDs) may behave as Kv7 channel openers. Interestingly, diclofenac and meclofenamic acid reproduced the effect of retigabine in a dose-dependent manner but XE991 failed to reverse this effect, suggesting that NSAIDs decrease SCIN excitability through a Kv7 independent mechanism. These results implicate Kv7 channels and NSAIDs targets as key regulators of SCINs excitability.

P165.-Histamine potentiates acid sensing ion channels (ASICs) currents at the giant Calyx of Held synapse.

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ASICs play an important function in physiologic processes and signal transduction associated with local and global extracellular pH variations during normal and pathological neuronal activity. We have identified homomeric ASIC1a-mediated currents during synaptic transmission at the calyx of Held synapse, suggesting an acidification of the synaptic cleft due to the co-release of neurotransmitter and H+ from synaptic vesicles. ASIC-1a current amplitudes are small relative to glutamatergic AMPA mediated excitatory postsynaptic currents. It is possible that some endogenous ligands may modulate ASICs and enhance their responses to physiologically significant levels. Indeed, we have found that micromolar concentrations of histamine significantly potentiate ASIC-1a currents. This potentiation may be due a shift of the activation dependence of ASIC-1a channels to less acidic conditions, increasing pH sensitivity. Histamine is involved in the immune and inflammatory response, and it also plays a role of a neurotransmitter in the central nervous system, regulating numerous physiological functions. The fact that histamine can target ASIC-1a channels is of great relevance since both histamine and ASIC receptors are implicated in many pathologies such as epilepsy, Alzheimer's disease, attention-deficit hyperactivity disorder, schizophrenia and multiple sclerosis.


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