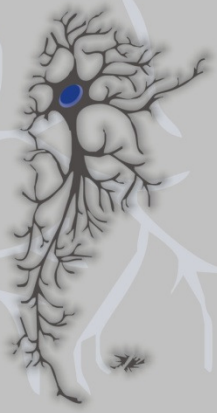
XXVIII CONGRESO ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN EN NEUROCIENCIAS

&

Reunión Satélite / Neurobiología del Comportamiento:
"Neuroetología y Neurobiología de la Memoria en el Cono Sur"

Septiembre 30 - Octubre 4, 2013, Huerta Grande, Córdoba, Argentina.



SAN

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XXVIII CONGRESO ANUAL DE LA
SOCIEDAD ARGENTINA DE INVESTIGACION EN NEUROCIENCIAS

&

Reunión satélite sobre Neurobiología del Comportamiento:
"Neuroetología y Neurobiología de la Memoria en el cono sur"
Un homenaje a Héctor Maldonado

PROGRAM

Monday September 30th: SATELLITE DAY 1

09:00: **Registration**

10:30: **Introduction**

11:00: **Symposium on Neurobiology of Memory I - International Society for Neurochemistry Symposium (**Room A)
Chair: Arturo Romano
Jorge Quillfeldt, Dep. de Biofísica, PPG Neurociências ICBS. Universidade Federal de Rio Grande do Sul, Brasil.
"Exploring the possible physiological roles of memory reconsolidation: reativation enables updating, precision-keeping and strenghtening"
Arturo Romano, IFIBYNE-CONICET, FCEN-Universidad de Buenos Aires, Argentina
"Enduring memories and the NF-kB-dependent chromatin regulation"
Rafael Pagani, Departamento de Cs Fisiológicas, FMED-Universidad de Buenos Aires, Argentina.
"Understanding Learning Disability"
Valeria Della Maggiore, Departamento de Cs Fisiológicas, FMED, Universidad de Buenos Aires, Argentina.

"Temporal course of functional connectivity during motor memories consolidation"

11:00 **Symposium on Neuroethology I** (Room B)

Chair: Lidia Szczupak

Angel Caputi, Departamento de Neurociencias Integrativas y Computacionales, Instituto Clemente Estable, Montevideo, Uruguay

"Action, sensation, cognition and evolution. What a mess!"

Fernando Locatelli, IFIBYNE-CONICET, FCEN-Universidad de Buenos Aires, Argentina.

"Experience dependent tuning in olfactory processing"

Daniel Olazábal, Departamento de Fisiología, Facultad de Medicina, Universidad de la República, Uruguay.

"Comparative and developmental analysis of the role of oxytocin in the facilitation of spontaneous parental responses"

Lidia Szczupak, IFIBYNE-CONICET, FCEN-Universidad de Buenos Aires, Argentina

"Organization of neuronal networks underlying locomotion in the leech"

13:00 **Lunch**

14:30: **Symposium on Neurobiology of Memory II** (Room A)

Chair: María Eugenia Pedreira

Jimmy Stehberg, Departamento Ciencias Biológicas, Universidad Andres Bello, Chile.

"A role for astrocytes in memory, stress and stress-induced memory enhancements"

María Eugenia Pedreira, IFIBYNE-CONICET, FCEN-Universidad de Buenos Aires, Buenos Aires, Argentina.

"Reconsolidation: a long way from crabs to humans"

Magdalena Sanhueza, Laboratorio de Fisiología Celular**,** Universidad de Chile, Santiago, Chile

"Regulation of synaptic memory by an endogenous CaMKII inhibitor?"

Lucas de Oliveira Alvares, Dep. de Biofísica, PPG Neurociências ICBS Universidad Federal de Rio Grande do Sul, Brasil.

"Effect of histone acetylation on physiological and pathological memories"

14:30: **Symposium on Neuroethology II** (Room B)
Chair: M. Fernanda Ceriani
José Alves-Gomes, Laboratório de Fisiologia Comportamental e Evolução, Instituto Nacional de Pesquisas da Amazônia, Brasil.
"Behavioral and evolutionary aspects of the genus Microsternarchus in the Brazilian Amazon"
Michel Borde, Departamento de Fisiología, Facultad de Medicina, Universidad de la República, Uruguay.
"Dedicated vs multifuncional neural networks for behavior: examples from the fish and rat brainstem"
Jorge Mpodozis, Departamento de Biología, Facultad de Ciencias, Universidad de Chile, Chile.
"Plasticity vs. conservation in the ammniote visual system. Some explicit examples"
Javier Nogueira, Departamento de Histología y Embriología, Facultad de Medicina, Universidad de la República, Uruguay.
"The role of a one-spike-neuron in implementing a sensory filter"
M. Fernanda Ceriani, Instituto Leloir-CONICET, Buenos Aires, Argentina.
"Circadian control of output pathways in Drosophila: from structure to behavior"

16:30**: Coffee break**

17:00: **Poster Session I**

19:00: **Symposium on Neurobiology of Memory III** (Room A)
Chair: Alejandro Delorenzi
Ramiro Freudenthal, IFIBYNE-CONICET, FCEN-Univerisidad de Buenos Aires, Argentina.
"Dynamics of synaptic NF-kappa B during inhibitory avoidance long term memory consolidation"
Daniela Barros, Instituto de Ciências Biológicas, Laboratório de Neurociências Universidade Federal do Rio Grande, Brasil.

"Memory persisitence: stress participation and the cholinergic system"
Alejandro Delorenzi, IFIBYNE-CONICET, FCEN, Universidad de Buenos Aires, Argentina.
"Memory reactivation goes far beyond expression"
Pedro Bekinschtein. IBCN-CONICET, FMED, Universidad de Buenos Aires, Argentina.
"Consolidating unique memories: BDNF interacts with adult-born immature neurons in the dentate gyrus during spatial pattern separation"

19:00: **Symposium on Neuroethology III** (Room B)
Chair: José Luis Peña
Nelson Velásquez, Programa de Fisiología y Biofísica, Facultad de Medicina, Universidad de Chile, Santiago, Chile.
"Divergence in the acoustic communication of a chilean anuran (Pleurodema thaul)"
Natalia Uriarte, Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República, Uruguay.
"Early experience and transgenerational transmission of maternal styles in the overlapping-litter model in rats "
Pablo Guerenstein, Universidad Nacional de Entre Ríos, Argentina.
"Behavioral responses of kissing bugs (Triatomines) to odors and odor
mixtures"
María Castelló, Departamento de Neurociencias Integrativas y Computacionales, Instituto Clemente Estable, Uruguay.
"Postnatal development of the electrosensory system in weakly electric fish"
José Luis Peña, Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, USA
"The biased owl"

21:00: Dinner

Tuesday October 1st: SATELLITE DAY 2

09:00: **Symposium on Neurobiology of Memory IV** (Room A)

Chair: Mariano Boccia
Olavo Amaral, Instituto de Bioquímica Medica, Universidade Federal do Rio de Janeiro, Brasil.
"Parallel systems for labilization and reinforcement of synaptic plasticity during memory retrieval"
Mariano Boccia, Departamento de Farmacología, FFyB, Universidad de Buenos Aires, Buenos Aires, Argentina.
"Memory neuropharmacology of consolidation and reconsolidation"
Diana Jerusalinsky, IBCN-CONICET, FMED, Universidad de Buenos Aires, Argentina.
"NMDA receptor subtypes and the "previous experience effect" on memory"
Víctor Molina, FCQ, Universidad Nacional de Córdoba, Argentina.
"Stress and retrieval interaction in fear memory: neurobiological mechanism"

09:00: **Symposium on Neuroethology IV** (Room B)
Chair: Ana Silva
Martín Berón de Astrada, IFIBYNE-CONICET, FCEN-Universidad de Buenos Aires, Argentina.
"Behaviorally related neural plasticity in the arthropod optic lobes"
Mario Penna, Programa de Fisiología y Biofísica, Facultad de Medicina, Universidad de Chile, Santiago, Chile.
"Propagation and reception patterns of acoustic signals in anurans"
Violeta Medán, IFIBYNE-CONICET, FCEN-Universidad de Buenos Aires, Argentina.
"Sensory Integration in a command neuron"
Ana Silva, Unidad Bases Neurales de la Conducta, Universidad de la República-Instituto Clemente Estable, Uruguay.
"Neuroendocrine bases of social behavior in weakly electric fish"

11:00: Coffee break
11:30: **Symposium on Neurobiology of Memory V** (Room A)
Chair: Noelia Weisstaub
Noelia Weisstaub, IBCN-CONICET, FMED, Universidad de Buenos Aires, Argentina.
"Role of serotonin in memory interference processes"

Walter Farina, IFIBYNE-CONICET, DBBE-FCEN, Universidad de Buenos Aires, Argentina.
"Behavioral and neural plasticity caused by early social experiences: the case of the honey bee"
Ramón Bernabeu, Departamento de Fisiología FMED, Universidad de Buenos Aires, Argentina.
"Smoke like a fish"
Martin Cammarota, Memory Research Laboratory, Brain Institute - UFRN - Natal, Brazil.

11:30: **Symposium on Neuroethology V** (Room B)
Chair: Matías Pandolfi
Eliane Gonçalves de Freitas, Departamento de Zoologia e Botânica, Universidade Estadual Paulista, Brasil.
"Nest digging, aggressiveness and androgen releasing in cichlid fish"
Mariana Lozada, Universidad del Comahue, Argentina.
"Learning from an exotic social wasp"
Laura Quintana, Unidad Bases Neurales de la Conducta, Instituto Clemente Estable, Uruguay.
"Roles of glutamate receptor subtypes in electric fish courtship signals"
Gabriela Hermitte, IFIBYNE-CONICET, FCEN, Universidad de Buenos Aires, Argentina
"The cardiac response in Neohelice granulata. Unravelling a crustacean neuroautonomic system"
Matías Pandolfi, DBBE-FCEN, Universidad de Buenos Aires, Argentina.
"Dominant and subordination: how fish control their access to reproduction?"

13:30: **Lunch**

15:00: **Symposium on Neuroethology VI** (Room B)
Chair: Daniel Tomsic
Leonel Gómez, Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República, Uruguay

"Dynamic perceptual cues for approaching an object in weakly electric fish"
Gonzalo Marín, Departamento de Biología, Facultad de Ciencias, Universidad de Chile, Chile
"Bottom-up and top-down attentional modulation: lessons from a neural circuit from the avian midbrain"
Gabriel Mindlin, DF-FCEN, Universidad de Buenos Aires, Argentina.
"Motor coordinates in the study of the neuronal code used in bird song"
Daniel Tomsic, IFIBYNE-CONICET, FCEN, Universidad de Buenos Aires, Argentina
"Predator avoidance and prey capture behaviors: from ecology to neurons and back"

17:00: Coffee break

17:30: **Poster Session II**

21:00: **Dinner + Discussion session**

The International Society of Neuroethology in South America

Neurobiology of Memory & Neuroethology in the Southern Cone. Current situation & Perspectives.

Wednesday October 2nd: SAN MEETING DAY 1

09:00 **Registration**

10:00 **Welcome by Organizers**
Tribute to Professor Héctor Maldonado
Closure of the Symposium on Neuroethology and Memory / Opening Lectures of the XXVIII SAN Meeting
Allocution of disciples and friends

10:15 **Conference on Neuroethology - Chair:** Daniel Tomsic (IFIBYNE-CONICET, FCEN-UBA)

- **Randolf Menzel**, Freie Universität Berlin, Germany

"Neuroethology of Learning and memory: the honeybee as a model system"

11:15 **Conference on Neurobiology of Memory - Chair:** Daniel Tomsic

- **Yadin Dudai,** Weizmann Institute, Rehovot, Israel

"The Beginning and the End of Memory Consolidation"

12:30: **Lunch**

14:00: **Short talks selected from poster abstracts** (two parallel thematic sessions in **Rooms A & B**)

16:00: **Poster session I & Coffee break**

18:30: **Symposium I: Information processing in cortical circuits**

Chairs: Emilio Kropff (Instituto Leloir, Buenos Aires), Antonia Marín-Burgin (IBIOBA-CONICET)

- **Emilio Kropff**, Instituto Leloir, Buenos Aires

"Modulation of activity by running speed in the circuits of the rat entorhinal cortex"

- **Alessandro Treves**, International School for Advanced Studies, Trieste, Italy

"Computational analysis of entorhinal lamination"

- **Hillel Adesnik**, University of California, Berkeley, USA

"Spatial coding by horizontal and vertical circuits in the somatosensory cortex"

- **Dan Shulz,** Unit of Neuroscience Information & Complexity, CNRS, Gif-sur-Yvette, France

"Exploring apparent motion in the tactile modality: A combined electrophysiological, imaging and modeling approach"

21:00: Dinner

Dinner activity: eat with the big shots I !

Students and postdocs can sign up to share the table with lecturers and symposia speakers

23:00: Party

Thursday October 3rd: SAN MEETING DAY 2

09:00: **Symposium II - International Society for Neurochemistry Symposium: Sensation, perception and neural representation of the environment: olfaction as case study**

Chairs: Alejandro Delorenzi, Fernando Locatelli (IFIByNE-CONICET, FCEN-UBA)

- **Lorena Rela**, Facultad de Medicina, Universidad de Buenos Aires

"Glial networks and the wiring of olfactory circuits"

- **Paul Szyszka**, Zoology and Neurobiology Universitaet, Konstanz, Germany

"Dealing with a turbulent odor world: Smelling fast and segregating objects"

- **Brian Smith**, School of Life Sciences, Arizona State University, USA

"The role of distributed neural plasticity in recognition of natural floral odors"

- **Randolf Menzel**, Freie Universität Berlin, Germany

"Olfactory coding at the input and the output of the honeybee mushroom body"

11:30: Coffee break

12:00: **Eduardo de Robertis Plenary Lecture in Neuroscience I** - **Chair:** Alfredo Cáceres (IMyMF, Córdoba)

- **Lily Y. Jan**, Univ. of California, San Francisco

"Neuronal signaling modulation by potassium channels and chloride channels"

13:30: Lunch

15:00: **SAN Award to the Best Doctoral Thesis in Neuroscience 2013** - **Chair:** Dan Shulz (Gif-sur-Yvette)

- **Estefanía Bello**, INGEBI-CONICET

"Functional study of the dopamine D2 receptor (D2R) in the central nervous system by inducible mutant mice"

15:30: **Young Investigator Symposium** (15-min talks from senior postdocs and junior group leaders) - **Chair:** Lionel Muller Igaz (FMed-UBA)

- **Paola V Plazas**, Neurobiology Section, Div. of Biological Sciences, UCSD, La Jolla, CA, USA; Departamento de Farmacología, FMed- UBA, Buenos Aires

"Electrical activity regulates Plexin A3-mediated axon pathfinding in developing zebrafish spinal motor neurons"

- **Mauricio Galiano**, CIQUIBIC - Dto. de Química Biológica, Fac. Cs.Químicas, UNC, Córdoba

"Assembly of the Axon Initial Segment (AIS): role of a distal axonal cytoskeleton"

- **Elena Avale**, INGEBI-CONICET, Buenos Aires, Argentina.

"Reprogramming of Tau isoforms by RNA trans-splicing: Towards a plausible therapeutical approach for tauopathies?"

- **Cynthia Katche**, Instituto de Biologia Celular y Neurociencias, FMED-UBA, Buenos Aires

"Challenging the view of the cortex in memory: essential role of retrosplenial cortex in memory formation, storage and retrieval"

- **Guillermo Solovey**, Columbia University, NY, USA

"Low attention impairs optimal incorporation of prior knowledge in perceptual decisions"

- **Cecilia Inés Calero**, Laboratorio de Neurociencia Integrativa, (FCEN-UBA/ CONICET)

"Children are natural pedagogues"

17:30: **Poster Session II & coffee break**

19:45: **Eduardo de Robertis Plenary Lecture in Neuroscience II** - **Chair:** Santiago Quiroga (CIQUIBIC-CONICET, Córdoba)

- **Yuh Nung Jan**, Univ. of California, San Francisco

"Dendrites: from form to function"

21:00: Dinner

Dinner activity: eat with the big shots II!

22:30: **SAN Business Meeting**

Friday October 4th: SAN MEETING DAY 3

08:30: **Symposium III: Axonal regeneration and remyelination: fact or fiction?**

Chair: Patricia Setton (Dept Quím. Biológica, FFyB-UBA, IQUIFIB-CONICET)

- **Paula Monje**, University of Miami, Miller School of Medicine.

"Plasticity and therapeutic potential of peripheral myelinating glia"

- **Felipe Court**, Facultad de Biología, Pontificia Universidad Católica de Chile

"The intimate relationship between glia and axons during degenerative and regenerative programs"

- **Rosalía Mendez-Otero**, Inst. de Biofísica Carlos Chagas Filho, UFRJ, Brazil

"Cellular therapies in neurological diseases"

- **Ana Adamo**, Dept Quím. Biológica, FFyB-UBA, IQUIFIB-CONICET

"Notch signaling pathway in the demyelination-remyelination process of the central nervous system"

11:00: **Poster session III and coffee break**

13:00: **Ranwel Caputto Plenary Lecture - Chair:** Alejandro Schinder (Instituto Leloir, Buenos Aires)

- **Marcelo Rubinstein**, INGEBI-CONICET, Buenos Aires

"Molecular and Functional Genetics of Food Intake and Body Weight Regulation"

14:00: **Closing remarks by organizers and farewell barbecue**

16:00: **Meeting adjourns**

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PLENARY LECTURES AND SYMPOSIUMS ABSTRACTS

Wednesday October 2nd / 10:15hs

Conference on Neuroethology - Chair: Arturo Romano

Neuroethology of Learning and memory: the honeybee as a model system

Randolf Menzel

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Where do the research questions come from in neuroscience? The concepts of neuroethology offer a rich repertoire of approaches into the brain. Observations of and experimentation with animals under natural conditions pose the questions to be addressed when searching for neural mechanisms. Equivalent laboratory model conditions are then devised that are compared and influenced by the results from the field, ensuring that appropriate paradigms are applied. The research by Hector Maldonado and his co-workers is a wonderful example for the success of this approach. I shall report examples of our work on honeybee learning, memory formation and memory retrieval focusing on the search for the olfactory engram in the bee´s mushroom bodyThe memory trace in the calyx is characterized by the high order combinatorial integration of multiple sensory inputs. Mushroom body extrinsic neurons are tentatively related to multiple processing categories that represent the acquired values and provide neural commands for goal directed behavior and decision making.Specifically, extrinsic neurons of the mushroom body encode cues and contexts differently. Memory processing is exemplified by rate changes in an inhibitory recurrent pathway that peak at discrete time windows over three days. Thus the MB input receives highly selective information about learned stimuli, and this information depends on consolidation of multisensory memory over the range of days. A model will be presented that aims for capturing the multi-faceted and distributed nature of the engram and may help to guide our future search of the engram at a systems level.

Wednesday October 2nd / 11:15hs

Conference on Neurobiology of Memory - Chair: Lidia Szczupak

The Beginning and the End of Memory Consolidation

Yadin Dudai

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Memory consolidation is the hypothetical process in which a memory item is transformed from a short- into a longer-term form. The process is conventionally described at two levels of analysis: "synaptic" or "cellular", involvingstabilization of use-dependent changes at local nodes in the neuronal circuits that encode the memory; and "systems", referring to reorganization of internal representations over distributed brain circuits.Cellular consolidation serves as a subroutine in systems consolidation.

The beginning of consolidation is reflected inmolecular processesstarting right after encoding of the new information. The end of consolidation is, however, more of an enigma. Ample evidence indicates that consolidation can linger for long and also reboot ("reconsolidate")once long-term memory is reactivated.Second, systems consolidation ofone-shot eventstransforms the quality of the stored information from an episodic toa semantic form, which is integrated into a more general accumulated body of knowledge. This again questions the notion that the consolidation of a distinct memory item ever ends. This transformationis reflected in decreased activation of retrieval circuits in the brain on the one hand, but enhanced correlation of theiractivity with correct recollection on the other.

All in all, understanding memory consolidation at different levels of brain and cognitionilluminatesthe mechanisms and function of memory systems, and contributes to the understanding of memory phenomena of great importance in real life, such as the resilience of traumatic memories and the widespread occurrence of false recollection.

Selected References: Lamprecht R, et al. (1997) J Neurosci17, 8443; Eisenberg M, et al. (2003) Science 301, 1102; Ben-Yakov A, Dudai Y (2011)J Neurosci 31, 9032; Furman O, et al. (2012)Learn & Mem 19, 575; Dudai Y (2012) Annu Rev Neurosci35, 227.

Wednesday October 2nd / 18:30hs

Symposium I: Information processing in cortical circuits

Chairs: Emilio Kropff (Instituto Leloir, Buenos Aires), Antonia Marín-Burgin (IBIOBA-CONICET)

Modulation of activity by running speed in the circuits of the rat Entorhinal Cortex

Emilio Kropff

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The Entorhinal Cortex of the rodent brain contains neurons - grid cells - whose activity correlates outstandingly with the position of the animal in space, disregarding all other behavioral variables. It has been proposed that they form a Cartesian-like frame of reference that serves as the main source of spatial input to the Hippocampus, though the exact mechanism that allows this is not yet clear. Some of the main current theoretical models that account for grid cell firing state that these neurons integrate a velocity signal that is coded either in the population oscillations of the network at the theta frequency band or in the firing rate of a selected group of Entorhinal cells, suggesting that running speed is a crucial element of the network dynamics. Following the introduction of a novel experimental setup that allows us to control the running speed of rats while we record their neural activity, we will evaluate how well the current perspectives of circuit oscillation and single cell coding can explain our results, thus closing the loop between experiments and theory.

Computational analysis of entorhinal lamination

Alessandro Treves

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Joint work with Dr Bailu Si, Weizmann Institute, Israel.

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The multiple layers of medial entorhinal cortex (mEC) contain cells that differ in selectivity, connectivity, and cellular properties. Grid cells in layer II and in the deeper layers express triangular grid patterns in the environment. The firing rate of the conjunctive cells found in layer III and below, on the other hand, show grid-by-head-direction tuning. In this study, we model the differentiation between grid and conjunctive cells in a network with self-organized connections. Arranged into distinct `layers', the model grid units and conjunctive units develop, with a similar time course, grid fields resulting from firing rate adaptation and competitive learning. Grid alignment in both layers is
delayed with respect to the formation of triangular grids. A common grid orientation among conjunctive units is produced, in the model, by head-direction modulated collateral interactions, while the grids of grid units inherit the same orientation through connections from conjunctive units. Grid units as well as conjunctive units share a similar spacing but show a random distribution of spatial phases. Grid units however carry more spatial information than conjunctive units, thus providing better inputs for the hippocampus to form spatial memories.

Spatial coding by horizontal and vertical circuits in the somatosensory cortex

Hillel Adesnik

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How does the brain accurately localize objects in space? Many animals use active sensory systems, in which sensory organs scan the environment to acquire sensory information, to better localize objects in the external world. This process is exemplified by both primate vision - where the eyes move - and rodent somatosensation - where the whiskers sweep nearby space at a high rate. Each whisker is topographically mapped onto an individual column in the rodent somatosensory 'barrel' cortex, but horizontal circuits between neighboring cortical columns are thought to be critical for coordinating input from multiple whiskers to generate accurate perceptions. Yet how these horizontal interactions govern the representation of objects in space is poorly understood. Here we take advantage of the discretized nature of the mouse whisker system and optogenetic control of specific cortical layers to address how intracortical horizontal projections control the cortical representation of object location.

Exploring apparent motion in the tactile modality: A combined electrophysiological, imaging and modeling approach

Daniel E. Shulz

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Our sensory percepts contain more explicit spatial and temporal information than the sensory stimuli on which they are based. This *constructive* aspect of perception, described by the Gestalt School of Psychology more than a century ago, predicts the emergence of a coherent percept of global shape and continuous motion from the temporal staggering of static presentations of elementary spatial features along a virtual trajectory (e.g. the apparent motion illusion). Although, at each moment in time, the image is stationary, subjects report the perception of a continuous motion of the object.

How sensory systems extract information about emerging properties of an object? Is there a tactile counterpart of the visual apparent motion illusion?

Using the somatosensory vibrissal system of rodents as a system model, our research is centered on the study of the propagation and integration of neuronal information in the trigeminal and thalamic nuclei as well as the primary somatosensory cortex and the emergence of collective neuronal properties in response to spatially distributed stimuli on the receptor surface.

To that purpose a 24 whisker stimulation matrix has been developed based on piezoelectric technology giving us an unprecedented possibility to apply complex stimuli spanning the entire sensory input space of the vibrissal system. Using the matrix in combination with multiple single-unit electrophysiological recordings, voltage sensitive dye imaging, 2-photon imaging and computational approaches, we tackled these scientific questions.

We show that the system, at its different levels, is selective to emergent properties of a tactile scene providing a neurophysiological basis for Gestalt perceptive phenomena.

References

Jacob V., Le Cam J., Estebanez L. and Shulz D.E. (2008). Emergent Properties of Tactile Scenes Selectively Activate Barrel Cortex Neurons. *Neuron* 60: 1112-1125.

Jacob V., Estebanez L., Le Cam J., Tiercelin, J.Y., Parra, P., Parésys, G., and Shulz D.E. (2010). The Matrix: a new tool for probing the whisker-to-barrel system with natural stimuli. *J Neurosci Methods.* 189: 65-74.

Le Cam J., Estebanez L., Jacob V. and Shulz D.E. (2011). The spatial structure of multi-whisker receptive fields in the barrel cortex is stimulus-dependent. *J. Neurophysiol.* 106:986-998.

Ego-Stengel V., Le Cam J., and Shulz D.E. (2012). Coding of apparent motion in the thalamic nucleus of the rat vibrissal somatosensory system. *J. Neuroscience* 32: 3339-3351.

Estebanez L., El Boustani S., Destexhe A. and Shulz D.E. (2012). Correlated input reveals coexisting coding schemes in a sensory cortex. *Nature Neuroscience* 15: 1691-1699.

Thursday October 3rd / 09:00

Symposium II - International Society for Neurochemistry

Symposium: Sensation, perception and neural representation of the environment: olfaction as case study

Chairs: Alejandro Delorenzi, Fernando Locatelli (IFIByNE-CONICET, FCEN-UBA)

Glial networks and the wiring of olfactory circuits

Lorena Rela

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The rodent olfactory epithelium sustains neurogenesis throughout adulthood. New sensory neurons grow an axon along the olfactory nerve to the olfactory bulb where they synapse. Olfactory ensheathing glial cells (OECs) wrap the axons of olfactory sensory neurons, promote axon growth both in vitro and when transplanted to sites of injury, and are proposed to generate a permissive environment for axon growth in the adult olfactory nerve. OECs form gap junction-coupled glial networks and express high levels of connexin 43, a glial gap junction protein with cell adhesion properties involved in a diversity of functions like potassium buffering, support for synaptic transmission, and development of cortical circuits. We are interested in determining the role of glial connexins and glial network remodeling in the plasticity of olfactory circuits. Our results show that genetically modified mice with reduced expression of connexin 43 in OECs display markers of a deficient sensory input to the olfactory bulb. In addition, we observed that the wave of degeneration/regeneration produced by olfatotoxins in the olfactory epithelium correlates with indicators of glial network remodeling. The identification of mechanisms underlying neurotrophic properties and plasticity of OECs is not only relevant to understand determinants of neural circuit formation but also for those interested in using OECs for cell therapy in degenerative or traumatic damage to the central nervous system.

Dealing with a turbulent odor world: Smelling fast and segregating objects

Paul Szyszka, Jacob Stierle, Rick Gerkin, Brian H. Smith, C. Giovanni Galizia

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Odors carried in air plumes quickly break up into thin filaments that spread out across short distances from the odor source. The ability to track the fast temporal structure of filaments in a plume is essential for animals to locate the odor source and for segregation of concurrent odors that arise from different sources. It is not clear whether transduction times and tracking rates of olfactory receptor neurons are fast enough to allow insects to use the higher frequency components of information present in odor plumes. We probed the limits of insects` olfactorytemporal resolution by delivering high frequency odor pulses and found that transduction times and pulse tracking capabilities of olfactory receptor neurons are 10 to 20 times faster than previously thought.We show that the insect olfactory system uses millisecond stimulus-onset asynchronyfor odor-segregation, similar to figure-groundsegregation in the visual system and concurrent soundsegregation in the auditory system:Honeybees can use 6-millisecond-short asynchrony between the components of an odor mixture to segregate a learned odor from it. Using *in vivo* calcium imaging ofprojection neurons in the antennal lobe, we found thatprojection neurons can resolve 5-millisecond-stimulus asynchrony, suggesting that odorsegregation is possible at the level of the antennal lobe.

Plasticity in early olfactory processing in the brain and its role in analyzing complex natural odors

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Natural odors are typically blends of many different chemical constituents. Slight variation in the blend composition, either by changing components or changing the relative amounts of components, can alter the blend's perceptual qualities. Moreover, odors are carried in a turbulent airstream, such that odors emanating from a point source quickly break up into thin filaments. An animal moving upwind would only be exposed to an odor for a few to at most a few tens of milliseconds when it encounters a filament. In spite of this complexity animals are very good at recognizing odors and locating the source. I study floral odor recognition by honey bees as a basic research model for understanding how animals locate and identify an odor given the complexity of the odor 'scene'. The central hypothesis of my research is that different forms of plasticity driven by specific biogenic-amine based modulatory pathways are necessary for solving these odor problems. My laboratory uses electrophysiological recordings, bioimaging and neuroanatomical analyses to reveal plasticity and its potential neural targets in early processing stages in the antennal lobe, which is the insect analog to the mammalian olfactory bulb. This plasticity is correlated to manifestations of behavioral plasticity toward odors. We employ pharmacological and molecular genetic techniques designed to disrupt neural plasticity as a way to evaluate the causal relationship between behavioral and neural plasticity. We have also recently begun to test these hypotheses developed from basic research in animals that are important for biomedicine. We are evaluating plasticity in the mouse olfactory bulb in regard to its relation to neurological disorders such as Alzheimer's and Parkinson's diseases. We plan to soon begin work on plasticity in the central brain of mosquitos because of its potential role in odor-guided behaviors at different stages in the life cycles (e.g., oviposition, host location) of important vectors of disease to humans and livestock.

Olfactory coding at the input and the output of the honeybee mushroom body

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The mushroom body in honeybees is the convergence site of highly processed multisensory input. We ask how olfactory stimuli are processed and stored within the mushroom body network by comparing the processes in the input site (calyx) and the output site (alpha lobe). At the input side olfactory coding and associative effects will be compared at the presynaptic (projection neuron) level and the postsynaptic (Kenyen cell) level. Special emphasis will be given to the role of GABA related inhibition in the microcircuits of the microglomeruli. Ca^{2+} imaging of calyx lip region is applied to elucidate the mechanisms of sparse coding in Kenyon cells, and relate it both to ionotropic GABA-A receptors and to intrinsic firing rate adaptation. Extrinsic neurons of the alpha lobe as recorded by intra- and extracellular electrodes do not code odors in a specific way. Rather they reflect the meaning of olfactory stimuli in associative contexts. Specifically responses of a recurrent pathway to the learned odor are enhanced, and a highly generalized odor is responded to more strongly than a weakly generalized odor. We conclude that the recorded recurrent neurons feed information back to the mushroom body about already learned and context related odor stimuli.

Thursday October 3rd / 12:00

Eduardo de Robertis Plenary Lecture in Neuroscience I - **Chair:** Alfredo Cáceres (IMyMF, Córdoba)

Neuronal signaling modulation by potassium channels and chloride channels

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In order to study voltage-gated potassium channels and other ion channels one at a time so as to learn about channel function and regulation, my long-term collaborator Yuh Nung Jan and I began our studies with molecular identification of the founding members of voltage-gated potassium channels in the 1980s, inwardly rectifying potassium channels in the 1990s and calcium-activated chloride channels in this millennium.

Whereas Kv1 channels of the Shaker family are targeted to invertebrate and vertebrate axons to control action potential propagation, our study of voltage-gated potassium channel local translation revealed dendritic localization of Kv1.1 mRNA and Kv4.2 mRNA, with their local translation under synaptic regulation involving signaling molecules linked to diseases with elevated risk for epilepsy and autism. Our study of EAG2 voltage-gated potassium channel upregulation in medulloblastoma revealed its involvement in volume regulation crucial for cancer cell proliferation and migration. Whereas ATP sensitive potassium channels in pancreatic beta cells control insulin release, our study of midlife obesity uncovered an upregulation of this inwardly rectifying potassium channel in hypothalamic POMC neurons.

Our study also uncovered some unusual features of the novel ion channel family, namely the TMEM16 family of “transmembrane proteins with unknown function” that is highly conserved among eukaryotes: whereas TMEM16A and TMEM16B form calcium-activated chloride channels (CaCC) in central neurons and other cell types, TMEM16F forms a novel small-conductance calcium-activated non-selective cation channel (SCAN) linked to a bleeding disorder while TMEM16C modulates pain processing in the dorsal root ganglion neurons by enhancing sodium-activated potassium channel activity.

Thursday October 3rd / 19:45

Eduardo de Robertis Plenary Lecture in Neuroscience II - Chair: Santiago Quiroga (CIQUIBIC-CONICET, Córdoba)

Dendrites: from form to function

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In our brain, neurons communicate with one another with their axons and dendrites. Axons are used to send signal to other neurons whereas dendrites, the neuron's antennae, are used to receive signals from other neurons. Even a relatively simple nervous system is composed of a vast number of neurons with strikingly different dendritic morphology. Dendrite arborization patterns are critical determinants of neural circuit formation and influence the type of synaptic or sensory inputs a neuron is able to receive. Moreover, dendrite defects have been implicated in certain human mental disorders such as autism. Although considerable progresses have been made recently, we still know relatively little about the molecular mechanisms that control dendrite development.

We have developed the dendritic arborization (da) neurons, a group of sensory neurons in the *Drosophila* peripheral nervous system (PNS), as a model system for a genetic dissection of dendrite development. By using those neurons, we have gained some insights over the past twelve years about dendrite development including how axons and dendrites are made differently, how a neuron acquires its neuronal type specific morphology, how the dendrites of different neurons are organized, how the size of a dendritic arbor is controlled, and how the pruning, remodeling and regeneration of dendrites are regulated during development.

To fully understand dendritic morphogenesis, we need to know how the dendrite morphology affects the function of a neuron. In the past few years, we have begun to study the functions of da neurons, especially their roles in mechano-sensation. Of all our senses, mechano-sensing is the least well understood as compared to other sensory modalities such as vision, taste and olfaction. Part of the reason is our lack of knowledge of the mechanical transducing molecules. Recently, *Drosophila* has emerged as an excellent system for studying mechanosensation. I

will describe our progress in uncovering molecular mechanisms underlying *Drosophila* larvae's responses to a variety of mechanical stimuli.

In parallel, we have been trying to extend our findings about dendrite morphogenesis from our *Drosophila* studies to the mammalian central nervous system. I will present some of our recent progress.

Friday October 4th / 08:30

Symposium III: Axonal regeneration and remyelination: fact or fiction?

Chair: Patricia Setton (Dept Quím. Biológica, FFyB-UBA, IQUIFIB-CONICET)

Plasticity and therapeutic potential of peripheral myelinating glia

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Adult peripheral nerve Schwann cells (SCs) provide a unique advantage for autologous transplantation in the treatment of spinal cord and peripheral nerve injuries. Whereas regeneration and remyelination of axons are increased after SC transplantation, functional outcomes remain modest, which highlights the need for combinatorial therapies and methods to improve the therapeutic potential of the transplanted cells. Precursor SCs from embryonic nerves have shown great promise for CNS repair, yet their potential clinical use may be limited. This talk will discuss how in vitro systems designed to manipulate the cellular plasticity of adult SCs can be used as a means to change the state of differentiation of the cells prior to transplantation and thereby alter their potential to foster CNS repair. Specifically, the development of clinically relevant methods to convert adult SCs into precursor SCs suitable for transplantation in the injured spinal cord will be presented and discussed.

The intimate relationship between glia and axons during degenerative and regenerative programs

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Axonal degeneration and regeneration are processes associated to neurodegenerative conditions (1) and functional recovery after nervous system damage, respectively. Both neuronal degenerative and regenerative programs are regulated by cell autonomous mechanisms as well as by tissular factors, in which glial cells have a predominant role. In this presentation, the role of glial cells in degenerative programs activated by axonal injury will be presented, and a novel mechanism for enhancement of axonal regeneration by transcellular vesicular transfer will be advanced (2).

References

(1) Court FA & Coleman MP (2012) Mitochondria as a central sensor for axonal degenerative stimuli. Trends Neurosci. 35(6):364-72.

(2) Lopez-Verrilli MA & Court FA (2012) Transfer of vesicles from schwann cells to axons: a novel mechanism of communication in the peripheral nervous system. Front Physiol 3:205.

Cellular therapies in neurological diseases

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Neurological diseases have a high prevalence, mortality and social cost both in developed and developing countries. In Brazil, cerebrovascular diseases are the leading cause of death with approximately 90,000 deaths/year and effective pharmacological therapies are unavailable. In this context, stem cells have been considered as potential therapies and although promising, many questions must be answered before entering clinical practice. In this presentation we will show the results of our studies in which we have used animal models of neurological diseases in order to investigate the possible therapeutic role of stem cells. For example, in animal models we were able to show that cell therapy with bone marrow derived cells decreases brain injury and increases functional recovery after focal ischemia. The mechanisms of action involved in the beneficial effect of bone marrow derived cells seems to be related to paracrine release of trophic and/or neuroprotective factors which decrease neuronal death and/or modulate microglia reactivity. We have also investigated the biodistribution and therapeutic effects of the cells delivered by intra-arterial or intravenous injections and we showed that brain homing and therapeutic efficacy are similar in both routes.

The observations from the preclinical studies allowed us to performclinical studies to assess the safety and feasibility of transplantation of autologous bone marrow derived cells in patients with middle cerebral artery ischemic stroke. The results from these studies showed that this therapy is feasible and safe in patients with moderate to severe stroke both in the acute and subacute phase. We will discuss future possible clinical studies to assess the efficacy of this treatment approach in several lesions and diseases of the nervous system.

Notch signaling pathway in the demyelination-remyelination process of the CNS

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Oligodendroglial damage and demyelination are common pathological features characterizing white matter and neurodegenerative disorders. Identifying the signaling pathways involved in myelin repair through oligodendroglial progenitor cell (OPC) maturation is essential for the development of new therapies. We have investigated the role of the Notch signaling pathway in CNS demyelination and apotransferrin (aTf)-induced remyelinationin two experimental models, focal lysolecithin (LPC)-induced and generalized cuprizone (CPZ)-induced demyelination in rats.Notch was found activated in Nestin-expressing neural progenitor cells and in NG2-expressing OPC in the subventricular zone (SVZ) and corpus callosum (CC) in both models. Notch activation seemed to be driven by Jagged1, which led to a high expression of downstream gene Hes5 in the SVZ of LPC-treated rats, and Hes1 in CPZ-demyelinated animals. aTf injection induced remyelination, while the injection of the γ-secretase inhibitor reversed this effect. In addition, 24 h after aTfinjection, evidence showed Notch activation concomitantly with an increase in F3/contactin levels and the upregulation of the myelin-associated glycoprotein gene in the SVZ and CC of demyelinated rats. Collected evidence supports the participation of both canonical and non-canonical Notch signaling pathways in demyelination/remyelination. During demyelination, Notch activation was found to trigger Hesgene expression, which might promote OPCproliferation. During aTf-induced remyelination, Notch activation seemed to be mediated by the expression of F3/contactin, which might induce aTf-mediated oligodendroglial maturation.

Friday October 4th / 13:00

Ranwel Caputto Plenary Lecture - Chair: Alejandro Schinder (Instituto Leloir, Buenos Aires)

Molecular and Functional Genetics of Food Intake and Body Weight Regulation

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The vertebrate brain regulates the energy balance by integrating afferent neural signals with peripheral information that reaches the mediobasal hypothalamus in the form of circulating nutrients and hormones. Within this brain area, a population of neurons expressing the proopiomelanocortin gene (*POMC*) senses most of these signals and mediate satiety responses. *POMC* encodes a prohormone that is enzymatically processed to produce the anorectic melanocortin peptides α- and β-MSH and the opioid peptide β-endorphin. The physiological relevance of POMC-derived peptides in the brain can be readily appreciated in mice lacking central *Pomc* expression, which are hyperphagic and display early onset severe obesity, similarly to what has been observed in humans carrying *POMC* null alleles. In the Ranwel Caputto 2013 lecture I will take the opportunity to present work done in my laboratory studying the transcriptional regulation of *Pomc* in the brain at the molecular, evolutionary and behavioral level. *Pomc* is highly expressed in the pituitary gland and arcuate nucleus of the hypothalamus by means of independent cis-acting modules scattered along its 5' flanking region. A proximal promoter controls *Pomc* expression in the pituitary gland whereas hypothalamic *Pomc* expression is controlled by two upstream distal enhancers, named nPE1 and nPE2, which are highly conserved in mammals. Expression studies in transgenic mice showed that nPE1, as well as nPE2, is sufficient to independently drive reporter gene expression to POMC neurons when placed upstream of minimal heterologous promoters. Moreover, both enhancers drive identical expression patterns in the mammalian hypothalamus, starting at embryonic day 10.5, when endogenous *Pomc* expression commences. This overlapping enhancer activity is maintained throughout hypothalamic development and in adulthood.

During mammalian evolution, nPE1 and nPE2 were exapted (co-opted) as neuronal enhancers into the *POMC locus* after the sequential insertion of two unrelated retroposons indicating that nPE1 and nPE2 are functional analogs that represent an authentic example of convergent molecular evolution of cell-specific transcriptional enhancers. Insertion of a loxP-flanked neo cassette in the vicinity of the neuronal enhancers allowed the generation of a reversible monogenic severe obesity model that revealed the critical importance of early intervention for the prevention of subsequent allostatic overload that auto-perpetuates obesity. In the last part of this lecture I will present unpublished studies on the regulation of *Pomc* at the vertebrate extremes (teleosts vs. mammals), on transcription factors of the mediobasal hypothalamus controlling *Pomc* expression in the developing and adult arcuate nucleus, and about the adaptive value of having two enhancers, instead of one, driving neuronal *Pomc* expression.

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Symposium on Neurobiology of Memory

ABSTRACTS

Exploring the possible physiological roles of memory reconsolidation: reativation enables updating, precision-keeping and strenghtening

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Do memory reconsolidation have just one or many different physiological roles? Simplification is not always the best course to take. We have considered the hypothesis of multiple, complementary functions and studied the possibility of three processes related to memory – updating, precision-keeping and trace strengthening – sharing a common pathway mediated by reconsolidation, in particular the underlying activation of calcium channels during reactivation / destabilization phase, at least in contextual fear conditioning. We found that memory reactivation in a situation not matching the original information induces changes in memory content (updating). However, when the contextual condition matches the original one, memory reactivation contributes either to the strengthening of memory trace, or to the maintenance of content precision over time. The suggestion of a common mechanism – reconsolidation - for these three important mnemonic functions comes from the fact that the L-type voltage-gated calcium channel antagonist nimodipine blocked all these effects, suggesting that supporting these processes.

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Co-authors of this publication publication:

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Enduring memories and the NF-kB-dependent chromatin regulation

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Memory consolidation requires gene expression regulation by transcription factors, which eventually may induce chromatin modifications as histone acetylation. This mechanism is regulated by histone acetylases and deacetylases. It is not yet clear whether memory consolidation always recruits histone acetylation or it is only engaged in more persistent memories. To address this question, we used different strength of training for novel object recognition task in mice. Only strong training induced a long-lasting memory and an increase in hippocampal histone H3 acetylation. Histone acetylase inhibition in the hippocampus during consolidation impaired memory persistence, whereas histone deacetylase inhibition caused weak memory to persist. Nuclear factor kB (NF-kB) transcription factor inhibition impaired memory persistence and, concomitantly, reduced the general level of H3 acetylation. Accordingly, we found an important increase in H3 acetylation at a specific NF-kB-regulated promoter region of the Camk2d gene, which was reversed by NF-kB inhibition. These results show for the first time that histone acetylation is a specific molecular signature of enduring memories.

Understanding Learning Disability

Alvaro San Martin[1°] , Sergio E. Lew[2°], Leonardo R. Ruzzi[1°], Verónica Cattaneo[1°], Bruce D. Gelb[3°], Mario R. Pagani[1°]

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Learning disability, commonly known as mental retardation in the International Classification of Disease (ICD-10) (World Health Organization, 1992), is the term that describes an intellectual and adaptive cognitive disability that begins in early life during the developmental period. The terminology and definitions in this field have changed many times over the last hundred years. Currently the terms intellectual disability or learning disability are the preferred ones. Although our understanding of the physiological basis of learning disability is poor, a general idea is that such condition, when results from genetic mutations, is quite permanent. However, investigations in animal models suggest that learning disability can be functional in nature and as such reversible through pharmacology or appropriate learning paradigms.

This presentation will describe our effort in understanding the molecular pathogenesis of Noonan syndrome and related disorders, a set of developmental disorders with common biochemical and phenotypic alterations. Using a Drosophila model system and a multidisciplinary approach we found evidence that learning problems in Noonan syndrome can be reversible and identified potentially new molecular components previously not associated with these disorders.

Memory consolidation in motor learning: the case for visuomotor adaptation

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Our body changes and so does our environment. The maintenance of accurate motor control despite this variable scenario is possible thanks to the establishment of new sensorimotor maps through adaptation learning. A typical experiment involves a session of familiarization during which subjects reach to visual targets in native –unperturbed- sensorimotor coordinates (null trials), followed by an adaptation session to a visual perturbation. Although abundant evidence points to the formation of long-term motor memories, several previous studies have failed at characterizing the time course of memory consolidation using behavioral protocols of retrograde interference (A-B-A). This may stem from the fact that proactive interference from B to A is much stronger than retroactive interference in this kind of learning. In my talk, I will present data from my lab that challenges current knowledge on how memories are formed and consolidated in motor adaptation. First, I will show that practice in native coordinates leads to the formation of long-lasting motor memories in the same way as reaching under perturbed coordinates. Second, null trials are not innocuous: like counterperturbations, they can interfere anterogradely both with new learning and memory retrieval through a mechanism involving the primary motor cortex. Third and last, I will show that the time course of memory consolidation can be nicely revealed using protocols of anterograde instead of retrograde interference.

A role for astrocytes in memory, stress and stress-induced memory enhancements

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Recent evidence has shown that astrocytes respond to neurotransmitters released at synapses through calcium waves and concomitantly release gliotransmitters into synapses to influence synaptic transmission. Previous studies have shown that glutamate, GABA, ATP and d-serine among others are released by astrocytes to mediate synaptic plasticity, suggesting important roles in learning and memory. Here we shall summarize present evidence for the role of astrocytes in memory, including fear memory consolidation blockade in the basolateral amygdala as a result of blocking astrocites´ release of gliotransmitters through connexin hemichannels. We shall also analyze preliminary evidence suggesting that astrocytes are involved in acute and chronic stress responses and a possible role for astrocytes on stress and arousal induced memory enhancements.

Reconsolidation: a long way from crabs to humans

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After being stored, memories can be modified through further experience. Thus, inactive memories can be reactivated through the presentation of cues (reminders) that were presented during acquisition. This presentation results in memory reactivation (labilization), followed by a process of re-stabilization known as reconsolidation. From the beginning two questions have emerged recurrently. First, Is this process triggered every time a memory is retrieved? And second, what is the function of memory reconsolidation? This talk is going to be centered in the main results of our group, trying to answer these queries. Here, we showed in crabs and humans that the reconsolidation process is only triggered under certain circumstances, when memory retrieval involves an experience that engages new learning (a discrepancy between expected and current events). Finally, we described our contribution to the description of one of the proposed reconsolidation functions: the role and dynamic of strengthening in this process using the declarative memory paradigm. We demonstrated that the strengthening via reconsolidation not only increased the memory precision but also improved its persistence. Moreover, memories strengthened by repeated labilization reconsolidations are more resistant to be interfering by a second task.

Regulation of synaptic memory by an endogenous CaMKII inhibitor?

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Ca2+/calmodulin-dependent kinase II (CaMKII) is critical for long-term potentiation (LTP) and memory. During LTP induction CaMKII is autophosphorylated and persistently translocated to synapses, where it binds to the NMDA-receptor subunit GluN2B. This binding is disrupted by CaMKIIN, an endogenous CaMKII inhibitor. CaMKIIN is widely expressed in the brain and it is transiently upregulated after behavioral conditioning. Transient treatment of hippocampal slices with CN peptides derived from CaMKIIN, persistently disrupts basal CaMKII-GluN2B binding and depresses synaptic strength by a mechanism different from other known forms of long-term depression. Moreover, LTP is enhanced after CN exposure and remarkably, it can be reinduced in previously saturated synapses. To further unravel the molecular and physiological mechanisms of these effects, we evaluated changes in critical synaptic proteins as glutamate receptors, PSD-95, and total/phosphorylated CaMKII, by western blot detections in synaptoneurosomes obtained from slices transiently preincubated with CN or control peptide. We observed a significant decrease in specific AMPA- and NMDA-receptor subunits (GluA1 and GluN1, respectively) and a reduction in synaptic phospho-CaMKII. Moreover, preliminary electrophysiological data shows a decrease in miniature synaptic currents amplitude. CaMKIIN protein thus emerges as a potential key regulator of hippocampal synaptic plasticity by affecting CaMKII localization and activity.

Effect of histone acetylation on physiological and pathological memories

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Memory consolidation requires de novo gene expression, in which is regulated by epigenetic machinery, including histone acetylation. Histone acetylation is a chromatin modification critically involved in hippocampus-dependent memory. It has been shown that the increase in histone acetylation is associated with memory enhancement. In the present study, we examined the role of histone deacetylase (HDAC) inhibitor Trichostatin A (TSA) and Sodium Butyrate (NaB) during initial learning in the maintenance of memory precision over time, forgetting, age-associated memory impairment and Alzheimer's disease (AD) rat model. We first show that TSA and NaB increase histone H3K9K14 acetylation following contextual fear conditioning and object location task in the hippocampus. Next, we show that NaB injection maintains contextual precision over time and prevents memory forgetting. Moreover, rats injected with HDAC inhibitors rescued memory deficits in AD model and middle-aged animals. Further, decreasing H3 acetylation by infusing garcinol into the hippocampus impairs memory formation. This data strongly support that the histone acetylation levels during consolidation plays a critical role in the memory quality, strength and persistence. These findings suggest that inhibition of HDAC enhances memories in physiological and pathological conditions and might be a suitable therapeutic strategy for neurodegenerative diseases and aged-associated learning and memory.

Dynamics of synaptic NF-kappa B during inhibitory avoidance long term memory consolidation

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Since the discovery that long term memory is dependent on protein synthesis, several transcription factors have shown to participate in the transcriptional activity needed for its consolidation. NF-kappa B, among them is a constitutive transcription factor whose nuclear activity has proven to be necessary for the consolidation of inhibitory avoidance in mice. This transcription factor has a wide distribution in the nervous system, with a well reported presence in dendrites and synaptic terminals. Here we report changes in synaptosomal NF-kappa B localization and activity of during long term memory consolidation. Activity comparison of synaptosomal and nuclear NF-kappa B, indicates different dynamics for both pools. Possible implication of synaptosomal NF-kappa B redistribution and activity during consolidation are discussed

Memory persistence: participation of stress and cholinergic system

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The role of stress and the cholinergic activity on the persistence of memory were evaluated. For this, we performed the treatments 9 or 12 h after acquisition and the memory tested 2 or 7 days after inhibitory avoidance (IA) training. We also investigated the interactions between the stress by immobilization (IS) and its effect on the persistence of memory and a possible effect mediated by β-adrenergic modulation. An enhancement on long-term memory (LTM) persistence caused by stress through immobilization applied 12 h after IA training was observed when the animals were submitted to 15 min or 1 h of IS, but not to 3 h. The reversal of this memory enhancement caused by IS was observed by propranolol infused prior to stress. Transitory inactivation of medial septum (MS) with lidocaine 12 h after IA training disrupted memory persistence at the 7th day, The role of cholinergic system was evaluated through muscarinic and nicotinic cholinergic receptors of CA1 area. Scopolamine and mecamylamine infusions, 12 h post-training impaired LTM persistence on the 7th. The same effects were found with pirenzepine, an M1 antagonist. No effects on the formation and persistence of memory on the 2nd and 7th days were demonstrated after DHβE infusions (nAChRs subtype antagonist □4□2, □3□2). These findings suggest that moderate stress, mAChh, nAChR at the CA1 area, and also MS activation, are required for the persistence of memory.

Memory reactivation goes far beyond expression

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The reconsolidation hypothesis has challenged the traditional view of consolidation, including the notion that consolidated memories are fixed and established. In this talk I will discuss our reconsolidation's studies that support the idea that there is dissociation between the mechanisms mediating memory reactivation and that underling the behavioral expression of memory. Although the absence of memory expression is largely insufficient to imply that memory traces are lost, our studies support the view that memory expression is not a requirement for long-term memories to be reactivated and labilized. Memory expression is not a boundary condition for reconsolidation: memory expression is indeed unnecessary for reconsolidation in crab and human. Our exceptional teacher and friend H. Maldonado and group elegantly showed that mismatch between what is expected and what actually occurs is a necessary condition to trigger memory reconsolidation. Key results of our studies show that even when memory expression does not take place, evaluation of mismatch conditions is a requirement for memory labilization both in crabs and humans. Moreover, in a recent study in crabs we show that even though expression can be disrupted by glutamate receptors antagonists at retrieval sessions, memory can undergo the reconsolidation process. So, retrieval and memory expression therefore appear not to be interchangeable concepts. Expression is just one of the possible fates of a reactivated memory.

BDNF interacts with adult-born immature cells in the dentate gyrus during consolidation of pattern separated memories

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Successful memory involves not only remembering information over time but also keeping memories distinct and less confusable. The computational process for making representations for similar input patterns more distinct from each other has been referred to as 'pattern separation'. Although adult-born immature neurons have been implicated in pattern separation, the precise role of these neurons and associated molecules in the processing of pattern-separated memories is unknown. Using a new paradigm that allowed us to manipulate the load for pattern separation and to study the effects of manipulations at different stages of memory, we provide experimental evidence that BDNF-dependent pattern separation occurs in the dentate gyrus during the encoding/consolidation, but not the retrieval stage of memory. We also found that BDNF may be expressed on an "as-needed" basis for pattern separation. Finally we provide evidence that consolidation of pattern-separated memories requires the action of BDNF on immature neurons specifically.

Parallel systems for labilization and reinforcement of synaptic plasticity during memory retrieval

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Memory reconsolidation and extinction have received increasing attention in recent years, as their potential clinical applications begin to be uncovered. Both processes seem to be dependent on more than one component – reconsolidation involves distinct biochemical systems to generate memory labilization and reinforcement, while extinction within a single behavioral session or across multiple sessions have been reported to depend on different molecular requirements. Through the use of a computational model based on attractor dynamics, we have proposed that the two processes depend on the same basic plasticity mechanisms, albeit operating in different synapses, and that this might explain why both can be affected by the same pharmacological agents. We now show further experimental evidence that fear extinction is dissociable into short and long-term components, which are differentially modulated by the phosphatase calcineurin. We believe that viewing reconsolidation and extinction from a unified perspective in terms of plasticity mechanisms would represent an interesting paradigm shift that can improve our understanding of memory modification processes and our ability to modulate them.

Memory neuropharmacology of consolidation and reconsolidation

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Experimental and clinical evidence has given support to the hypothesis that cerebral acetylcholine plays a role in mnemonic phenomena. Thus, central or systemic administration of anticholinergic drugs or lesions of the cholinergic system cause memory impairment while drugs that enhance cholinergic activity improve memory. Most of these studies have dealt with the acquisition and consolidation of memory and less attention has been paid to the retrieval and extinction processes. Several reports suggest that when a well – consolidated memory is recalled it becomes sensitive to disruption to the same treatments that affect consolidation. This new window of susceptibility is now referred as reconsolidation. In the present work it will be presented experimental evidences that suggest a possible role of central cholinergic mechanisms not only on memory consolidation, but also in memory processes that take place after memory recall.

NMDA receptor subtypes and the “previous experience effect” on memory

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The blockade of hippocampal N-methyl-D-aspartate receptors (NMDAR) usually impairs memory consolidation in rodents, while their stimulation improves it. However, adult rats that explored once or twice an OF before training in an inhibitory avoidance (IA) task, exhibited IA long-term memory (LTM), in spite of the hippocampal administration of the NMDAR channel blocker MK801 at the IA early consolidation period. On the other hand, the selective blockade of GluN2B-containing-NMDAR with ifenprodil into the hippocampus, promoted IA consolidation. This suggested that hippocampal GluN2B-R negatively modulate IA memory.

The analysis of protein extracts from the hippocampus of rats exposed to the OF, revealed an increase of GluN1 and GluN2A subunits 70 min after the OF session, without changes in GluN2B (Baez et al.). Then, the temporal course and localization of these changes were analyzed in various experimental models, after learning and after synaptic plasticity. The increase in GluN1 and GluN2A is transient, returning to basal levels 4 h after the OF. The underlying mechanisms seem to be different for each subunit.

We hypothesize that these changes could be involved in the “anti-amnesic effect” of the previous experience: During a certain period, an increase in GluN1 –and GluN2A- would lead to a rise in membrane NMDARs, while an increase in GluN2A/GluN2B ratio could also protect the synapse and the already established plasticity, perhaps saving a specific trace for a time.

Stress and retrieval interaction in fear memory: Neurobiological Mechanism

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The present study investigated the fear memory resulting from the interaction between a stressful experience and the retrieval of a fear memory trace in adult rats. Our behavioral data showed that such interaction enhanced both fear expression and fear retention. This facilitated memory is accompanied by an increased number of total and mature dendritic spines in dorsal hippocampus (DH). In addition, the current study assessed the effect of Midazolam (MDZ) intra-basolateral amygdala (BLA) infusion prior to the restraint session on the resulting fear memory after retrieval. The stress-induced enhancing effect on both fear memory and the density of mature spines was attenuated by MDZ, suggesting the involvement of a stress-induced reduction of the GABAergic transmission in BLA in both effects. Next, we test a potential BDNF role in the stress-induced promoting influence on fear memory by the intra-DH infusion of a BDNF antisense oligonucleotide. The knockdown of hippocampal BDNF mitigated the stress-induced facilitating influence on fear retention. Moreover, the retrieval experience elevated BDNF level in DH at 60 min after recall exclusively in stressed animals. These findings suggest the involvement of a hippocampal BDNF sensitive mechanism in the stress-promoting influence on the fear memory following retrieval.

Role of Medial Prefrontal Cortex Serotonin 2A Receptors in the Control of Retrieval of Recognition Memory in Rats

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Retrieval cues are not uniquely related to one specific memory, which could lead to memory interference. Controlling interference is particularly important during episodic memory retrieval or when remembering specific events in a spatio-temporal context. Despite a clear involvement of Prefrontal Cortex (PFC) in episodic memory in human studies, information regarding the mechanisms and neurotransmitter systems in PFC involved in memory is scarce. Although the serotoninergic system has been linked to PFC functionality and modulation, its role in memory processing and particularly is poorly understood. We hypothesized that the serotoninergic system in PFC, particularly the 5-HT2A receptor could have a role in the control of memory retrieval. In this work we used different versions of the object recognition task in rats to study the role of the serotoninergic modulation in the medial PFC (mPFC) in memory retrieval. We found that blockade of 5-HT2A receptor in mPFC affects retrieval of an object-in-context memory in a spontaneous novelty preference task, while sparing single item recognition memory. We also determined that 5-HT2A receptors in mPFC are required for hippocampal-mPFC interaction during retrieval of this type of memory suggesting that the mPFC controls the expression of memory traces stored in the hippocampus biasing retrieval to the most relevant one.

Behavioral and neural plasticity caused by early social experiences: the case of the honeybee

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Early experiences play an important role in shaping the future behavior in mammals but also in insects. In holometabolous insects, which suffer profound changes during metamorphosis, the effect of experiences acquired during pre-imaginal stages on the adultÂ´s cognitive abilities is still unclear. Additionally, whether precocious appetitive experiences occurred in recently emerged adults affect learning performances has not yet been deeply studied. Honeybee is an excellent model for assessing the role of experiences on later behavior due to its versatility to respond under different experimental situations. Taking advantage of the fact that honeybees extend their proboscises as a reflex response to antennal stimulation with a sufficiently concentrated sugar solution, their olfactory memories can be analyzed, as bees that have associated a conditioned odor with sugar reward, protrude their proboscis when that stimulus is delivered onto the antennae. By using this procedure we found that pre-imaginal odor-rewarded experiences lead to olfactory memories in young adults. These precocious experiences also improve adult learning performance and memory retention to known and novel odors. Moreover, rewarded experiences occurred during the first week of the adult; enhance retention performance in elder conditioned bees. Our results show that precocious experiences may allow honeybees to assess food-related information very early in life with consequences during their adulthood.

Smoke like a fish

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One study using zebrafish have demonstrated that nicotine induces a unbiased Conditioned place preference (CPP). Because in rodents biased procedures was suggested to be more effective for nicotine, we decided to setup a biased CPP task for zebrafish. Our results demonstrated that zebrafish exhibited putative nicotine biased CPP to an initially aversive compartment (nicotine-paired group). A counterbalanced nicotine control group provided evidence that the preference shift in the nicotine-paired group was not due to a reduction of aversion for that compartment. Zebrafish nicotine's preference was corroborated by behavioral analysis of several indicators of drug preference, such as time spent and number of entries to the drug paired side, and distance traveled. The results provided strong evidence that zebrafish develop a preference for nicotine, although the drug was administrated in an aversive place for the fish. The behavioral results were further supported by molecular studies. Real-time PCR analysis depicted a significant increase in the expression of 7 and 6 but not 4 and 2 subunits of the nicotinic receptor in nicotine-paired zebrafish brains. Moreover, CREB phosphorylation, an indicator of neural activity, accompanied the acquisition of nicotine-CPP. The results suggested that zebrafish exposed to nicotine in an unfriendly environment can develop a preference for that initially aversive place, which is likely due to the rewarding effect of nicotine.

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ABSTRACTS

Action, sensation, cognition and evolution. What a mess!

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Along the last 25 years our group has used electric fish as a model for studying action, sensation, perception and evolution. I have seen the progressive growth of neuroethology and cognitive neurosciences in the different countries of south cone. Now is time to start tearing down frontiers and getting together paving the way for the integration of the scientific community in this region. In this context, the aim of this talk is to introduce the diverse driving forces determining the ongoing rhumb of our lab. I will focus on their reciprocal interaction and the main recent results that should motivate discussions at the posters. On the motor side we continue exploring the neural organization of the electric organ discharge of weakly electric fish, a model of fixed motor pattern. Lately we have described the commonalities and differences among the electrogenic systems of species of the two largest groups of pulse gymnotiformes (Gymnotus and Brachyhypopomus) and some of these data is presented here within a evolutionary context. On the sensory side we contienue studying the central processing of electtrosensory images and recent findings derived from unitary recordings from the freely moving fish. Last but not least, I should introduce a novel branch of the lab focused on human motor control and cognition. Novel data dealing with processing of logic propositions will be presented.

Experience dependent tuning in olfactory processing

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Animals live in a world of countless olfactory stimuli presented forming variable mixtures. In case of specialist animals, whose success depends on detection of defined molecules, odor detection is optimized by specific receptors. In the present work we asked if detection of relevant odors can be also optimized when the category “relevant or irrelevant” is not fixed but depends on the experience of each individual. Honey bees provide a good model for this study, because their foraging behavior depends on generalist olfactory receptors and because they are able to learn the predictive value of the odors. Olfactory stimuli to which bees are normally exposed are mixtures, in which relevant odors can be masked by the presence of irrelevant ones. The significance of odors may change and bees have to keep their olfactory sense adjusted to these changes. The antenal lobe is the first olfactory neuropil were olfactory sensory neurons synapse projection neurons that convey olfactory information to other brain areas. We perform calcium imaging in projections neurons of the antennal lobe and measured the neural representation of mixtures and the pure components to test the hypothesis that relevant components are preferentially represented in the pattern of the mixture. We compared mixture patterns from naïve and trained bees and found that in trained animals the representation is more similar to the odor that predicts a reward. The results are consistent with a model in which plasticity in the antennal lobe can redefine the perceptual space according to experience.

Comparative and developmental analysis of the role of oxytocin in the facilitation of spontaneous parental responses

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Parental behavior (PB, commonly displayed by progenitors) is critical for the survival of mammalian species. However, PB can also be displayed by other individuals genetically related (e.g. siblings, aunts, uncles), or not, with the newborn. That behavior is commonly called alloparental or adoptive behavior, and it is indistinguishable from the behavior of progenitors. We hypothesizes that species that live in groups, where other non-reproductive members cooperate with caring activities, have brain adaptations to promote or facilitate those behavioural responses. We are investigating those adaptations and the neural basis of PB in non-reproductive animals. We will show evidence that supports the implication of the nucleus accumbens (NA) in species and individual differences in PB. In particular, we will discuss the action of oxytocin (OXT) in the NA to facilitate PB in non-reproductive animals. First, we will show how species (rats, prairie voles, meadow voles, and mice) and individual differences (prairie voles) in the incidence and quality of alloparental behavior are associated with different density of OXT receptors in the NA. Then, we will show how mice parental and infanticidal behaviors develop and discuss the role of OXT in the mediation of these behavioural responses. Finally, we will propose strategies to continue testing our working hypothesis and discuss the implication of our studies for human behavior.

Organization of Neuronal Networks underlying locomotion in the leech

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Neuronal networks underlying motor behaviors are thought as highly hierarchical: at the base, numerous motoneurons govern the activity of the muscles and, at the top, a few neurons "decide" the initiation of the behavior. Whether the decision to generate a particular locomotion is deposited in a few neurons or whether motoneurons are only executors of upstream commands is a matter of intense debate today. Moreover, how different aspects of behavior are actually controlled is poorly understood. The leech is an extraordinarily suited organism to address this question. The relative simplicity of its nervous system allows an analysis of motor networks from behavioral to subcellular levels. We have investigated the role of the lower levels of the hierarchy, motoneurons and premotor neurons, in the organization of the neuronal network underlying a terrestrial locomotive behavior, crawling. Crawling can be studied in the isolated nervous system, in chains of ganglia or in the isolated ganglion, indicating that the central pattern generator (CPG) is present in each ganglion and intersegmental elements coordinate the activity along the cord. We have found that motoneurons participate in the CPG of crawling (see poster by Schneider & Szczupak) and that premotor neurons operate as modulators of the rhythmic activity. The presentation will focus on how nonspiking premotor neurons modulate a rhythmic motor pattern and how they help us to explore the structure of the locomotive network.

Evolutionary and behavioral aspects of the electric fish genus Microsternarchus (Hypopomidae, Gymnotiformes) in the Brazilian Amazon

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The diversity of electric fish in South America has been historically underestimated. New taxonomic tools such as DNA markers are revealing a large number of morphologically similar, but genetically distant lineages that constitute different, sibling species. The gymnotiform genus Microsternarchus is one good example of this phenomenon and, therefore, becomes a good model to study how a behavior (Electric Organ Discharges - EODs) may vary between closely related clades, and to what extent it may contribute to sexual isolation. In the last ten years, more than 70 tributaries of the Negro river were sampled in a river stretch of approximately 1200 km. From the fish collected, EODs were recorded, DNA sequences obtained and animals were transported alive to captivity, for further behavioral experiments. Here are presented results about the distribution of the genetic diversity of Microsternarchus in the Negro river basin, as well as the first experiments on Jamming Avoidance Response (JAR) in this genus. The JAR experiments were performed with two types of jamming signals (constant frequency and constant phase differences) and revealed that Microsternarchus can modulate its EODs' rates similarly to other pulse-type gymnotiforms, including slow and rapid frequency rises, phase locking, chirps and complete interruptions. However, no stops following decelerations of the EOD rate were elicited. These preliminary results indicate similar but not identical neuronal mechanisms between Microsternarchus and other pulse-type gymnotiforms. Interpreting these similarities and differences under an evolutionary perspective can elucidate further the phylogenetic trends and the generation of distinct behaviors in the gymnotiform brain.

Dedicated Vs Multifunctional neural networks for behavior: Examples from the fish and rat brainstem

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The study of the neural bases of behavior is a major challenge in Neuroscience. From this study, dedicated and multifunctional networks emerged as two different neural strategies commonly used in the vertebrate CNS with different adaptive and functional consequences. Examples of such neural designs are currently analyzed in our lab. One experimental model includes the central components of a well known dedicated neural network that organizes the escape response in most teleosts fish. In Gymnotus omarorum, a south-american pulse-type weakly electric fish, activation of the Mauthner cells, the command neurons for motor escape, also triggers an abrupt and prolonged increase in the active electrosensory sampling of the fish environment, most probably involved in motor sequencing and in the selection of escape trajectory. As a model of a neural plan that organizes a more complex behavior, we also deal with the analysis of a neural network located in the mesopontine junction in the rat. This region is thought to be both necessary and sufficient for the generation of rapid eye movement (REM) sleep suggesting a dedicated neural network design. However, the existence of modulatory cholinergic and monoaminergic inputs to the mesopontine network with different behavioral consequences suggests that the network may exhibit different functional configurations. State-dependent changes of synaptic contacts within the network may play a pivotal role in mesopontine network multifuncionality.

Plasticity vs. conservation in the ammniote visual system. Some explicit examples

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The expression “phylogenetic plasticity” refers to an organic structure that exhibit different attributes among members of different taxa, while remains very constant among members of the same taxa. It is self-evident that the understanding of brain evolution requires the prior establishment of the magnitude and the direction of the phylogenetic plasticity of the different brain structures, as well as an elucidation of the main factors influencing such phylogenetic plasticity. In these later years we have performed some comparative studies that reveal that different structural aspects of the visual system of ammniotes, ranging from retinal specializations to central visual projections exhibit a variable degree of phylogenetic plasticity, among and within taxa. I will present examples of these studies, along with the suggestion that the main constraints underlying this process of phylogenic change/conservation do not are neither ecological nor developmental, but historical, that is, derived from the historical dynamics of the organism/medium relationship.

The role of a one-spike-neuron in implementing a sensory filter

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Spherical neurons of the electrosensory lobe of the weakly electric fish Gymnotus omarorum belong to the one-spike-onset phenotype expressed at the early stages of signal processing in various sensory modalities in diverse taxa. Membrane intrinsic properties play a fundamental role in the sensory processing of self-generated signals along the fast electrosensory pathway in weakly electric fish. Our results indicate that such role depends mainly on the presence of two resonant currents that tend to clamp the voltage near the resting potential: a low threshold potassium current sensitive to 4-amynopiridine and a mixed cationic current sensitive to cesium chloride. The dynamic filtering of self-generated signals is based on the presence of a long refractory period caused by the previously mentioned low threshold potassium current. The filtering effect implies the blockage of the pathway after being activated by the self-generated electric organ discharge and the facilitation of self-generated electrosensory information, in the context of allo-generated interference. This report shows that the spherical neuron membrane intrinsic properties determine a novel one-spike-onset neuron 'response function', specifically adapted to this circuit and task. This supports the idea that the one-spike-onset neuron phenotype may play several functional roles in animal sensory behavior dependending on the neuron and its functional context.

Circadian control of locomotor output: from structure to behavior

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Circadian rhythms regulate physiology and behavior through the action of self-sustained transcriptional feedback loops of clock genes operating in discrete groups of neurons. In Drosophila, about 150 neurons in the central brain are implicated in the circadian regulation of rest-activity cycles, but a small subset known as the small ventral lateral neurons (sLNvs) are essential. Preservation of molecular oscillations within this cluster is key to command rhythmic behavior in the absence of environmental cues. The sLNvs transmit time-of-day information releasing a neuropeptide known as pigment dispersing factor (PDF), and other yet unidentified classical neurotransmitters. The sLNv axonal terminals in adult brains also undergo extensive remodeling on daily basis, and such structural plasticity could provide an alternative means of encoding time-of-day information. We have recently carried out an unbiased screen to map the connectivity of sLNv neurons using GRASP (GFP reconstitution across synaptic partners). Remarkably, GRASP analysis revealed that sLNv terminals contact different target cells along the day, thus extending the impact of core pacemaker neurons to circuits beyond the circadian network. This finding opens the attractive possibility that circadian structural remodeling provides a mechanism by which a neuron can exert sequential control of different target circuits along the day.

Divergence in the acoustic communication of a Chilean anuran (Pleurodema thaul)

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Communication, the transmission of signals from senders that induces behavioral changes in receivers, plays a fundamental role in the evolution of species. These signals present intra-specific geographic variations, which generates mismatches between senders and receivers. Pleurodema thaul (Anura: Leiuperidae) is as an excellent model for communicational studies because during the reproductive season males emit calls which signal territories and attract females. These calls show a clear geographic variation pattern in three bioacoustic groups concordant with genetic groups within this species. Evoked vocal responses of males show strong differences between the three groups. The morphology of male's vocal apparatus could to show a corresponding divergence. In contrast, females present similar phonotactic responses to calls, indicating the absence of preferences for signals of any of these three groups. These results stress the role of male recognition and intra-sexual selection and points to a reduced importance of inter-sexual selection in the evolution of sound communication of this species.
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Early experience and transgenerational transmission of maternal styles in the overlapping-litter model in rats

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In the rat, mating at the postpartum estrus, results in the temporal overlapping of successive litters within the maternal nest. Thus, the mother will raise pups from different ages, with dissimilar sensory traits, physiological demands and behavioral capabilities at the same time. These mothers adapt their behavior according to the characteristics and needs of the two different-aged litters. Interestingly, during the overlapping of litters (OL), juveniles develop maternal like-behavior towards their younger siblings, licking them and spending significant amounts of time in the nest. Despite this "extra" source of stimulation, neonates reared in OL do not receive higher amounts of licking, as mothers lick them less than mothers with single litters. As early-life experience modulates rodents' brain function, and maternal behavior (MB) is transmitted through generations, this is a valuable model to study the effects of early experience on neuroendocrine development. We found that when adults, virgin OL females show long-term alterations in their behavioral and endocrine response to stressors and decreased reproductive behavior. However, during lactation, postpartum OL females do not modify their MB or aggression. These results show that the long term changes induced by OL varies according to reproductive states. Thus, it appears that the behavior displayed by juveniles is sufficient to compensate the effects of decreased MB on the behavior of postpartum rats during lactation.

Behavioral responses of kissing bugs (Triatomines) to odors and odor mixtures

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Using a dual-choice olfactometer in which attracted bugs get trapped, we aim at optimizing the performance of a CO2-free synthetic host odor blend to attract triatomines. We first tested a CO2-free synthetic host-odor commercial lure for mosquitoes consisting on ammonia, lactic acid and hexanoic acid (all triatomine-detected odors) and found it significantly attractive. This attraction proved to be the result of a synergistic interaction between the responses to the three odors. We then developed different blends consisting on ammonium hydroxide, lactic acid and pentanoic acid varying the total mass of compounds and their proportions. Results indicate that the proportion at which the odors were delivered has a major role in determining the attraction and capture level. Addition of a fourth triatomine-detected host odor to one of the attractive synthetic blends did not result in increased attraction as capture was even reduced by 60 %. This negative synergy or hypoadditivity depended on the odor blend to which the new odor was added, implying variability in the stability of the response to odor blends. As expected, the building of a multicomponent attractive odor blend is not a linear process. In another set of experiments using IR video recordings we compared the suitability (i.e., specificity) of different variables commonly used to measure attraction in insects.

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Ontogeny of weakly electric fish electrosensory system

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Understanding the neural basis of behavior, through integration of behavioral, physiological and anatomical studies, also leads to questions about the developmental and evolutionary history of the neural networks. Our research group's main aim is to contribute to the understanding of the development and evolution of the electrosensory system in weakly electric fish. We use two species, Gymnotus omarorum and Mormyrus rume, as their electrosensory system evolved independently, attaining different networks to tackle similar computational problems.

To determine the relative development of electrosensory and electromotor brain networks and centers, from early (M. rume), and late larval (G. omarorum) stages to adult, we combined neuroanatomy (immunohistochemistry -IHC, tract tracing, electronmicroscopy and 3D-reconstruction) with in vivo electrophysiology. To analyze the role of cell proliferation in the relative growth of brain centers involved in the electrosensory system, we described the spatial-temporal distribution and composition of brain proliferation zones by using BrdU and double-thymidine analog labeling techniques and quantification by confocal stereology. The phenotypes of proliferating and derived cells were further identified by double or triple IHC. We expect to contribute in the future to the comparative analysis of the role of local signals and incoming information in the regulation of postnatal cell proliferation-differentiation as a cue to act on its modulation.

The biased owl

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Although owls can accurately localize sounds near the center of gaze, they systematically underestimate the direction of sound sources in the periphery. Other species including humans also underestimate peripheral sound directions. This behavior and the underlying neural implementation can be predicted by statistical inference, where errors in the periphery may actually improve performance in frontal space. We found how statistics about the sensory environment and sensory input could be encoded in the owl's brain. In the presence of noise, owls would rely more strongly on prior information, leading to a bias toward the front. We have followed this work investigating how the auditory system of the owl synthesizes a representation of natural statistics.

Behaviorally related neural plasticity in the arthropod optic lobes

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Object motion detection provides essential cues for a wide variety of animal behaviors such as mate, prey, or predator detection. In insects and decapod crustaceans, visual codification of object motion is associated to visual processing in the third retinotopic optic neuropil, the lobula. In all the studied species (hoverflies, locusts, crayfishes and crabs) the repetitive presentation of object motion stimuli induces a retinotopic specific reduction in the response of lobula tangential neurons that would account for the reduction in the animal response to the visual stimulation. Whether the circuitry plasticity observed at the lobula tangential neurons first arises at these neurons themselves or as a consequence of plastic changes occurring in their presynaptic columnar neurons has been an elusive issue. Thus, we developed a simply methodology to directly address this issue recording the activity of columnar elements with calcium optical recordings. We found that the calcium response of the columnar neurons rapidly declines to repetitive motion stimulus presentations. In correspondence with animal behavior and with the activity of lobula tangential neurons, the response of the presynaptic columnar elements completely recovers after fifteen minutes and the reduction in response is retinotopic specific. Our results show that visually guided behaviors can be determined by neural plasticity that occurs surprisingly early in the arthropod visual pathway.

Propagation and reception patterns of acoustic signals in anurans

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Propagation and reception patterns of acoustic signals in anurans
Propagation patterns of acoustic signals and auditory sensitivity provide insights into the evolution and adaptation of sound communication systems. Calls produced by 16 E. calcaratus males and 17 E. emiliopugini males recorded at 0.25-8.0 m show larger average amplitudes at 0.25 m for E. emiliopugini (83.5 dB SPL) than for E. calcaratus (75.9 dB SPL), and the amplitude of both signals decreases with distance (ANOVA $F(3,75) = 314.50$, $P < 0.00001$). In the tonal calls of E. calcaratus, the amplitude ratios: harmonic 2/harmonic 1 and harmonic 2/harmonic 3 decrease with distance. The pulsed calls of E. emiliopugini show a decrease in amplitude modulation depth from about 90% at 0.25 m, to 70% at 4 m. Auditory thresholds for conspecific vocalizations measured with midbrain multi-unit recordings are about 60 dB SPL for E. calcaratus and 44 dB SPL for E. emiliopugini. These results combined reveal remarkable differences in active spaces: E. emiliopugini communicates beyond 8 m, while E. calcaratus is restricted to distances of about 2 m, implying different communication strategies in these anurans. Males give similar vocal responses to degraded and non-degraded conspecific signals, which may contribute to maintain chorusing in different aggregation densities. Supported by FONDECYT Grant 1110939.

Dendritic membrane properties influence multimodal integration in the escape circuit of goldfish

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Animals integrate information from different sensory modalities to form percepts that allows adaptive behavioral decisions. Great advances have been made by studying sense organs one at-the-time. However, understanding of multimodal integration and its role in decision-making has lagged behind. Our goal is to extend our knowledge on the contribution of single neurons to multimodal integration. We try to understand how neurons process multimodal sensory input with variable temporal dynamics and if dendrites show specific adaptations according to their input sensory modality. These questions are typically studied in vitro. We use however, an in vivo model system, the Mauthner cell (M-cell) circuit, responsible of triggering the escape response of the goldfish combined with biologically relevant stimuli. Interestingly, the M-cell receives anatomically segregated visual and auditory inputs in two distinct dendrites. This allows us to study how visual and auditory stimuli propagate towards the soma and how electrical and anatomical properties of the two dendrites determine which stimuli can be effectively integrated. We found differences in the passive spread of visual and auditory signals partly accounted for by anatomical differences between the dendrites. In addition, computer modeling of the Mauthner cell will test if anatomy is enough to explain the observed differences or that differential expression of active/passive conductances is also required.

Neuromodulation of non-breeding territorial aggression

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We are interested in the study of the neural basis of reproductive and aggressive behavior in two species of electric fish with different sociality, combining field work, behavioral recordings, pharmacological modulations, electrophysiology and cellular approaches. We focus on the identification of the neural features that underlie the gregarious behavior and seasonal aggression of Brachyhypopomus gauderio, and the high year round aggressiveness and territoriality of Gymnotus omarorum. The non-breeding intra and intersexual aggression displayed by the solitary G. omarorum is an unique model of non-sex biased territorial aggression in which we aim to demonstrate the distinct spatio-temporal pattern of activation of the social behavior network that characterizes it by exploring its modulation by both serotonin (5-HT, main inhibitor of aggression in vertebrates) and arginine-vasotocin (AVT, known to underlie sexual, individual, and social context differences in behavior). Serotonergic modulation through 1A receptors inhibited aggression in the injected fish and evoked social-mediated changes in its partner. AVT injection increased the motivation towards aggression and modulated the electric submission observed in G. omarorum. The advantages of our model species allowed us to identify precise target areas and neuromodulation mechanisms of territorial aggression that may represent more general and conserved strategies of the control of social behavior among vertebrates.

Nest digging, aggressiveness and androgen releasing in cichlid fish

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Cichlid fish interact aggressively to keep a territory wherein nests are built. Nests, in turn, act as a site of mating and caring for offspring. As nest building is an energetic costing behavior for fish, we hypothesized it could be involved in the metabolic processes that regulates aggressive interaction. Additionally, fish agonistic interaction modulates androgen releasing, such as testosterone (T) and 11-ketotestosterone (11KT). Thus, if nest building regulates aggressiveness, possibly also regulates androgen levels (Challenge Hypothesis prediction). I will show results of studies from our laboratory, with Nile tilapia social groups (males and females) as experimental models. First, we tested nest deprivation on aggressive behavior of males and found out that nest building reduces overt fighting frequency, probably by metabolic signalization. Afterwards, we tested the predictions of the "Challenge Hypothesis" by addressing social groups to three types of nesting substrates and also to nest deprivation. Androgens were measured in basal, reproductive and social challenge conditions. We found out nest deprivation did not affect T levels, but reduced 11KT levels. Contrary to Challenging Hypothesis predictions, increased aggressiveness was not followed by androgen increasing. Then, we suggest nest digging take part in regulation of aggressiveness and androgen releasing in Nile tilapia, probably by different mechanisms involving HPG axis.

Learning from an exotic social wasp

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I will present findings on behavioral plasticity in the wasp Vespula germanica. We investigated cognitive processes related to its foraging behavior, analyzing the effects of past experience on wasp response to change. This species makes consecutive flights between an undepleted resource and the nest. In our experiments, individual wasps collect food from a feeder located in a certain position in relation to a colored array. We found that when food was removed after wasp departure, on its return, wasps continued searching for the resource for a length of time which depended on the number of previous feeding experiences. We also found that, when food was displaced to a distance of 60 cm and an empty dish was placed at the original feeding site, on its next visit, wasps visited the empty feeder without noticing the nearby presence of food, even with only one previous experience. These findings indicate how previous experience seems to condition perception, delaying the detection of more rewarding contexts. What seems paradoxical is why returning foragers do not discover the available meat, but search over a site which no longer offers food, despite the fact that odour cues have great saliency for this species. We also found that when the colour of the array was changed when the food was displaced, on its next visit, wasps detected the novel food site more quickly than if contextual conditions remained unaltered. In sum, our studies show how this wasp deals with uncertainty.

Roles of glutamate receptor subtypes in electric fish courtship signals

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Weakly electric fish modulate their electric organ discharge (EOD) to produce social electric signals. EOD rate is governed by a hindbrain pacemaker nucleus (PN), which contains spontaneously active dorsal pacemaker neurons and ventral relay cells. Courtship in Brachyhypopomus gauderio includes sexually dimorphic electric displays: chirps in males and offs in females. In an in vivo preparation, the PN displays sex-specific responses to glutamate injection: EOD rate increases and interruptions can be elicited in both sexes when the PN is stimulated but only males produce chirps when stimulated in a restricted ventral and rostral portion of the PN. In an in vitro preparation containing the PN, sexually dimorphic responses arise after the injection of glutamate, AMPA and NMDA in different sites of the PN, suggesting that differences in AMPA-mediated activation are underlying the male-exclusive mechanisms of chirp production. We further explored the amount of GluR2B transcripts (AMPA receptors common subunit) by in situ hybridization in breeding males and females. Pacemaker and relay neurons of the PN from both males and females show Glur2B RNA but no significant differences were found in the quantity of transcripts between males and females. Our results highlight one of the few vertebrate groups in which the control of relevant behavioral displays can be reliably traced to a spatially restricted site within a central nucleus, and to AMPA-mediated responses in identified neurons.

Behavioral and neuroautonomic responses occur together during fear conditioning in the crab Neohelice granulata

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Reports on experience-dependent changes in invertebrate neuroautonomic function are few. We studied the context signal memory (CSM) of the crab Neohelice, usually assessed by a behavioral parameter, considering both the escape response and the concomitant heart rate adjustments. The results supported the view that the same memory process brings about changes in both parameters. We investigated the classical conditioning of the cardio-inhibitory response (CIR) and found that after CS-US pairing, an initially neutral stimulus triggered a significantly stronger CIR compared to controls. We examined the cardiac response to different stimulus modalities and found that significant CIRs of different intensities were elicited by all the stimuli investigated. Conspicuous heart arrests which are revealed by an increase in the magnitude of cardiac interbeat intervals were partially abolished by picrotoxin suggesting that these rapid responses of the crab's cardiac system to environmental disturbances, reminiscent of an autonomic-like regulation associated with flight or fight, may be extrinsically regulated by the GABAergic system. We provided an anatomical description of the cardiac system in Neohelice and evidence of the presence of GABA by means of immunohistochemistry, strengthening our previous results that suggested the GABAergic system mediates CIR upon sensory stimulation.

Dominant and subordination: how fish control their access to reproduction?

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Social interactions with the outcome of a position in a dominance hierarchy can have profound effects on reproductive behavior and physiology. Cichlid fish (Perciformes) are intensively studied in the field of social control of reproduction. The most studied species to date have been Astatotilapia burtoni from Tanganika Lake and the tilapia Oreochromis mossambicus. We are studying New World cichlids using the South American cichlid Cichlasoma dimerus (â€œchanchitaâ€) as a biological model. This substrate breeding fish has biparental care of the fry and presents a dominance hierarchy that determines access to breeding territories among males, and to males with territories among females. Female and male individuals who were located on the top rank of the social hierarchy, ascended in social status when the opportunity arose, therefore indicating that dominance is directly correlated with social ascent likelihood. Dominance was positively correlated with size in males but not in females, suggesting for the latter a relationship with intrinsic features such as aggressiveness or personality rather than to body and/or ovarian size. In order to perform these studies we developed different tools that will be presented: histological atlas from brain, gonads and different endocrine glands (pituitary gland, pineal complex and interrenal gland), ethograms, characterization of genes involved in behavior, stress and reproduction. Using all this information together we try to understand how social interactions control fish access to reproduction. Also we are trying to obtain useful information in order to improve the culture of cichlid fish that are economically relevant for our country.

Dynamic perceptual cues for approaching an object in weakly electric fish

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Pulse type weakly electric fish Gnathonemus petersii actively sense the environment using a self-emitted electric organ discharge (EOD) that produces an electric field around the fish. Nearby objects modulate the local intensity of the field at the skin of the animals and this modulated distribution is called the electric image (EI). Each EI can be characterized by a set of parameters that have been linked experimentally with the perceptual capabilities of the fish. Most of those relations have been established in static conditions, focusing on the spatial properties of electric images based on single EODs.

In this work we modelled sequences of EIs based on video sequences, triggered by the EOD, during object approximation. This experimental design allows us to study the sensory-motor, iterative, loop used by the fish to approach objects. Kinematic parameters were obtained from the sequence of video frames and reconstructed EIs. Electric image parameters and position of the fish in relation with the object, were systematically explored. The sequence of actions and sensory inputs that the fish gets as a result of this, enables us to infer the implicit decisions made by the fish and the possible rules that support them. The evidence suggest that the fish "checks and corrects" using a rule based interactive strategy with the environment. The behavioural rules obtained were used to to design a similar approaching strategy in a robot, to test its efficacy and robustness.

Bottom-up and top-down attentional modulation: lessons from a neural circuit in the avian midbrain

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When an animal attends to a certain location in the visual field neural responses within visual areas representing the attended location are enhanced at the expense of responses representing non-attended regions. The neural mechanisms behind this feat are not yet well understood. I review our work in pigeons, describing the operation of a mesencephalic network that selectively controls the ascending transmission of visual inputs, thereby emerging as a model circuit allowing competitive stimulus selection and spatial attention in birds and other vertebrates. The circuit is formed by the nucleus isthmi parvocellurais (Ipc) and nucleus isthmi magnocellularis (Imc), both reciprocally connected to the optic tectum (TeO), the main visual center in most vertebrates. We have shown that bursting feedback signals from the nucleus isthmi pars parvocellularis (Ipc) selectively boost the propagation of ascending visual inputs from the optic tectum (TeO, superior colliculus) to higher visual areas. Long-range inhibitory interactions mediated by the nucleus isthmi magnocellularis (Imc) focus the feedback from the Ipc to those locations in TeO receiving the strongest visual stimulation. This circuit also receives top-down signals from the arcopallium in the thelencephalon, which may bias stimulus competition according to the ongoing behavior. We propose that the ascending visual pathway controlled by this mesencephalic network is specially related to avoidance and escape behaviors.

The neuroscience of birdsong production in motor coordinates

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Quantitative biomechanical models can identify control parameters that are used during movements, and movement parameters that are encoded by premotor neurons. We fit a mathematical dynamical systems model including
subsyringeal pressure, syringeal biomechanics and upper-vocal-tract filtering to the songs of zebra finches. This reduces the dimensionality of singing dynamics, described as trajectories (motor 'gestures') in a space of syringeal
pressure and tension. In this work we describe our work testing this model through the study of song selective neurons to synthetic song, as well as the use of the predicted physiological parameters in the understanding of the motor neural code.

Neurobiology of visually guided prey and predator behaviors

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The semiterrestrial crab Neohelice (previously Chasmagnathus) granulata is predated by gulls, while in turn this crab predates upon smaller crabs. Both, predatory and prey behaviors of Neohelice are visually guided. Field experiments revealed that a small dummy moved 10 cm above the ground reliable elicits the escape response, whereas the same dummy moved at ground level elicits strong chasing responses. In the laboratory, the crab's escape is readily evoked by computer-generated images simulating predator attacks. The time course, speed and trajectory of the response can be precisely measured in a treadmill like device. This allowed us to investigate the visuomotor transformations involved in escaping from visual stimuli. Moreover, we identified a group of lobula giant (LG) neurons that respond to the various simulations of predatory attacks, whose firing rates match the temporal course of both the stimulus motion and the crab's speed of escape. But escaping in not the only strategy available to crabs to avoid a predator. In fact, field and laboratory experiments show that upon the sight of a predator crabs can freeze, escape or defend themselves by raising their claws. In the lab, the probability of switching among these three strategies can be biased by adjusting the image parameters that simulate a predator approach, which allows studying the decision making processes involved in crab's avoidance behavior. Additionally, in a visually homogeneous context, the image of a predator approaching right from above elicits the animal escape to its left or right side with equal probability. The decision to choose a particular escape side can be biased by creating contextual asymmetries (e.g. differences in luminance; object shapes; polarization patterns) or by conditioning the animal using an electrical shock. We are currently investigating the involvement of LG neurons in these decision making processes.

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Young Investigator Symposium

ABSTRACTS

Electrical activity regulates Plexin A3-mediated axon pathfinding in developing zebrafish spinal motor neurons

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One of the puzzles in neurosciences is how neuronal circuits are formed during the development of the nervous system. While the role of genetic programs in this process is well understood, evidence for a role of electrical activity is quite limited. In zebrafish embryos, each spinal hemisegment contains 3 primary motorneurons (PMN), named CaP, MiP and RoP, and ~30 secondary motorneurons (SMN). We simultaneously characterized PMN axon outgrowth and Ca2+ activity during pathfinding behavior in transgenic Hb9:Gal4/UAS:GCaMP3 embryos. Between 17 hr (PMN axonogenesis) and 24 hr post fertilization, PMN display two types of spontaneous Ca2+ transients. Ca2+ waves are generated in both PMN and SMN, with similar durations and frequencies. In contrast, only PMN exhibit specific patterns of Ca2+ spiking activity at different developmental stages. Suppression of Ca2+ spiking activity by stochastic expression of inward rectifier K+ channels (hKir) in single PMN led to errors in MiP and RoP axon pathfinding. Errors comprise aberrant branching in 30% of MiPs and intraspinal pathfinding mistakes in 26% of RoPs. Misguided RoP axons either extend towards the endogenous exit point but bypass it or orient away from it. Axon trajectories of hKir-expressing PMN were restored to normal when the activity of nearby cells was also suppressed; suggesting that an activity-based competition rule is a key regulator of PMN axon pathfinding. The guidance receptor PlexinA3 plays a major role in PMN axon pathfinding. Coinjections of PlexinA3 morpholino (MO) with hKir cDNA induced a synergistic effect in the incidence of pathfinding errors compared with embryos injected either with PlexinA3 MO alone or hKir cDNA alone. Moreover, whole mount in situ hybridizations showed that PlexinA3 expression is not regulated by activity. Our results provide an in vivo demonstration of the role of spontaneous electrical activity in axon pathfinding, modulating PlexinA3 signal transduction pathway.

Assembly of the Axon Initial Segment (AIS): role of a distal axonal cytoskeleton

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The AIS is a specialized domain located at the initial portion of the axon with essential roles on action potential firing and maintenance of neuronal polarity. The formation and maintenance of the AIS mainly depends on the enrichment of the membrane adaptor protein Ankyrin-G (AnkG), which clusters ion channels at this domain and organizes a specialized cytoskeleton beneath the AIS. This study focused on how ankG is recruited to the AIS. By immunohistochemical analysis was observed that after axonal specification, AnkG is clustered at the same axonal location proximal to the cell body, during development. In this sense, it was defined a distinct submembranous cytoskeleton comprised of Ankyrin-B, αII-spectrin and βII-spectrin, that is formed from the distal axon generating an intra-axonal boundary that restricts AnkG to AIS. The overexpression of these individual components of distal cytoskeleton modified the location of this boundary altering the AIS length. As well, after knockdown of Ankyrin-B, αII-spectrin or βII-spectrin, a strong impairment of AnkG clustering at the AIS was observed. Moreover, disrupted AIS were also observed in αII-spectrin and βII-spectrin deficient mice supporting these findings. Thus, AnkG clustering at the AIS takes place by an exclusion mechanism driven by the distal axonal cytoskeleton.

Reprogramming of Tau isoforms by RNA trans-splicing: Towards a plausible therapeutical approach for tauopathies?

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Tauopathies are major neurodegenerative diseases, including Alzheimer's disease (AD), characterized by the presence of intraneuronal aggregates of the protein tau in neurofibrillary tangles. Tau is a microtubule-associated protein predominantly expressed in neurons, which participates in a myriad of cellular functions such as microtubule polymerization and stabilization, neurite outgrowth and axonal transport. Human Tau, encoded by the MAPT gene, comprises 16 exons. Alternative splicing of exons 2, 3 and 10 gives rise to six tau isoforms in the adult brain. Particularly, the alternative splicing of exon 10 (E10) produces tau isoforms with three (3R) or four (4R) microtubule binding repeats. Tau 3R and tau 4R are expressed in equal amounts in the normal adult human brain. Several human tauopathies are associated with mutations in the MAPT gene which interfere with exon 10 alternative splicing, leading to an imbalance between the 3R and 4R isoforms, and thus disrupting the normal 3R/4R ratio. Correction of that imbalance between Tau isoforms might represent a potential therapeutic approach for those tauopathies. Ideally, such a therapeutical restoration has to be achieved by a versatile strategy. RNA reprogramming is a promising alternative to this end, because it offers several advantages over conventional therapies: RNA therapy avoids side effects of drugs and most importantly, the repaired product is under endogenous transcriptional control and has the same expression pattern as the normal transcript. The aim of our work is to use a strategy to modulate Tau 4R/3R ratio by reprogramming the inclusion of E10 in the endogenous Tau transcript, via spliceosome-mediated RNA trans-splicing (SMaRT). SMaRT creates a chimaeric mRNA through a trans-splicing reaction between an endogenous mRNA and an exogenously delivered RNA pre-trans-splicing molecule (PTM). Tau-PTMs were delivered into differentiated primary neurons by lentiviral vectors. The trans-spliced product was detected both at the RNA and protein level, demonstrating efficient isoform conversion between 3R and 4R Tau and translation of the chimaeric RNA to Tau protein. Tau trans-splicing was also tested in a pilot in vivo study, by sterotaxical delivery of Tau-PTMs into the brain of a mouse model of tauopathy, carrying the human MAPT gene (hTau mice). So far, our results provide evidence for the potential of SMaRT to correct tau mis-splicing and raise promising perspectives about the use of RNA reprogramming for tauopathies. Our work in progress aims to elucidate if RNA reprogramming is a suitable tool to achieve a relevant phenotypic recovery in the hTau mouse model.

Challenging the view of the cortex in memory: essential role of retrosplenial cortex in memory formation, storage and retrieval

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The retrosplenial cortex (RSC) plays a role in a range of cognitive functions, includingepisodic-like memory. However, its precise involvement in memory processing is unknown. Using microinfusions of antisense oligonucleotides to locally knockdown cFos in the anterior part of RSC (aRSC), we found that c-Fos expression is necessary around training, and again 12 h thereafter to maintain for many days a fear-motivated memory. Long-lasting memory storage is regulated by D1 dopamine receptors in aRSC and depends on the interplay between dorsal hippocampus and aRSC. Experiments also show that recently acquired and consolidated fear memory requires macromolecularsynthesis in aRSC and that its reversible inactivation impairs recall of recent and remotememories. The present data challenge the generally accepted idea that neocortical areasare slow encoding systems that participate in the retrieval of remote memories.

Low attention impairs optimal incorporation of prior knowledge in perceptual decisions

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Non breeding territorial aggression is an uncommon feature whose underliyng mechanisms are under ongoing research in birds and mammals. The weakly electric fish Gymnotus omarorum is the only teleost species studied to date that displays non-breeding territorial aggression irrespective of sex, and thus constitutes an interesting model system to study the neuro-endocrine mechanisms of territoriality. With the aim of exploring the determinants of territory value and individual spacing, we studied a natural population of G. omarorum during the non-breeding season. We carried out a diurnal electrical census of 7 homogeneous sites in Laguna del Sauce, Uruguay; and performed ecological, morphological, electrophysiological, and hormonal assays. In a first attempt to characterize the species' habitat, we found that oxygen concentration and aquatic vegetation density are variables influencing spatial distribution of G. omarorum. In particular, oxygen saturation had predictive value on territory size, stressing the importance of this parameter as indicator of territory value. The expected positive relationship between body size and territory size was found, while other variables such as in situ discharge frequency (indicator of social hierarchy) did not show significative correlation nor with territory size or body size. In addition, we correlated plasmatic levels of steroid hormones with territory size, morphometric and physiological traits and with environmental parameters. Supported by ANII_FCE_2011_6180

Children are natural pedagogues

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Human communication is adapted to transmit opaque knowledge which is hard to acquire by pure observation (Csibra et al, 2006). In particular, infants and young children are sensitive to communication cues – called ostensive cues- which are directed to them and specify a learning context (Csibra et al, 2009; 2010; Senju et al, 20084). They can recognize the communicator by identifying the ostensive nature of his actions. And then, can attempt to infer the content of the information when the signals used unambiguously mark them as the recipient of the message (Csibra et al, 2010). They are prepared to be at the receptive side of natural pedagogy (Csibra et al, 2009). However, whether children are tuned to efficiently communicate in the emitter side of natural pedagogy remains unknown. In the present work, we will show that young children are capable of generating ostensive signals when teaching. Adopting a simple experimental setup which originality put kids -3 to 7- years old- in the place of teachers, we found that they can not only detect, recognize and react to ostensive communication (Gegerly et al, 2005) but furthermore, that they can efficiently utilize this strategy to denote their own pedagogical intention. We examined their use of ostensive cues in a game in which a rule had to be inferred (Schulz et al, 2004) before being taught to an adult. Children modified their behavior -changes in body orientation, eye-contact and eyebrow-raising - to fulfil an informative intention to their addressee. Our results strongly demonstrate that kids can actively transmit opaque knowledge to others using well-known ostensive cues. Here we show for the first time that young children efficiently use these signals, placing themselves in the emitter side of natural pedagogy. Given that, it has been proposed that natural pedagogy enable the transmission of cultural knowledge in humans (Csibra et al, 2011), studying the kids' role in this process is fundamental.

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SAN Award to the Best Doctoral Thesis in Neuroscience 2013

Functional study of the dopamine D2 receptor (D2R) in the central nervous system byinducible mutant mice

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Suboptimal or excessive dopamine (DA) release are characteristic of a number of verycommon diseases, including Parkinson's disease, schizophrenia, attention deficit disorder with hyperactivity (ADHD) and compulsive self-administration of drugs of abuse. In this work, we study the role of D2R by generating mutant mice. First, we generated micelacking D2R in dopaminergic neurons (autoreceptors). These mice have increaseddopamine synthesis and release, are hyperactive and hypersensitive to the psychomotoreffects of cocaine, and show enhanced motivation to work for food. Second, we generateda model that allows us to eliminate D2R of adult animals normally developed. The abruptremoval of the D2R in adulthood causes a marked decrease in locomotion, severe learningproblems and motor coordination routines. In some cases, it can induce rigidity and tremorat rest. These results demonstrate the importance of the strict regulation mediated by theD2R (pre-and postsynaptic) in the control of locomotor activity, sensitivity to drugs ofabuse and particularly in the motivational state of animals.

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Short talks / Session A

ABSTRACTS

Dissecting reactive astrogliosis: The conversion of astrocytes towards a reactive phenotype

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Reactive astrogliosis (RA) is a generic response to brain injury mediated by reactive astrocytes. It is proposed that, during activation, astrocytes suffer a de-differentiation process. Evidence shows that RA contributes to neuronal protection as well as with expansion of focalized brain lesions. However these antagonizing roles of RA and the underlying mechanisms are still on debate.

Here we show in vivo that reactive astrocytes (hypertrophied GFAP+ cells) overexpressed nestin in a time dependent manner after the onset of experimental brain ischemia. We were able to purify these cells in vitro by applying a protocol for establishment of primary cultures. Only ischemic tissue (but not control) was capable of rising proliferative cultures. Immunofluorescence studies for nestin, vimentin, GFAP and BrdU incorporation revealed an undifferentiated astrocytic phenotype and a high proliferation rate compared to primary astrocytes. Even more, conditioned medium obtained from these cells induced the RA and proliferation of naïve astrocytes, proliferation, but also neuronal protection to OGD.

Our results indicate that the proinflammatory environment generated after ischemic stroke induces activation of astrocytes towards a reactive and undifferentiated phenotype. These reactive astrocytes proliferate in vitro and have the potentiality of activating naïve astrocytes probably by secretion of proinflammatory cytokines thus contributing to sustain RA.

Pea3 transcription factor family members, Etv4 and Etv5, mediate retrograde signaling and axonal growth of DRG sensory neurons in response to NGF

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Nerve Growth Factor (NGF) is a target-derived neurotrophic growth factor that controls many aspects of sensory and sympathetic neuronal development. The identification of transcription factors and downstream target genes that mediate NGF-dependent neuronal differentiation and target field innervation is currently a major challenge. Here, we show that the Pea3 transcription factor family members, Etv4 and Etv5, are expressed by developing TrkA-positive dorsal root ganglion (DRG) neurons during the period of target innervation. Real time PCR assays indicated that Etv4 and Etv5 mRNAs are significantly induced by NGF in different neuronal cells, suggesting that they could be involved in the biological responses induced by this neurotrophin. Interestingly, distal axon application of NGF in compartmentalized cultures of rat DRG sensory neurons was sufficient to induce a significant increase in Etv4 and Etv5 mRNA expression. Pharmacological assays also revealed that activation of MEK/ERK (MAPK) pathway is required for Etv4 and Etv5 gene induction in response to NGF. Downregulation of Etv4 and Etv5 using small interference RNA knockdown experiments inhibited NGF-induced neurite outgrowth of rat sensory neurons, while overexpression of full-length Etv4 or Etv5 potentiated neuronal differentiation in response to this neurotrophin. Together, these data establish Etv4 and Etv5 as essential molecules of the transcriptional program linking neurotrophin signaling to sensory neuronal differentiation, and suggest that they can be involved in NGF-mediated target innervation.

Tyrosine 251 at the C-terminus of Neuronal Glycoprotein M6a is Critical for Neurite Outgrowth

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Recent findings associate polymorphisms in human GPM6A with mental illnesses such as claustrophobia, schizophrenia and bipolar disorders. Neuronal glycoprotein M6a is involved in neuronal plasticity promoting neurite and filopodia outgrowth and synaptogenesis. Nevertheless, the molecular bases underlying these observations remain unknown. Previously, we documented that M6a depends on the association of membrane
lipid microdomains and activation of Src and MAPK kinases for filopodia induction. In silico analysis of phosphorylation of the tyrosine-251 at the C-terminus of M6a showed that it could be a target of Src kinases. We examined whether phosphorylation at Y251 of M6a affects neurite and filopodia outgrowth and the targets involved in their signal propagation. We found that phosphorylation of Y251 contributes to neurite extension in hippocampal neurons and N2a cells. In addition, Src and AKT are phosphorylated and recruited to the cell membrane. Expression of a non-phosphorylatable form of M6a arrested neurite outgrowth. In contrast, phosphorylation state had no effect on M6a-stimulated filopodia formation. PI3K inhibitors dramatically blocked filopodia induction in M6a-overexpresing neurons. We suggest that phosphorylation of M6a at Y251 is critical for a specific stage of neuronal development and triggers redundant signaling pathways such as Src and PI3K/AKT, leading to neurite extension.

Identification and characterization of genes involved in the pro-neurogenic effect of TGFβ1

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The adult brain possesses neurogenic regions that contain adult neural stem cells (NSC), which are able to proliferate and generate new neurons, astrocytes and oligodendrocytes. The molecular mechanisms of this differentiation process aren't yet completely known.
Our lab demonstrated that immune system cytokines participate in the neurogenic niche, regulating the neuronal differentiation. In particular, we demonstrated that TGFβ1 induces neurogenesis in vivo and increases the ratio of neuronal progenitors (Tuj1+ cells) obtained from NSC in vitro.
The aim of this project is to identify molecules participating in the pro-neurogenic process induced by in vitro. Through a functional genomics assay, we detected 10 genes with differential expression induced by TGFβ1, and validated them by qRTPCR. We selected Fibulin 2 (Fbln2, which exhibited the highest induction rate) as a candidate for a functional validation of its potential role in the neurogenic process. We silenced Fbln2 expression with specific siRNA during the neural differentiation process induced by TGFβ1 in NSC primary cultures. The specific Fbln2 siRNA, but not the scramble, blocked the pro-neurogenic effect of TGFβ1. Notably, Fbln2 induction was observed specifically in Tuj1- cells, suggesting an indirect effect over the neuronal progenitor population. These results indicate Fbln2 as a candidate to mediate TGFβ1 neurogenic effect, attributing it for the first time a role in neurogenesis.

Role of 5-HT1A and 5HT2A in the modulation of GABA release from the thalamic reticular nucleus

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Methylphenidate (MPH), a drug widely used to treat children diagnosed with ADHD, and cocaine (Coc) inhibit the re-uptake of dopamine and norepinephrine. Cocaine, unlike MPH, also inhibits the re-uptake of serotonin (5-HT). Previously, we observed that the frequency of spontaneous GABA release from thalamic reticular nucleus (Ret) neurons is increased in slices from mice treated with a Coc binge, but not in those from animals treated with MPH, suggesting that the effect of Coc is mediated by changes in serotonergic transmission.We recorded miniature inhibitory post-synaptic potentials (mIPSPs) from ventrobasal nucleus neurons in the presence of 5-HT and 5-HT1A or 5HT2A/2C agonists ((±)-8-OH-DPAT, (±)-DOI hydrochloride; both 10μM) and antagonists (ketanserin, NAN-190 hydrobromide; both 25μM). Our results show that the effect of bath–applied 5-HT (100 μM) on mIPSP frequency resembles that of Coc, and that even though both types of agonists lead to an increase in frequency, the effect of the 5-HT1A agonist was stronger. Surprisingly, the 5HT2A antagonist also had the same effect, which could be explained by a biphasic behavior of the 5HT2A receptors in Ret neurons' GABAergic terminals.Our findings suggest that Coc-induced effects on thalamic serotonergic transmission might be mediated by presynaptic 5-HT receptors (on the terminals of Ret neurons) and that these effects could be responsible for the thalamocortical dysrhythmia observed in humans and animal models of Coc use.

Suprachiasmatic astrocytes modulate the circadian clock in response to TNF-alpha

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Circadian rhythms in mammals are orchestrated by a master oscillator that resides in the hypothalamic suprachiasmatic nuclei (SCN) and drives a number of physiological and behavioral rhythms. The immune and the circadian systems interact in a bidirectional fashion and the SCN responds to both peripheral and local immune stimuli. Astrocytes exert immune functions in the central nervous system, and there is growing evidence demonstrating multiple roles of these cells in the regulation of circadian rhythms. The aim of this work was to assess the response of SCN astrocytes to the proinflammatory cytokine TNF-alpha with focus on the effects on the circadian clock. SCN astrocytes cultures from PER2::luc knock-in mice treated with TNF- showed changes in either phase or amplitude of PER2 expression rhythms, depending on the phase of the treatment. We also analyzed if SCN astroglia could secrete factors that alter circadian physiology in response to TNF-alpha. Conditioned media from SCN astrocytes transiently challenged with TNF-alpha induced an increase in Per1 expression in NIH-3T3 cells, as well as phase delays in both, PER2 expression rhythms in the SCN and behavioral circadian rhythms when applied intracerebroventricularly in mice. Moreover, we found that these effects were dependent on TNF-alpha secreted by the astrocytes. In conclusion, SCN astrocytes respond to TNF- alpha by showing an alteration on its own molecular clock, and modulating in vitro and in vivo circadian physiology.

Mature and immature hippocampal granule cells activation profiles are dictated by local inhibitory circuits

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Neurogenesis in the adulthood provides the dentate gyrus (DG) of the hippocampus with pools of granule cells (GC) which integrate into the preexisting network. It has been widely shown that newly born GC are necessary for many types of memory, but how these neurons contribute to the hippocampal function is unknown. In this work, we propose that it is when they are still immature that newly born GC provide the network with a specific processing function. We injected a retrovirus in the adult mice DG to label new GC by the expression of fluorescent markers. We performed calcium imaging and elecrophysiological recordings from immature newly born GC (iGC) and mature GC (mGC) on acute hippocampal slices. Upon stimulation of the afferent pathway, iGC require weaker input strengths to be activated than mGC. This difference is due to the fact that iGC receive a slower and weaker inhibition. In addition, we showed that iGC could respond to independent inputs, acting as good integrators of afferent information, while mGC are more specific in their responses. Last, we evaluated the responses of iGC and mGC to stimulation at different frequencies. While both populations differentially responded to distinct frequencies, iGC showed higher activation levels. Inhibitory circuits play a main role in generating these differences. Our results show iGC emerge as a population of GC with different activation properties since they escape from the generalized high levels of inhibition of the DG.

Neurotoxicity of glyphosate involved Wnt-CAMKII signalling pathway

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Glyphosate (Gly) formulations (Round Up) are used as non-selective herbicides for controlling the growth of weeds. Mammals and humans are exposed to high levels of Gly herbicides due to agriculture activity. Up to date, very few scientific evidences have been reported about its toxicity. In this work, we study the potential effect of Gly on nervous system during development through in vivo and in vitro studies. We found that rats exposed to Gly during gestation stage showed signs of neurotoxicity, such as defect on reflex responses, lower motor activity and memory impairment. In order to identify the cellular mechanism inducing the Gly neurotoxicity we performed assays using cultured neurons. We found that hippocampal pyramidal neurons exposed to Gly showed a delay on the development characterised by a decrease in axonal growth and neuronal complexity. Wnt proteins function as key modulators for the formation and functioning of neuronal circuits. Particularly, Wnt5a is involved in axonal growth and guidance. We observed that the expression of Wnt5a decreased in neurons treated with the herbicide. Moreover, Gly treatment induced a significant inhibition of CaMKII, a key effector of the non canonical Wnt pathway. Importantly, this effect was reverted when exogenous Wnt5a was added to the medium and neurons developed a morphology similar to controls. These findings suggest that Gly affects neuronal development and function through changes in the non-canonical Wnt signaling pathway.

SAN
SOCIEDAD ARGENTINA DE
INVESTIGACIÓN EN NEUROCIENCIAS

Short talks / Session B

ABSTRACTS

Brain functional connectivity in patients with disorders of consciousness: towards novel dynamical approaches

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Severed brain injury can lead to disorders of consciousness (DOC) in which there is an absence of awareness of the self and the environment. Resting-state (RS) functional studies using functional magnetic resonance imaging (fMRI), explore the spontaneous activity of the brain by obtaining the fluctuating temporal series of neural activity and study their behavior, and this approach appears to be of great value for the study of unresponsive DOC patients. Many studies show that the brain functional connectivity is altered in patients with DOC. In the present study we calculated the FC on fMRI data from healthy subjects and patients in DOC state using a classical approach of linear correlations and a novel measure from Information Theory field, the transfer entropy. FC was assessed among time series of the blood oxygenated level dependent (BOLD) signal from 98 regions. These time series were used to estimate FC using two approaches: Partial Linear Correlation (PLC) and Transfer Entropy (TE). FC was examined within and between brain hemispheres as a measure of the integrity of brain function.
PLC pattern was altered in DOC patients in comparison to controls. In particular, between homotopic areas of different hemispheres and within hemispheres. On the other hand, TE was also altered in DOC patients, suggesting a disruption in information flow from left hemisphere to right hemisphere and in the opposite direction.

Role of medial prefrontal cortex (mPFC) in aversive memory processing

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In the systems consolidation theory, the hippocampus is seen as a sparse and fast learning structure which encodes an event using separated representations minimizing interference, whereas the neocortex is a distributed, overlapping and gradually integrating information structure with a low learning rate. Nevertheless, recent results provide evidence for alternative views which propose that the neocortex may have a crucial role from initial steps of memory formation.Recently, we described a late stabilization phase required for the persistence of the long term memory (LTM) in the hippocampus. We also demonstrated that maintenance of LTM depends on activation of ventral tegmental area (VTA)/hippocampus dopaminergic connections. In this work we present evidence in agreement with emerging views, demonstrating that mPFC supports learning and permanent storage of two types of aversive memory: inhibitory avoidance (IA) and conditioned taste aversion (CTA). In addition, we show that early after training, mPFC dopaminergic system plays a specific role controlling LTM maintenance, but not memory formation, and modulates the hippocampal late phase. Importantly, with our results we accomplish to dissociate the mechanism underlying LMT consolidation from LTM persistence in mPFC in the moment of the memory acquisition.

Cool songs: stretching and breaking syllables in birdsong

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Birdsong is a complex learned behavior generated by a network of forebrain nuclei that generates the coordinated motor patterns for song. However, nature of telencephalic control over premotor and motor circuits is debated. Hypotheses range from complete usurping of downstream circuitry to highly interactive control mechanisms [1,2]. We show theoretically and experimentally, that telencephalic song motor control in canaries is achieved by a highly interactive strategy. As predicted from a theoretical model of respiratory control [2-5], mild cooling of a forebrain nucleus (HVC) led to song stretching, but further cooling caused progressive restructuring of song, consistent with the hypothesis that respiratory gestures are subharmonic responses to a timescale present in the output of HVC. This interaction between a life-sustaining motor function (respiration) and telencephalic song motor control suggests a more general mechanism of how nonlinear integration of evolutionarily new brain structures into existing circuitry gives rise to diverse, new behavior.

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The involvement of the GABAergic system in the formation and expression of the extinction memory in the crab Neohelice granulata

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Extinction memory usually occurs after repeated or prolonged presentation of a conditioned stimulus (CS) that was previously associated with an unconditioned stimulus (US). It is widely accepted that fear extinction involves a new association between the CS and the absence of the US rather than the erasure of the CS–US association. We have demonstrated that an agonist of mammalian GABAA receptors impaired memory consolidation and reconsolidation, whereas an antagonist improved both processes. Considering that its assumed that extinction is a process based on inhibitory association, it seems possible to speculate that inhibitory mechanisms may be required in order to acquire a memory that is inhibitory in nature. Using a combination of behavioral protocols and pharmacological treatments, we investigated the role of the GABAergic system in the different phases of the extinction memory in the crab Neohelice granulata. We show that the stimulation of the GABAergic system facilitates and its inactivation impairs the extinction memory acquisition, and that diminishing the GABAergic tone before extinction test block its expression. These results allow us to conclude that an active GABAergic system is necessary for the acquisition and expression of the extinction memory. This detailed description may contribute to understand the role of the GABAergic system in diverse aspects of the extinction memory.

Lateral Habenula regulates the maintenance of fear long-term memory

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Memory definition implies the temporal persistence of a mnemonic trace; however the mechanisms that ensure memory stability over time are not well understood. One crucial finding in this regard was that a dopaminergic signal arriving from the Ventral Tegmental Area (VTA) to the hippocampus during a defined period of time after acquisition is critical for the definition of how long a memory will persist (Rossatto et al., 2009). Lateral Habenula (LHb) is a small epithalamic structure that codifies negative motivational value and exerts a powerful control over VTA dopaminergic neurons. Recently it has been shown that LHb activation is sufficient to induce aversive associative learning; however the key question about whether LHb activation is required for a memory to be formed during adversive associative learning has not been addressed. In our experiments we used the Inhibitory Avoidance (IA), a protocol in which a single electric shock exposure induces a persistent contextual aversive memory, to study the relationship between LHb and memory formation in rats. Our results show that inhibition of LHb during memory acquisition does not impair IA memory formation but reduces its temporal stability. This effect posses a striking parallelism to reducing IA memory salience by reducing electric shock intensity suggesting that LHb activation during training conveys a salience signal that ensures temporal stability of the newly formed memory.

Alterations in frontal cortex synaptosomes from rats with experimental autoimmune encephalomyelitis

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Experimental autoimmune encephalomyelitis (EAE) is an animal model of the human disease multiple sclerosis. Both are inflammatory demyelinating pathologies of the central nervous system associated with motor, sensory, and cognitive deficits. In the last years gray matter damage has increasingly received attention as they may contribute to disease progression and emergence of cognitive deficits. Herein we analyze functional and morphological changes in isolated presynaptic terminals (synaptosomes) from frontal cortex of rats with acute EAE. We show impairment in Ca2+-dependent L-glutamate releaseconcomitant with alterations in the levels and phosphorylation state ofsynapsin I and kinasesof the release machinery (Erk1/2 and CaMKII). These changes rapidly reverse when the animals begin to recover from the clinical signs of the disease. Our results indicate the release machinery is altered in the frontal cortex of rats with EAE. Furthermore,electron microscopy studies revealed differences in synaptic vesiclesdistribution and PSD size in EAE group. These are the first evidences unraveling the molecular mechanism of presynaptic dysfunction in frontal cortex during the course of EAE.

Involvement of PFC´s Wnt/bcatenin pathway in cocaine induced sensitization

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Wnt factors are cistein rich secreted proteins that interact with their receptors: Frizzled, Ryk, and Ror. As a result of the interaction, Dishevelled is activated, and, consequently, one of three pathways: Wnt/βcatenin, Planar Cell Polarity, or Wnt/calcium pathways. Wnt signaling pathways are essential for mammalian brain development. However, little is known regarding its role in adulthood. Recently we showed a decrease in Prefrontal Cortex (PFC) βcatenin levels in cocaine sensitized animals. Since our main goal was to elucidate the role of Wnt/βcatenin pathway in cocaine sensitization, we evaluate PFC´s GSK3β activity levels of sensitized animals as well as βcatenin levels in nuclear fraction. Adult male Wistar rats received daily cocaine injections for 7 days, were tested for locomotor sensitization and sacrificed 24hs after last injection. Our results showed an increase in GSK3β activity levels associated with a decrease in βcatenin levels in the nucleus, indicating an inhibition of Wnt/βcatenin pathway in PFC. Then, we evaluate if these PFC changes were necessary for cocaine sensitization. To do it, rats received an intra-PFC infusion of Sulindac an hour before cocaine between day 2 and 6 of the treatment. The data showed that blocking PFC Wnt/βcatenin pathway with Sulindac, prior to cocaine injections, enhances the development of behavioral sensitization. So far our data suggests that cocaine sensitization is associated with an inhibition of PFC Wnt/βcatenin pathway

The Role of Acetaldehyde in Ethanol Behavioral Efects during Early Ontogeny

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Central effects derived from ethanol exposure varies across ontogeny. The catalase system, wich metabolizes EtOH into ACD in the brain, is more active during the first 10 days of life. We have found that ACD is necessary for the acquisition of an appettitive conditioning in newborn rats. Here, we analyze the role of CD in EtOH induced locomotion and sedation in infant rats. In Experiment 1, infants received EtOH (i.g.: 0.0; 0.5; 1,5 and 2,5 g/kg) one hour after cianamide administration (0 or 10 mg). Five and 45 minutes later, locomotive activity was rated in an open field during 5 minutes. Results: EtOH significantly increased locomotive activity shortly after administration (min 5-10, doses 1.5 and 2.5 g/kg). During postadministration time 45-50, cianamide significantly decreased motor activity in pups administered with EtOH (0.5; 1.5; and 2.5 g/kg), compared to control siblings (group 0.0 g/kg EtOH). In Experiment 2, locomotive activity was assessed in EtOH administered 15 day old rats (0.0 and 2.5 g/kg), wich received cianamide or cianamide plus 4-metylpirazol (0 or 10 mg). Whereas cianamide potentiated EtOH reduction of motor activity, 4-MP blocked this effect. Experiment 3 assessed EtOH blood levels after receiving manipulations similar to those used in experiment 2. Cianamide administration significantly decreased circulating levels of EtOH, 4MP blocked this effect. Present results indicate that ACD accumulation decreased locomotion, but ETOH accumulation reverts this effect.

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INVESTIGACIÓN EN NEUROCIENCIAS

POSTER ABSTRACTS

Cellular and Molecular Neurobiology
Poster Number 1/ Session 1

Agonist-induced melanocortin type 4 receptor (MC4R) activity specifically inhibits neuronal CaV2.2 channels

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MC4R is a G-protein coupled receptor involved in food intake and energy expenditure. MC4R is expressed at brain nuclei that operate as centers of body weight regulation, such as PVN of the hypothalamus, amygdala and NTS. MC4R activation modifies neuronal activity but the molecular mechanisms by which this process occurs remain unclear. Here we studied how MC4R evoked activation can regulate voltage-gated calcium channels (VGCC). Using patch clamp we found that MC4R activation by MTII, a MC3/4R agonist, inhibited CaV2.2 current in transiently transfected HEK293 cells. This inhibition was concentration-dependent, voltage-independent and occluded by cholera toxin (Gαs inhibitor). Moreover, we found that MTII specifically inhibited native CaV2.2 currents from mouse cultured amygdalar neurons in a concentration-dependent manner. Then we compared the effect of mouse icv injections of the MC4R specific agonist (RO27-3225) and CaV2.2 blocker (ω conotoxinGVIA). RO27-3225 activated mice neurons in several amygdalar subregions while ω conotoxin GVIA mimicked the increase of c-Fos expression induced by RO27-3225 exclusively in the Central Amygdala nucleus (CeA). Our data shows that a presynaptic VGCC subtype, the CaV2.2, is specifically inhibited by MC4R activation. From our in vitro and in vivo studies on amygdalar neurons, and since CeA has abundant GABAergic innervations, we postulate that inhibition of CaV2.2 by MC4R could reduce the GABA release decreasing the inhibitory tone on CeA

Cellular and Molecular Neurobiology
Poster Number 2 / Session 2

Does Gymnotus carapo show a mixed neuro-myogenic type of electric organ?

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Electric fish have evolved 2 strategies for electrogeneration. In most cases the effector units – electrocytes- are myogenic syncitia that have lost their contractile machinery. In adults Apteronotidae the electric organ (EO) consists of parallel bundles of electromotor axons having 2 enlargements arranged in parallel (neural electrocytes). Gymnotus carapo (L), emits a pulse with 6 deflections in head-to-tail recordings. Like other species, five of these deflections result either from direct neural activation of electrocyte membrane faces oriented perpendicular to the main axis or from the propagation of action potentials to the opposite electrocyte face. The first positive phase (V1ct), is characteristic of a clade within the genus. The aim of this study was to unveil the origin of V1ct combining anatomical, electrophysiological and computational analysis. Electrophysiological data show that v1ct is originated very early in the EOD, at the transition between the central region and the tail. In this place, Cajal photographic techniques show axon enlargements in the large electromotor nerves (PEN) inervating the tail portion of the EO. These enlargements may act as 'neural electrocytes' suggesting that carapo´s clade may have a mixed form of electrogeneration. Computational modeling confirm that V1ct may be explained by the activation of these structures.

Cellular and Molecular Neurobiology
Poster Number 3 / Session 3

Novel axonal transport motion regimes of the proteasome complex analyzed by a newly design tracking system using high spatial and temporal resolution

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While the ubiquitin-proteasome system (UPS) is the major route for cytosolic protein degradation, local accumulations of poly-ubiquitinated proteins in neurodegenerative diseases suggest that protein turn over by the proteasome might be impaired during Alzheimer disease (AD). Local clearance by the UPS depends on the correct delivery and positioning of the proteasome complex. Our previous results showed UPS transport throughout axons; however, proteasome distribution was not fully understood. We performed live imaging experiments of fluorescent proteasomes in primary hippocampal neurons. High temporal resolution movies (50 frames per second) were analyzed with a high spatial resolution tracking system allowing the subpixel identification of particle position. Through a set of computer scripts we tracked individual proteasome particles and based on the mean square displacement we classified them in three motion categories: actively transported, diffusive and confined motion. We revealed from active proteasomes a distribution of segmental velocities according to molecular motor-dependent transport. Proteasome diffusion coefficient was obtained and was consistent with proteasome size. Finally a cage of confinement was obtained for restricted movement. This new approach allowed the characterization of at least three proteasome motion regimes that support proteasome distribution in axons and might provide clues about the defects associated with local protein accumulation in AD.

Cellular and Molecular Neurobiology
Poster Number 4 / Session 1

Demyelination-remyelination in the CNS: possible participation of Notch signaling pathway

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In the CNS the oligodendroglial cell is responsible for normal myelination. Demyelination is a pathological process characterized by myelin loss around axons. Demyelination is followed by remyelination, during this process myelin sheets are restored around demyelinated axons resolving the functional deficit.
In this work we examined the Notch signaling pathway involvement in the demyelination-remyelination process in a toxic model of demyelination induced by CPZ ingestion. Twenty-one-day-old Wistar rats were fed with a diet containing 0.6% (w/w) CPZ during 2 weeks. Demyelinated animals were sacrificed 7d before CPZ withdrawal (-7d), the day of CPZ withdrawal (0d), and 7d after (+7d). Control animals were sacrificed at the same time. We characterized Notch signaling in the SVZ and CC throughout NICD level and the non canonical Notch ligand F3/Contactin by WB and IHC analysis. We also evaluated the expression of Notch down stream genes Hes1, Hes5 and MAG in SVZ and CC of control and demyelinated animals by Real Time-PCR.
Results showed Notch pathway activation in response to CPZ induced demyelination in SVZ and CC. IHC analysis showed this activation in NG2+ and Olig2+ cells being the percentage of Olig2+ oligodendroglial cells significantly higher than NG2+ oligodendroglial precursor cells (OPC). These results suggest that Notch signaling is involved in the demyelination/remyelination processes and that F3/contactin could mediate OPC differentiation.

Cellular and Molecular Neurobiology
Poster Number 5 / Session 2

Development of maternal behavior in female mice (C57Bl6) and its relationship to brain oxytocin receptors

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Naïve female mice behavior toward newborns varies from maternal to infanticidal. Oxytocin (OXT) is known to facilitate maternal behavior (MB); and brain OXTR distribution has been associated with intra- and inter-specific differences in MB. We investigated the development of MB in mice and its relationship with changes in OXTR density in the brain. We recorded MB (e.g. retrieving, licking, crouching) in juvenile (n=9, 20-22 days of age) and adult (n=10) naïve female mice exposed to newborn during 15 minutes. We found that 20% and 30% of adults showed full MB (FMB) and partial MB (PMB) respectively, while only 11% of the juveniles displayed PMB. Then, we determined if juveniles that cohabitated with their mother at the delivery of a second litter showed FMB. In contrast to juveniles from single offspring mothers (n=8, none maternal), 18% and 41% of those from overlapping litters (n=9) displayed FMB and PMB respectively ($p<0.01$). This suggests that juvenile mice are inhibited to display MB, and stimuli associated with parturition and early cohabitation with siblings remove this inhibition. Finally, we found that juveniles had higher OXTR density in most brain regions associated with MB (e.g. the cingulated cortex, lateral septum, and habenula) than adults with a few exceptions (e.g. < in the ventromedial hypothalamus). Therefore, OXT independent mechanisms might block the expression of MB in juvenile mice and mask OXT rapid induction of MB.
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Cellular and Molecular Neurobiology
Poster Number 6 / Session 3

Activity-dependent neuronal maturation in the adult hippocampus

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The adult dentate gyrus contains neural stem cells that generate neurons that develop and mature during several weeks. We have recently demonstrated that the rate of neuronal maturation is regulated by electrical activity in the local circuit; more active networks promote faster maturation rates. To investigate whether developing neurons display a critical period for their sensitivity to electrical activity we tested how increased neuronal activity by running during restricted time windows modulate neuronal maturation. Our data shows that developing neurons display a high sensitivity to network activity during the initial stages of maturation corresponding days 3 to 11 of neuronal development. To test the role of intrinsic activity on neuronal maturation we performed retroviral expression of RASSLs (receptor activated solely by synthetic ligands, synthetic hM3D-type receptor) to specifically activate newborn neurons during restricted time windows. Preliminary results indicate that an increase of intrinsic activity during the period of high sensitivity (days 3 to 11) causes an accelerated development. This preliminary data supports the hypothesis that intrinsic electrical signals control the rate of development of adult-born neurons. This mechanism could serve to facilitate the integration of new neurons into highly active dentate networks.

Cellular and Molecular Neurobiology
Poster Number 7 / Session 1

Role of copper and cholesterol association in the neurodegenerative process

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Age is one of the main factors involved in the development of neurological illnesses, in particular Alzheimer, and it is widely held that the rapid aging of the world population is accompanied by a rise in the prevalence and incidence of Alzheimer disease. However, evidence from recent decades indicates that Cu and Cho overload are emerging causative factors in neurodegeneration, a hypothesis that has been partially investigated in experimental models. The link between these two variables and the onset of Alzheimer disease has opened up interesting new possibilities requiring more in-depth analysis. The aim of the present study was therefore to investigate the effect of the association of Cu + Cho (CuCho) as a possible synergistic factor in the development of an Alzheimer-like pathology in Wistar rats. The results demonstrate the establishment of a pro-oxidative and pro-inflammatory environment after CuCho treatment, hallmarked by increased TBARS, protein carbonyls and nitrite plus nitrate levels in plasma and brain zones (cortex and hippocampus) with a consequent increase in the activity of calpains and no significant changes in caspase-3. A simultaneous increase in the plasma AÎ²1-42/AÎ²1-40 ratio was found. Furthermore, a slight but noticeable change in visuo-spatial memory was observed in rats treated with CuCho. We conclude that our model could reflect an initial stage of neurodegeneration in which Cu and Cho interact with one another to exacerbate neurological damage.

Cellular and Molecular Neurobiology
Poster Number 8 / Session 2

Requeriment of cAMP signaling for Schwann Cell differentiation restricts the onset of myelination

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Isolated Schwann cells (SCs) respond to cAMP by adopting a differentiated post-mitotic state that exhibits enhanced expression of myelin-specific proteins and lipids such as MAG and galactocerebroside (O1). Despite the molecular resemblance of this phenotype with the pro-myelinating SC of peripheral nerves, whether cAMP drives the process of myelin sheath formation is unclear. To address this question, we compared how SCs differentiate in response to cAMP while being in isolation and in co-culture with dorsal root ganglion neurons either in the absence or presence of ascorbate, a known inducer of myelination. We found that cAMP potently enhanced myelination by promoting the differentiation of axon-related SCs rather than directly inducing myelin basic protein (MBP) expression, the ensheathment of axons or the formation of a basal lamina. In fact, the attainment of an O1 positive state was the major cAMP-dependent rate limiting step for the onset of myelination. Experiments using transmembrane adenylyl cyclase (AC) agonists, such as forskolin and cholera toxin, together with type-selective AC inhibitors indicated a stepwise requirement for transmembrane (classical) and soluble (novel) AC activities during the initial stages of SC differentiation. Collectively, these studies suggest a temporally restricted role for cAMP signaling for cell cycle exit and differentiation prior to and likely independently of the onset of MBP expression and myelin membrane wrapping.

Cellular and Molecular Neurobiology
Poster Number 9 / Session 3

Altered expression of miRNA biogenesis components XPO5 and AGO2 in hippocampus of perinatal protein malnourished mice

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Early life stresses such as malnutrition during the critical perinatal period, which includes the development of the nervous system, modify cellular differentiation and neurogenesis programs promoting lifetime social and cognitive disturbances. However, the mechanisms linking malnutrition with cognitive and behavioral deficiencies are still unknown. This work aims to study the role of miRNAs as potential regulators involved in mentioned deficiencies caused by perinatal adversities, since they control multiple developmental processes. CF1 mice dams were fed with normal protein (NP) diet or low protein (LP, 40%) diet during pregnancy and/or lactation and the male offspring were analyzed. We observed that maternal protein restriction delayed physical growth and neurodevelopment of the offspring. Righting reflex showed significant differences while grip strength did not, suggesting that a neurological but not muscular deficit is produced. The expression of miRNA biogenesis components in the hippocampus were determined by RT-qPCR. XPO5 expression was reduced in LP mice, and the effect was more pronounced in the progeny of dams fed with LP diet only during lactation. Expression of AGO2, a component of RISC complex, showed an increase in LP mice. Both Microprocessor complex (Drosha/DGCR8) and Dicer did not change significantly their expression among groups.
These results suggest a relation between transport and miRNA activity in the hippocampus and perinatal malnutrition effects.

Cellular and Molecular Neurobiology
Poster Number 10 / Session 1

Gut feeling in Drosophila: orsai and anorexic larvae

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We study CG6115, which we named orsai, an uncharacterised Drosophila melanogaster gene. According to bioinformatics analysis, it has a central domain that belongs to the Complex I LYR family, proteins in this family have been identified as a component of the higher eukaryotic NADH complex, suggesting a role in cellular metabolism.

Once wild type D. melanogaster larvae reach a critical weight they molt from second instar to third instar. And once again, when critical weight is reached at this stage, they leave the food source and start burrowing, searching for a place away from the food, which precedes the wandering phase. Thus, only after they reached a critical weight third instar larvae start pupation.

Larvae with reduced orsai expression by mutation or tissue specific RNAi expression reached late second instar with a severely reduced weight compared to wild type, and display premature burrowing and abnormal wandering-like behavior. These larvae are found dead ≈ 75 hours after egg laying, still as second instars, even when age-matched controls have molted into third instars and are actively eating. Interestingly, orsai downregulation in gut muscles is sufficient to trigger this change in behavior.

Here we show that IHCs performed with orsai antibodies localise it in the larvae's gut, in a pattern similar to myosin, a central protein involved in muscle contraction.

Cellular and Molecular Neurobiology
Poster Number 11 / Session 2

GDNF/GFRα1 regulates cell proliferation and differentiation of cortical progenitors

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Glial cell line-derived neurotrophic factor (GDNF) was initially discovered as a survival factor for midbrain dopaminergic neurons. GDNF signals by binding to the glycosylphosphatidylinositol-anchored receptor GFRα1 in complex with the receptor tyrosine kinase Ret or the neural cell adhesion molecule (NCAM). In addition to midbrain dopaminergic neurons, GFRα1 is expressed by several different classes of neurons in the central and peripheral nervous system, indicating that GDNF has broader actions than initially proposed.

As GDNF and its receptor GFRα1 has been described to be expressed at early developmental stages in the forebrain, we asked whether GDNF signaling trough its GFRα1 receptor is important for embryonic forebrain precursor cell development. Interestingly, reverse transcription analysis of total RNA isolated from forebrain precursors maintained in proliferating conditions shows lower levels of GFRα1 expression than precursors maintained in differentiating conditions showing a clear correlation between GFRα1 expression and neuronal differentiation. Addition of GDNF to proliferating precursors resulted in the inhibition of neuronal precursor proliferation and in a significant increase in neuritic branch complexity and length of the differentiated neurons.

Thus, our results indicate that GDNF/GFRα1 signaling plays an essential role controlling the transition of the neuronal progenitors from a proliferative condition towards neuronal differentiation

Cellular and Molecular Neurobiology
Poster Number 12 / Session 3

Purification and quantification of acetylated tubulin

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Tubulin can be acetylated/deacetylated on Lys40 of the α-subunit. Studies on the role of the post-translational acetylation/deacetylation of tubulin using biochemical techniques require tubulin preparations enriched in AcTubulin (acetylated tubulin) and, for comparison, preparations lacking AcTubulin. Assembly–disassembly cycling of microtubules results in tubulin preparations that contain scarce or no AcTubulin. In the present study, we demonstrated that this result is due to the activity of HDAC6 present in the extracts. By inhibiting this HDAC6 activity with Trichostatin A (TSA) during the purification by assembly/disassembly, we obtained a 3 x cycled tubulin preparation that contains about 64% of Ac-tubulin with respect to total. This preparation was shown to have the same protein composition, same tyrosination state and same kinetics of assembly and disasembly as compared with a preparation obtained in the absence of TSA. We also developed a method to estimate the percentage of AcTubulin relative to total tubulin. The method is based on acetylation of a tubulin sample with acetic anhydride, Western blotting stained by anti-AcTubulin antibody, and comparison of the optical density of the AcTubulin band with that of a corresponding sample that was not chemically acetylated.

Cellular and Molecular Neurobiology
Poster Number 13 / Session 1

Differecences in lipid profile on distinct pluripotent cell population

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We have previously demonstrated the ability of bone marrow mononuclear cells (BMMC) to foster remyelination in the injured sciatic nerve, and we are currently conducting experiments to evaluate the same ability in bone marrow stromal cells (BMSC). Withthe appropriate stimuli, both BMMC and BMSC can differentiate into Schwann-like cells (SLC). For these reasons, the aim of the present work was to evaluate whether BMMC and BMSC change their protein expression and lipid composition once they differentiate into SLC.BMMC were isolated from tibia and femur bones of adult Wistarrats.BMSC were obtained through BMMC culture. SLC were obtained from BMSC differentiation. Schwann cells (SC)isolated from adult rat sciatic nerve were used as control. Protein expression was evaluated by Western blot and flow cytometry.Lipidcompositionwasdetermined by thin layer chromatography and later quantification. Results indicate that BMMC and BMSC express pluripotent cells markers (CD34 and CD90) but not SC markers (S100β and MBP).SLC increase the expression of S100β and decrease the expression of CD34 and CD90. When lipid composition was analyzed we found that BMSC have ten times more phospholipid (PL) and cholesterol (Cho) contents than BMMC. In contrast, triacylglycerol content in BMSC decreased by 40 % when compared to BMMC. The increase in PL and Cho contents in BMSC suggeststhe expansion of cellular membranes, which indicates morphological and, probably, physiological changes in BMSC.

Cellular and Molecular Neurobiology
Poster Number 14 / Session 2

Sex differences in Ngn3 expression in primary hypothalamic neurons is determined by sex chromosomes

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Brain phenotype is determined by the hormonal profile generated by the gonads during the critical period of development (E18-PN10). Over the years it has been accumulated evidence showing the existence of sex differences before this critical period. Previous works have demonstrated that male hypothalamic neurons, which show a retarded neuritic differentiation compared to female neurons, showed also decreased mRNA levels of the neuritogenic factor Ngn3. In order to study if cell autonomous actions of sex chromosomes are involved in the generation of sex differences in the brain we evaluated Ngn3 mRNA in neuronal cultures of transgenic mice which combine a deletion of the Sry gene from the Y chromosome with its reinsertion into an autosome. This model comprises XX and XY gonadal males (XXM and XYM) and XX and XY gonadal females (XXF and XYF). Neuronal hypothalamic cultures of E14 embryos were performed segregated by sex and genotype. After 72h in vitro RNA were extracted and cDNA obtained by reverse transcription. The mRNA transcript levels of Ngn3 were measured by qRT-PCR. Neurons carrying XY chromosomes (XYM and XYF) showed lower expression levels of Ngn3 than those carrying XX (XXM and XXF; $p<0.001$), irrespectively of the gonadal type. Our findings indicate that the expression of the autosomal Ngn3 gene must be downstream the expression of X or Y genes that results from the inherent sex difference in the number (two copies of X) and/or type (presence of Y) of sex chromosome.

Cellular and Molecular Neurobiology
Poster Number 15 / Session 3

Neurotrophins induce migration of reactive astrocytes

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Astrocytes respond to all forms of CNS insults through a process referred to as reactive astrogliosis. Reactive astrocytes are characterized by an increase in proliferation, size, migration to the injured zone and release of a plethora of chemical mediators that includes neurotrophins, such as NGF and BDNF. We have previously demonstrated that a brain injury induces the expression of the neurotrophin receptor p75 on hippocampal astrocytes and mediates the anti-proliferative effect of NGF.

The goal of this study was to investigate whether neurotrophins and their receptors influence the migration of reactive astrocytes from different brain areas. We used an in vitro scratch-wound assay made on confluent cultures of cortical, hippocampal and striatal astrocytes obtained from neonatal rats. We observed that a scratch lesion increased levels of p75 NTR, but not TrkB, in astrocytes from the three brain areas. When scratched astrocytes were treated with NGF or BDNF we found that striatal astrocytes responded to both neurotrophins by increasing the migration toward the injured area. This effect was blocked by an antibody against p75NTR indicating that this receptor mediates the effect of both neurotrophins on migration. Astrocytes from hippocampus or cortex also increased the migration in response to NGF but not to BDNF. These results are consistent with the idea that neurotrophin may serve to modulate different aspects of gliosis after injury.

Cellular and Molecular Neurobiology
Poster Number 16 / Session 1

Neurons specific requirements of KIF5B motor protein in mice showed by conditional deletions in dopaminergic neurons or throughout the brain

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Neurons have a highly polarized structure composed by a cell body, dendrites and a large axon. Several cargos such as synaptic vesicles and mitochondria must have a proper distribution along the cell. A coordinated axonal transport system, consisting of molecular motors which carry cargos along the microtubules, is fundamental for neuronal viability. Mice lacking the anterograde molecular motor subunit Kif5b are embryonic lethal, however, its relevance in the nervous system remains unclear. To determine whether Kif5b molecular motor is relevant for neurons of the nigrostriatal system we deleted Kif5b in dopamine neurons using conditional transgenic mice lines through Cre-LoxP technique. Open field assays were performed to determine spontaneous locomotion and the locomotor changes induced by amphetamine-increased dopamine release. Rotarod were used to study complex movement capacity and immunohistochemistry performed to analyze neurodegeneration of dopaminergic cells. Surprisingly, our results revealed that dopamine neurons devoid of Kif5b motor protein showed normal function in the substantia nigra. To unravel whether this phenomena is due to a specific ability of dopaminergic neurons, we deleted Kif5b protein throughout the brain. Abnormal neuronal pathology and locomotor behavior will be compared in non dopaminergic neurons and dopaminergic neurons. Our results will shed lights on the neuronal selective dependency of Kif5b function in the brain.

Cellular and Molecular Neurobiology
Poster Number 17 / Session 2

A preconditioning stimulus induces neuroprotection in a in vitro model of Status Epilepticus (SE)

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Previous studies from our laboratory have shown that 3 h neuronal hyperactivation in a co-culture of hippocampal neurons and astrocytes, induces an increase in neuronal cell death.
It is possible that molecular modifications given by a preconditioning (pre cond) prior to SE can result in increased neuronal survival. We evaluated whether a pre cond modifies neuronal death levels, levels of TrkB with other signaling molecules. We observed that a preconditioning induces neuroprotection only if performed 24 h before the beginning of SE. It was determined that a pattern of TrkB receptor activation was different depending on whether there was or not a preconditioning. By inmunocitochemestry, we determined that only the 24h pre cond maintain the TrkB levels while in the other conditions, such as pre 5 hr or SE without pre cond, the receptor protein levels decreases. TrkB receptor blockade by K252a inhibits the neuroprotective effect of 24 h preconditioning. It was observed that related signaling molecules such as neuronal survival Erk is differentially regulated depending on whether the culture was stimulated with 24 h pre, pre 5 h or without a pre cond. Further experiments will be conducted to establish the role of astrocytes in the development of neuronal death.

Cellular and Molecular Neurobiology
Poster Number 18/ Session 3

An alkaloid extract obtained from Huperzia saururus induces neuroprotection in an in vitro model of neuronal death

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Previous data shows that an (AE), obtained from the Lycopodium ferm Huperzia saururus has functions such as acetylcholinesterase inhibition, and also has an effect on learning and memory. The aim of this study was to determine if the AE has also a neuroprotective property in a in vitro model of neuronal death. We found that 24 hour after being added to hippocampal neuron culture, the AE induced a significative neuroprotection. As a possible mechanism of this effect we determine if the extract induced modifications in the well known survival protein the neurotrophin receptor TrkB. We found that AE induces a remarkable activation (phosporilation state) of TrkB. Also AE induces a significant increase in the survival of hippocampal neurons exposed to an environmental stress that induce cell death. These results together with those obtained by Montrull et al., suggests that AE may be a perfect candidate for use for protection of neuronal cell death in several neurological disorders in which there and neuronal death.

Cellular and Molecular Neurobiology
Poster Number 19 / Session 1

Incorporation of L-Dopa into the C-terminus of α-tubulin in cultured cells and in vivo

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We previously described that L-Dopa can be in vitro incorporated into the C-terminus of α-tubulin by "tubulin tyrosine ligase" (TTL). After its incorporation, Dopa cannot be released by "tubulin carboxypeptidase" (TCP), the other enzyme involved in the tyrosination/detyrosination cycle. Dopa-tubulin, was polymerized into microtubules as well as Tyr-tubulin, and both tubulin types disassembled similarly. To monitor and to measure the amount of Dopa incorporated into tubulin we used a method based the analysis of the tyrosination state (% tyrosinated, % detyrosinated tubulin with respect to total tubulin) of samples before and after Dopa incorporation.

We now report that Dopa incorporation into tubulin was also demonstrated to occur in cultured cells in the absence of "de novo" protein synthesis. Furthermore, once incorporated into tubulin of cultured cells, dopa could not be removed by subsequent incubation even in the presence of added tyrosine suggesting that dopa binds irreversibly to the COOH-terminus of α-tubulin blocking posterior incorporation of tyrosine. Similarly, after intracraneal microinjection of L-Dopa in rats and subsequent brain tubulin purification, we found that L-Dopa was incorporated in the COOH-terminal of tubulin.

Cellular and Molecular Neurobiology
Poster Number 20 / Session 2

Chronic restraint stress increases the density of mushrooms spines in nucleus accumbens core: Relevance for cross sensitization to cocaine

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Behavioral sensitization is an example of experience-dependent plasticity, induced by drug or stress, which has been suggested to involve cellular adaptations in excitatory transmission in the nucleus accumbens (NAc) (Nestler, 2005; Kalivas and O'Brien, 2008, Esparza et al., 2012). Like repeated drug administration, repeated exposure to stressors induced enduring adaptations in the shape and the number of spines in NAc (Robinson & Kolb, 2004; Shen et al., 2009; Christoffel et al. 2011). GABAergic medium spiny neurons are the predominant cells of the NAc and reside in two functionally and anatomically distinct subregions of the NAc: core and shell. Since the stress-induced changes in the neuronal architecture within NAc and their role in the cross-sensitization to cocaine are unknown, the purpose of the present study was to determine the structural changes that occur in NAc after seven daily restraint stress session and cocaine. We observed an increase in the density of mushroom spines in NAc core twenty-one days after chronic restraint stress, either after saline or cocaine challenge. Meanwhile, the total density of dendritic spines in the NAc core was not modified in these animals. This finding in the morphology of dendritic spines in core reminds to that observed following chronic cocaine (Shen et al., 2009), and could be also associated to previous findings showing a key role of core in the stress-induced cross-sensitization to cocaine (Garcia-keller et al., 2013).

Cellular and Molecular Neurobiology
Poster Number 21 / Session 3

Tau RNA reprogramming by trans-splicing

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The microtubule-associated protein Tau is predominantly expressed in neurons where it promotes microtubule polymerization and stabilization. Exclusion or inclusion of exon 10 (E10) by alternative splicing gives rise to Tau isoforms with either three (3R) or four (4R) microtubule-binding repeats. In the normal adult human brain the ratio 4R/3R is about 1. Recent genetic evidence demonstrated that some neurodegenerative diseases characterized by the intracellular aggregation of tau (tauopathies) are associated with aberrant splicing of E10, which alters the normal balance between 4R/3R isoforms.

Our goal is to modulate the inclusion of E10 in tau mRNA using a strategy that creates a chimaeric RNA through a trans-splicing reaction between the endogenous mRNA and an exogenously delivered RNA molecule (the pre-trans-splicing motif: PTM). We have used lentiviral vectors (LVs) to achieve efficient delivery and long-term expression of Tau-PTMs into differentiated neurons. We constructed LVs carrying PTMs that were tested in human neuroblastoma cells, mouse cultured primary neurons and into the mouse brain. Trans-spliced RNA products and efficient isoform conversion from 3R to 4R Tau were detected by RT-PCR. Together, our results provide a proof of concept for the use of LVs to reprogram Tau RNA in vivo and set the grounds to use RNA trans-splicing to achieve phenotypic recovery in models of tauopathy and other disorders linked to aberrant RNA processing.

Cellular and Molecular Neurobiology
Poster Number 22 / Session 1

Understanding orsai's role in neurodegeneration

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Through a behavioral screen we identified a gene involved in neurodegenerative processes that we named orsai (osi). Sequence analysis suggests osi is a component of the mitochondrial respiratory complex I, and as such is likely to play a role in cellular metabolism. Although it is conserved from yeast to humans, no ortholog has been characterized in depth.

To unravel orsai's function we carried out an enhancer/suppressor screen looking for its genetic partners. A collection of small chromosome deletions was combined with RNAi-mediated osi downregulation exclusively in the eye. orsai downregulation per se shows a rough eye phenotype, which could be rescued (¨improved¨) or enhanced (¨made worse¨) in the absence of additional proteins required for its function.

Potential candidate genes contained in the chromosome deletions were analysed using DAVID, a bioinformatic tool, in order to find the overrepresented categories. Genes singled out in such bioinformatic analysis were further verified in a secondary screen in the fly's eye, through co-expression of individual RNAis in the context of osi´s. In this step, we narrowed down to 17 positive hits, mostly related to Acyl CoA binding proteins, response to reactive oxygen species and tissue morphogenesis, highlighting potential processes underlying osi- mediated neurodegeneration.

Cellular and Molecular Neurobiology
Poster Number 23 / Session 2

Dendritic development is controlled by Wnt7b-Frizzled7 pathway involving the activation of CaMKII

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Wnts are glycolipoproteins that interact with receptors such as Frizzled, RYK and ROR2 to elicit intracellular responses. This interaction activates 3 cascades: Wnt/β-catenin, planar cell polarity and calcium pathways. In the nervous system, Wnts regulate axon pathfinding, dendrite morphogenesis and synapses formation. In this study, we try to identify the Wnt7b receptor and the role of CaMKII in dendritic development. We found that Wnt7b interacts with Frizzled-7 (Fz7) and increases dendrite complexity. Moreover, Fz7 requires the expression of Dishevelled (DVL), the first downstream effector of Wnt signaling, since a shDVL blocks the effect of Fz7 on dendrite development. In addition, the effect of Fz7 is blocked in neurons expressing the CRD-Fz7 or a shRNA-Fz7. These evidences suggest that Fz7 may act as a receptor of Wnt7b to regulate dendrite morphogenesis. To go further, we examine Wnt-Fz signaling involved in dendritogenesis. We observe that neurons exposed to Wnt show an increase in the level of pCaMKII, a Wnt effector. This effect is blocked when neurons are treated with shRNA against Fz7. Furthermore, treatment with KN-93, a specific CaMKII inhibitor, abolishes the effects of Wnt7b on dendrite growth. Blocking DVL expression by a shDVL inhibits the Fz effect on CaMKII activity. Taken together, our results suggest that Wnt7b-Fz7-Dvl signaling is critical to regulate dendritic development through the activation of CaMKII.

Cellular and Molecular Neurobiology
Poster Number 24 / Session 3

Cdk5/p25 Complex Modulates Morphological Plasticity of Dendritic Spines Induced by Amphetamine.

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It is known psychostimulant drugs alter synaptic transmission in reward centers of the brain, and that synaptic plasticity mechanisms in those regions are targets of drugs of abuse. The cellular and molecular processes underlying drug addiction are considered as maladaptive responses that hijack physiological mechanisms of synaptic plasticity. Several studies suggested cdk5 plays an important role in drug addiction. Our previous results demonstrate that 48hr exposure to Amphetamine 50uM (Amph) increased dendritic spine density in hippocampal slice cultures. Pharmacological inhibition of Cdk5 as well as, inhibition by expression of either a dominant negative mutant or siCdk5 during Amph exposure, prevented the increase on dendritic spine density. In this study we tested the participation of cdk5 activators p35 and p25 (proteolitic product of p35) in Amph-induced spine formation. Hippocampal slices maintained in organotypic tissue culture were biolistically-cotransfected with cDNAs coding for eYFP and either p35 or p25, and exposed to Amph for 48h. Quantitative analyses of dendritic spine density and morphology were carried in CA1 hippocampal pyramidal neurons. Our results showed that while over-expression of p25 accompanied Amph-induced spine formation, p35 prevented this effect. These results suggest that Amph-induced spine formation require intact cdk5 activity and this effect is mediated through cdk5/p25 complex.

Cellular and Molecular Neurobiology
Poster Number 25 / Session 1

Regeneration of the Olfactory Epithelium. Role of Wnt and Sox2 in the differentiation of the olfactory receptors neurons

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The olfactory epithelium (OE) has been known for its capability of actively generating olfactory receptor neurons throughout adulthood, and rapid neuronal regeneration after extensive damage to the tissue, due to the presence of neural stem cells (NSC) in the basal layer of the OE. Wnt promotes cell proliferation and regulates neurogenesis in multiple tissues. In the other hand, during neurogenesis, Sox2 antagonizes proneural genes in order to maintain progenitors. Therefore, in the last years a directional Wnt-Sox2-proneural pathway has been investigated in order to describe the regulation of the transition from proliferation to differentiation of NSC .In the present study, we analyzed the Sox2 expression in the olfactory basal cells and the activation of Wnt signaling pathways in normal and regenerating OE. We found that sox2 expression is significantly increased during extensive regeneration and would be regulated by Wnt. Immunohistochemistry and qRT-PCR showed that after Wnt inhibition, sox2 expression is significantly decreased during OE regeneration. Analysis of Wnt/B-catenin signaling pathway showed that B-catenin is not trans-located in to the nucleus in the Sox2+ cells. Moreover, analysis of Wnt/JNK pathway activation through the immunodetection of pJnk showed that neither this signaling would be activated by Wnt in the sox2+ basal cells. These results suggest that Wnt is regulating Sox2 expression in OE basal cells although through activation of another Wnt signaling pathway were B-catenin and pJNK are not involved.

Cellular and Molecular Neurobiology
Poster Number 26 / Session 2

Nitric oxide modulation of tonic and phasic responses mediated by GABA-A receptors in CA1 hippocampal pyramidal neurons

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Nitric Oxide (NO) is a gas messenger that can modulate the activity of neurotransmitter receptors. NO is produced by the nitric oxide synthase (NOS) in hippocampal pyramidal neurons at the postsynaptic active zones of both GABAergic and glutamatergic synapses (1). NO was shown to modulate GABaergic synaptic transmission during early development (1) and to increase frequency of spontaneous IPSC in cultured hippocampal cells (2).

In the present study, we examined if endogenously produced, or exogenously applied, NO can modulate tonic (bicuculline-sensitive holding currents) and phasic responses (puff-evoked) mediated by GABA-A receptors in CA1 cells of acute hippocampal slices.

L-NAME, a NOS inhibitor which blocks endogenous NO synthesis, produced a significant potentiation of both tonic and phasic current responses evoked by GABA. These results indicate that endogenous NO levels can modulate the activity of GABA-A receptors in the mouse hippocampus.

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2. S. Zanelli, M. Naylor, J. Kapur, Nitric oxide alters GABAergic synaptic transmission in cultured hippocampal neurons, Brain Res 1297, 23â€“31 (2009).

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Cellular and Molecular Neurobiology
Poster Number 27 / Session 3

Study of SNARE proteins involved in regulated exocytosis of plasmalemmal precursor vesicles (PPVs)

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Two different types of regulated exocytosis are known in neurons: well-studied secretory exocytosis (for release of synaptic vesicles) and non-secretory exocytosis (for enlargement of the plasma membrane). The last one is essential for neurite outgrowth and is sustained by the exocytosis of specific vesicles, named plasmalemmal precursor vesicles (PPVs). However, targeting mechanisms for PPVs to developing axon are barely understood. Previous results of our lab indicate that TC10 and exo70 (two components of exocyst complex) are necessary for tethering of PPVs and addition of new membrane, allowing axon elongation stimulated by IGF-1. But the SNARE proteins involved in docking and fusion of PPVs remains, so far, unidentified. The present study attempts to elucidate the SNARE proteins implicated in these steps and VAMP4, SNAP23 and Syntaxin6 were spotted as candidates. Data obtained showed that these SNAREs acquire polarized distribution in early stages of axonal development and, besides, are required for preferential insertion of IGF-1 receptor in plasma membrane of developing axon. Others SNAREs involved in axonal elongation like VAMP7, SNAP25 and Syntaxin1 seems are not essential in regulation of initial axonal outgrowth and, therefore, not necessary for the establishment of neuronal polarity.

Cellular and Molecular Neurobiology
Poster Number 28 / Session 1

Guillain Barré Syndrome-associated anti-glycan antibodies alter growth cone cytoskeleton from growing DRGs neurons

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Axon regeneration is a response of injured nerve cells critical for the restoration of structure and function after PNS or CNS injuries; this response is key to recover from the acute immune neuropathy called Guillain Barré Syndrome (GBS). Clinical studies associate the presence of anti-ganglioside antibodies (anti-Gg abs) with poor recovery in GBS. Passive transfer of mAb (GD1a/GT1b, clone 1B7) or patient-derived anti-Gg in an animal model halts axon regeneration. We developed an in vitro model of axon regeneration using organotypic co-cultures of dorsal root ganglion (DRG) explants with peripheral nerve. 1B7-treated explants show a ganglioside-dependent inhibition of axon regeneration associated with the presence of dysthrophic growth cones. Also, 1B7-treated dissociated DRG neurons cultures (DRGn) display reorganization of components of the growth cone cytoskeleton. Later DRGn were nucleofected with LifeAct-mCherry and tubulin-GFP and subject to time-lapse microscopy. 1B7 treatment induced growth cone collapse associated with activation of the small GTPase RhoA (measured by using a FRET-based biosensor based). Treatment with RhoA-associated kinase inhibitor prevented tubulin disruption and promoted neurite extension. Preliminary results suggest 1B7-induced microtubule disassembly is reached by phosphorylation of Collapsin-response-mediator protein-2 at T555. Overall, this data provide knowledge about the molecular mechanisms determining impaired nerve repair in GBS

Cellular and Molecular Neurobiology
Poster Number 29 / Session 2

Novel biological functions induced by the transmembrane protein Lrig1 in developing hippocampal neurons

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Recent studies show compelling evidence of transmembrane proteins containing extracellular leucine rich repeats (LRR) domains involved in neuronal connectivity, functioning as regulators of process like axon guidance, synapse formation and plasticity. Transmembrane LRR proteins are highly enriched in the nervous system, and their LRR domain frequently serves as protein-protein interaction site, suggesting a participation in the control of receptor signaling pathways. While the specific roles of certain LRR proteins have recently been addressed, others such as Lrig1, remains to be determined.

In the present work, we explore possible functions of Lrig1 in the nervous system. The prominent and tightly regulated expression of Lrig1 in pyramidal and granule hippocampal neurons prompted us to examine the biological contribution of this LRR protein during neuronal development. The role of Lrig1 was analyzed through RT-PCR, immunofluorescence and gain/loss of function assays, in primary hippocampal neuron cultures.

Cellular and Molecular Neurobiology
Poster Number 30 / Session 3

Origin and characterization of newborn cells in the olfactory bulb of juvenile Gymnotus omarorum

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Mammalian telencephalic subventricular proliferation zone (PZ) and zebrafish ventral telencephalic PZ were proposed to be analogs with respect to their role in postnatal generation of olfactory bulb (OB) neurons. To test the generality of this phenomenon, we analyzed the spatiotemporal distribution of OB and telencephalic PZ, and the neuronal fate of their progeny in juvenile G. omarorum. We labeled S-phase cells by administration of the thymidine analog 5-chloro-deoxyuridine (CldU). After a survival of 1, 7, 30 and 90 days, brain sections were processed by double immunohistochemistry to label CldU and neuronal markers doublecortin (DCX), HuC/D and beta III tubulin (bIII). 3D reconstructions of the OB were created in order to visualize the location of CldU+ nuclei and quantify them.

At 1 day survival, CldU+ cells were scarce, restricted to the surface of the OB, not constituting a typical PZ, but a clear PZ was present at the lining of the rostral telencephalic ventricle. CldU+ cells in the OB increased as a function of post-CldU survival. At longer survivals (7-90 days), CldU+ cells shifted medial-laterally, passing through the granular cell layer and reaching the internal cell layer. DCX and HuC/D showed a predominantly central and peripheral distribution, respectively, while bIII was evenly distributed in the OB.

These data are consistent with a process of tangential migration from the telencephalic PZ into the OB, followed by radial migration within the OB of G. omarorum.

Cellular and Molecular Neurobiology
Poster Number 31 / Session 1

Are bone marrow stromal cells better candidates than bone marrow mononuclear cells to foster remyelination in the peripheral nervous system?

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We have previously demonstrated the migration of bone marrow mononuclear cells (BMMCs) to the injured nerve both in an irreversible and areversible model of Wallerian degeneration (Setton et al., 2007; Usach et al., 2011). In the reversible model, once the cells arrive at the ipsilateral nerve, BMMCs colocalize with Schwann cell (S100β and MBP) and nerve fiber markers (PGP 9.5).Also, BMMCs are capable of acceleratingnerve degeneration to foster the regeneration process. BMMCs include a subpopulation of bone marrow stromal cells (BMSCs),which exhibit stem cell characteristics. In this context, the aim of this work was to comparethe participation of these cell groups in thesciatic nerve remyelination.
BMSCs were obtained from adult Wistar rat tibia and femurand maintained in culture until reaching confluence at passage 2. The cells were then transplanted to adult Wistar rats submitted to sciatic nerve crush.
BMSCs seemed to be more efficiently recruited than BMMCs, since more cells were found in the ipsilateral nerve even when a smaller number of cellswas transplanted. Five days after sciatic nerve crush, BMSCs also colocalized with Schwann cell and nerve fiber markers. BMSCs seemed to reduce the number of MBP clusters at 7 and 10 days post injury, suggesting an improvement in the regeneration process. However, more experiments will benecessary to confirmthe advantages of BMSC in the treatment of sciatic nerve injuries.

Cellular and Molecular Neurobiology
Poster Number 32 / Session 2

Cell lineages of the avian auditory nuclei

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The auditory systems of birds and mammals have undergone separate evolution since these lineages shared their last common ancestor 320 million years ago. While the common origin of the auditory end organ is well established, to date there is no consensus as to whether the first order auditory nuclei of birds and mammals are evolutionarily related. Electrophysiological recordings, together with morphological descriptions, have identified the neuronal types present in the first order Ventral and Dorsal Cochlear Nuclei of mammals and Nucleus Angularis and Magnocellularis of birds. Numerous similarities suggest that many of these cell types could share an origin in the ancestral amniote first order auditory nucleus. We propose to evaluate this plausible commonality in evolutionary origin by analysing the developmental genetic lineages that give rise to the different neuronal types of the avian nuclei and comparing them to the lineages of the mammalian nuclei. Here, we present preliminary data in which we show that hindbrain rhombic lip derived Atoh1+ neuronal precursors gave rise to neurons in both avian first order auditory nuclei. Further evaluation of genetic markers will allow us to assess whether the neurons identified are related to the atonal derived neuronal types of the cochlear nuclei of mammals and will ultimately establish the evolutionary origins of the amniote first order auditory nuclei.

Cellular and Molecular Neurobiology
Poster Number 33 / Session 3

GHSR1a-constitutive activity inhibits presynaptic voltage gated calcium channels in cultured hypothalamic neurons

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Within the hypothalamus, several peripheral signals have been shown to modulate neuronal activity, including the orexigenic hormone ghrelin. Ghrelin effects are mediated by Growth Hormone Secretagogue Receptor Type 1a (GHSR1a), the highest constitutively activated G-protein coupled receptors known. We have already demonstrated that GHSR1a-constitutive activity tonically inhibits presynaptic voltage gated calcium channels (VGCC), CaV2.1 and CaV2.2, in a heterologous system. Here, we aimed to determine if native levels of GHSR1a are enough to control basal CaV2.1 and CaV2.2 currents in hypothalamic neurons. We performed whole-cell patch-clamp recordings in embryonic hypothalamic neuronal cultures from GHSR-eGFP reporter mice. We found that eGFP(+) neurons (expressing GHSR) have 50 % less of total native VGCC current than eGFP(-) neurons (no expressing GHSR), whereas NaV currents were not different between groups. Also, the application of exogenous ghrelin inhibits 25 % of VGCC current only in GHSR-expressing neurons. Interestingly, we observed a specific reduction of ω-Agatoxin IVA and ω-Conotoxin GVIA (selective CaV2.1 and CaV2.2 blockers, respectively) sensitive CaV currents in GHSR-expressing neurons, while conotoxin/agatoxin insensitive CaV current remain unchanged. Our results demonstrated that GHSR1a constitutive and ghrelin-evoked activity specifically inhibit presynaptic VGCC in hypothalamic neurons.

Cellular and Molecular Neurobiology
Poster Number 34 / Session 1

Role of TDP-43 in post-transcriptional regulation: implications for neurodegeneration and plasticity processes

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TDP-43 protein has been identified as the main proteic component of the intracellular ubiquitinated inclusions in most cases of Amyotrophic Lateral Sclerosis (ALS) and frontotemporal dementia (FTD), two neurodegenerative processes that are encompassed by the term "TDP-43 proteinopathies". We are studying in vivo the intrinsic properties and physiological role of TDP-43 to define its involvement in neurodegenerative disease. Consequently, we propose to study in vivo TDP-43/mRNA and TDP-43/protein interactions in brain tissue from wild-type mice, with special emphasis on those genes involved in neuronal plasticity and survival. To do this, we are applying different techniques including single and double immunofluorescence, co-immunoprecipitation, immunoblotting, RT-PCR and subcellular fractionation by gradient centrifugation. To investigate the physiological role of TDP-43 and the contribution of TDP-43 in maintaining transcript and protein levels, we are using an antisense oligonucleotide (ASO) approach to stereotaxically infuse TDP-43 or control ASOs for region-specific knock-down of the protein. These studies will provide relevant information to understand the physiological functions of TDP-43 and the molecular mechanisms involved in the pathogenesis of TDP-43 proteinopathies and related neurodegenerative diseases, which in turn may provide the basis for new therapeutic approaches.

Cellular and Molecular Neurobiology
Poster Number 35 / Session 2

Ghrelin receptor (GHSR1a) constitutive and ghrelin-evoked activities inhibit calcium channels through different signalling pathways

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GHSR1a is a G-protein coupled receptor (GPCR) highly expressed at the hypothalamus and by contrast to the most GPCRs, it exerts a high constitutive activity. GHSR1a activity enhances neuronal excitability by acting on several postsynaptic structures. This receptor is also present at axonal terminals, but its physiological impact and the molecular mechanisms involved in its presynaptic actions have not been addressed yet. Here, we postulate that GHSR1a regulates presynaptic voltage-gated calcium channels (VGCC), the structure that controls neurotransmitter release. We performed patch clamp recordings and imaging analysis in HEK293t cells transiently transfected with GHSR1a or GHSR1a-A204E (mutant lacking constitutive activity), and CaV2.1 or CaV2.2 and its auxiliary subunits. We found that GHSR1a constitutive activity inhibits CaV2.1 and CaV2.2 currents. We also observed that GHSR1a constitutive activity acts through a GÎ±i/o voltage independent mechanism. On the other hand, we observed that GHSR1a ghrelin-evoked activity inhibits CaV2.1 and CaV2.2 by a different pathway that depends on GÎ±q, GÎ²Î³, and it is CaVÎ² subtype-dependent. Moreover, imaging analysis showed that GHSR1a constitutive activity impaired VGCC density at the plasma membrane, likely by reducing its traffic. Our results demonstrated that constitutive and ghrelin-evoked GHSR1a activities inhibit presynaptic calcium channels using different pathways.

Cellular and Molecular Neurobiology
Poster Number 36 / Session 3

Ephexin is downstream EPHA3-Regulated-EPHA4 forward signaling in the retinotectal mapping formation

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Eph/ephrins are expressed in complementary gradients in the retina and the tectum guiding retinotectal projections. Previously we showed that tectal EphA3 stimulates axon growth of nasal retinal ganglion cells (RGC) toward the caudal tectum preventing them from branching in the rostral tectum. The aim of this work was to study the molecular pathway which mediates the EphA3 action. We postulated that activation of axonal EphA4 rises the level of ephexin phosphorylation and decreases axon growth; tectal EphA3 increases axon growth by reducing axonal EphA4 and ephexin phosphorylation by competing with EphA4 for axonal ephrin-As.

We used cultures of retinal explants from chicken embryos treated with EphA3-Fc, Fc, or KYL (EphA4 inhibitor). We analyzed axon length and realized immunocytochemistry and Western blot. We showed that: a) Axonal response to EphA3 is associated to ephrin-A expression, EphA4 phosphorylation and the pattern of phosphorylated ephexin. b) The EphA3 decreases the EphA4 and phexin phosphorylation. c) Inhibition of EphA4 signaling recapitulates the effects of EphA3 on RGC axon growth and branching. The results support the idea of a novel molecular mechanism whereby tectal EphA3 increases axon growth toward the caudal tectum and inhibits axon branching in the rostral tectum by decreasing ephrin-A-mediated-EphA4 forward signaling. Furthermore, it is suggested that regulation of ephexin phosphorylation is downstream of EphA4 activation. Supported by CONICET-UBA.

Cellular and Molecular Neurobiology

Poster Number 37 / Session 1

Evidence for the involvement of SARA in neuronal migration and orientation through L1-CAM

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SARA (Smad anchor for receptor activation) localizes to early endosomes (EE) where it regulates their morphology and function. Its role in neuron and brain development has not yet been uncovered. *In situ* electroporation of mouse embryonic brains at ambryonic day E13.5 suggests a pivotal role for SARA in neuronal development. Three days after electroporation, control GFP expressing neurons migrated through the cortical plate showing proper pia-directed orientation. By contrast, neurons expressing sh-SARA-GFP failed to migrate as expected, acquiring a horizontal orientation. Quantitative analysis reveals that most of these neurons lack vertical orientation, being tilted with angles ranging from 0 to 45 degrees. We show that SARA silencing leads to increased surface L1-CAM levels at the axonal plasma membrane in stage 2-3 cultured neurons. To assess whether this was also the case in our in vivo experiments, we co-electroporated L1-CAM-GFP with control HcRed and found that this mimics the phenotype observed for shSARA-HcRed, that is neurons displaying: delayed migration and horizontal orientation around SVZ/IZ. Most interestingly, L1-CAM knock down in SARA-silenced neurons rescues the migration and orientation defects. Altogether, our results show that L1-CAM regulation by SARA controls neuronal positioning and orientation during brain development. It is likely that some of these functions could be related with a role of SARA as a regulator of endosomal trafficking. Supported by ANPCyT and CONICET to AC and CC

Cellular and Molecular Neurobiology
Poster Number 38 / Session 2

Multiple roles of a single compound in the cognitive modulation of the escape response in an insect

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Innate responses in animals can be modulated by experience. Disturbed adults of the triatomine bug Triatoma infestans release an alarm pheromone that elicits an escape response in conspecific larvae. The main component of this pheromone, the isobutyric acid (IsoAc), has already shown to generate an escape response in this species. We present here evidences of the cognitive capacities of T. infestans larvae in an escape context under different conditioning paradigms, including IsoAc in different roles.

In a non-associative context we found that a simple chemical pre-exposure event to IsoAc is enough for modulating the escape response of larvae to the same compound. Under a Pavlovian classical paradigm, an association between IsoAc and a second aversive stimulus can be created, increasing the magnitude of the escape response. Under a Skinnerian operant context, the occurrence of a self-action can be prevented by punishing it with IsoAc.

These results evince that IsoAc can attain multiple and different cognitive roles in the modulation of the escape response of triatomines and show how cognitive processes can modulate a key behavior for surviving, as it is the escaping response in presence of a potential danger in insects.

Cellular and Molecular Neurobiology
Poster Number 39 / Session 3

An alkaloid extract obtained from Huperzia saururus induces neuroprotection after Status Epilepticus

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Epilepsy is a common neurological disorder that affects 1-2% of people in the world. In animals, prolonged seizures induced by pilocarpine pre-treated with lithium leads to a condition called Status Epilepticus (SE), and result in both apoptotic and necrotic cell death. Huperzia saururus is commonly known as “cola de quirquincho” in Argentinean folk medicine. It has been demonstrated that a purified alkaloid extract (AE) obtained from this specie has an extended ethnomedical use mainly as aphrodisiac, but moreover, it is believed to improve memory retention and hippocampal synaptic plasticity. Given these functions we asked whether the AE was able to protect neurons after SE. To test this we administrated unilaterally the AE in the CA1 region of hippocampus immediately after SE. Animals were sacrificed 24h later and the neuronal damage was assessed by FJB. We found that the infusion of the AE immediately after SE induced a remarkable decreased in CA1 hippocampal neuronal death. Interestingly, we also found an important decrease in the number of FJB positive cells in the Entorhinal Cortex as compared with the contralateral. In contrast, no difference was observed in neuronal injury in the hilus of the dentate gyrus. These results suggest that AE has neuroprotective properties and could serve as a good potential use for several neurological disorders in which there are neuronal death and memory impairment.

Cellular and Molecular Neurobiology
Poster Number 40 / Session 1

Lentiviral-based expression system of ghrelin receptor in neurons

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Growth hormone secretagogue receptor type 1a (GHSR1a) activity modulates neuronal circuits that control appetite and energy expenditure, but the molecular mechanisms involved are currently unknown. GHSR1a is a G protein-coupled receptor that shows constitutive activity and ligand-evoked activation. Our research is focused in GHSR1a actions on the communication between neurons, specifically at the presynaptic level. Recently, we found that neuronal calcium channels, structures that control neurotransmitter release, are inhibited by GHSR1a constitutive and ligand evoked activity. Here we aim to develop a system suitable to evaluate the effect of GHSR1a on synaptic activity in mouse embryonic neuronal cultures. In order to measure electrical synaptic activity in vitro we need to express GHSR1a at native levels in a large amount of neurons and to identify the neurons expressing the receptor. Here we present a lentivirus-based expression system of GHSR1a tagged with yellow fluorescent protein (YFP) and an analog system for the GHSR1aA204E mutant that lacks constitutive activity. High neuronal transduction rates plus a weak promoter that ensure expression levels close to the native condition are some of the advantages of lentiviral systems. Furthermore, we used a third generation system to guarantee a high level of biosecurity. Here we present our clone strategy, protocols development and some preliminary data demonstrating the utility of our system.

Cellular and Molecular Neurobiology
Poster Number 41 / Session 2

Regulation of establishment of neuronal polarity by growth factors

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Neuronal polarity acquisition depends on axonal specification, whereby one of the undifferentiated neurites starts to grow rapidly and becomes an axon. The results obtained in our laboratory indicated that insulin-1 like growth factor (IGF-1) and its specific receptor would be essential for the establishment of neuronal polarity in cultured hippocampal cells (Sosa, Dupraz et al. 2006). Recently, however, a paper has been published in which propose that signaling transforming growth factor beta 2 (TGF-β2), specifies axons during brain development (Yi, Barnes et al. 2010). This has generated an interesting debate about the involvement of different growth factors in the regulation of axonal specification. The experiments designed in the herein project tend to re-examine the relationship of IGF-1 receptors and signaling pathways TGF-β2 in axon specification and establishment of polarity. After carrying out primary hippocampal cultures an “exo utero” or “in utero” electroporation in cortex, the axonal development will be examined though it or loss experiments receptor function of IGF-1 and TGF-β2. Therefore, new perspectives to this debate are expected to obtain.

Cellular and Molecular Neurobiology
Poster Number 42 / Session 3

p19INK4d avoids DNA damage-induced neurodegeneration in mice hippocampus and prevents loss of cognitive functions

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Defects in DNA repair have been linked to cognitive decline with age and neurodegenerative diseases, yet the mechanisms that protect neurons from genotoxic stress remain largely unknown. There are strong evidences that p19INK4d (p19), a member of the INK4-cell cycle inhibitor family, plays a crucial role in regulating genomic stability and cell survival in neuron primary cultures from rat hippocampus. In this work, we sought to examine whether the neuroprotective properties of p19 could be recapitulated in an in vivo mouse model. To do this, 0.5 nmol ss-DNA oligonucleotide containing an antisense sequence of p19 was laterally injected by stereotaxis in the dorsal hippocampus to selectively knockdown the p19 expression, after which 25 ng/ml NCS or saline solution was administered in each hippocampus. Brain sections were examined for □H2AX to label DNA damaged cells. □H2AX-positive cells in hippocampus from mice previously injected with p19 antisense (48.9±9.3%) was significantly increased ($p<0.001$) respect hippocampus injected with NCS alone (31.6±6.3%). Hippocampal-damaged mice were subjected to Y-maze spontaneous alternation or two-trial with clues tests, and fear conditioning test in order to evaluate their learning and memory performance. Mice with hippocampal p19-deficience showed an impaired performance in the proposed tasks.
We suggest that p19 confers resistance to DNA-damage mediated neurodegeneration reducing the adverse consequences on hippocampal functions.

Cellular and Molecular Neurobiology
Poster Number 43 / Session 1

KIF5C is essential for polarized insertion of IGF-1r in developing neurons

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In neuronal development occur early events of polarity in morphologically still-unpolarized neurons. As the segregation of active (phosphorylated) IGF-1 receptor in a single neurite. In the other hand, in axogenesis the cytoskeleton undergo to intense rearrangements such as increasing the stability of microtubule (MT) along the shaft of a single neurite. The preference of motor proteins by MT with increased stability or specific posttranslational modifications may mediate direct traffic in the axon. The experiments reported was designed to establish a correlation between these two early events in neuronal development. Application of low doses of the microtubule destabilizing nocodazole or stabilizing drugs taxol, the polarized distribution of active IGF-1r is modified. It was also observed that those neuritic processes in stage 2 of differentiation, with high accumulation of acetylated tubulin are coincident with process that has high levels of active receptor. This experiments suggested that the stable MTs would be an early marker for the polarized insertion of the receptor. We found that cells can't polarize in low concentration of insulin, even in presence of microtubule-stabilizing drugs. So, the stabilization of MTs plays an active role during axonal specification but not sufficient to stimulate neuronal polarity. Finally the kinesin KIF5C would essential for the establishment of neuronal polarity and for the polarized insertion of IGF-1 receptor in stage 2 neurons

Cellular and Molecular Neurobiology
Poster Number 44 / Session 2

Characterization of adult cerebellar proliferation zone in Gymnotus omarorum

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The cerebellum is one of the adult teleost´s brain regions with the highest proliferative activity in which cell proliferation-neurogenesis and regeneration were thoroughly studied, but the cellular composition of its proliferation zones remains to be characterized (Zupanc, 2006). We analyzed the cellular composition and fate of newborn cells at its most rostral division (corpus cerebelli, CCb) of adult pulse-type gymnotid Gymnotus omarorum. We used double thymidine analog labeling technique (Vega & Peterson, 2005) with short (24 hs) and long chases (30 days) between analog administration, and a 4 hs survival after the second analog. Proliferating cells were evidenced by double immunohistoquemistry and quantified by confocal stereology. CCb proliferation zone, located at the medial part of its molecular layer, was mainly composed of four cell types: actively and fast cycling, putative stem and quiescent cells. After 30 days chase, derived cells (migrating neuroblasts) predominated within the granular layer of CCb. Proliferation zone´s and derived cell types were further characterized by double or triple immunohistoquemistry. G. omarorum´s CCb proliferation zone presented a heterogeneous cellular composition consisting of the main cell types already described in amniotes and thus constitutes a good model for comparative studies of adult neurogenesis. Vega, C.J & Peterson, D.A. (2005), Nature Methods 2(3), 167-169. Zupanc, G.K.H. (2006), J. Comp. Physiol. A.192, 649–670.

Cellular and Molecular Neurobiology
Poster Number 45 / Session 3

Myelin-associated glycoprotein modulates apoptosis of motoneurons via NgR-Mediated RhoA Activation

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Myelin-associated glycoprotein (MAG) is a lectin present in the periaxonal layer of myelin that engages several axonal receptors including Nogo-receptors (NgRs). Pharmacological activation of NgRs has a modulatory role on p75NTR-dependent programmed cell death (PCD) of motoneurons (MNs). The small GTPase RhoA regulates apoptosis of MNs during embryonic development via Rho-associated kinase (ROCK). The aim of this study was to analyze a modulatory role of MAG on PCD of MNs via NgRs/RhoA signaling pathway during postnatal development. A time course study showed that early after birth Mag-null mice have a reduction in MNs count. Also Mag-null mice exhibit increased susceptibility in an in vivo model of PCD induced by a sciatic nerve crush. Pre-treatment with a soluble form of MAG (MAG-Fc) prevented MNs apoptosis. Studies using an in vitro model of p75NTR-dependent PCD on spinal cord organotypic cultures and a MN1 cell line confirmed the modulatory role of MAG. Infection of MN1 cells with lentiviral particles carrying shRNA sequences targeting NgRs abolished the protective effect of MAG. Treatment with ROCK inhibitor Y27632 blocked MAG protection against apoptosis in in vitro and in vivo settings. Using a RhoA biosensor and a FRET approach we have obtained evidence about the spatial/temporal analysis of RhoA activity. Overall these findings identify a new protective role of MAG as a modulator of apoptosis of MNs during postnatal development via NgR-mediated RhoA activation

Cellular and Molecular Neurobiology
Poster Number 46 / Session 1

Prenatal antiandrogen treatment resembles prenatal stress consequences on the mesocorticolimbic dopaminergic system development in the male offspring

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We have previously demonstrated that prenatal stress (PS) impaired midbrain dopaminergic (DA) system metabolism especially after puberty, suggesting a particular sensitivity of DA system to variations in gonadal hormones peaks. We further demonstrated that the reproductive axis of male rats exposed to PS was altered. PS was shown to disrupt perinatal testosterone surges and since DA system could be influenced by androgen exposure, the aim of this research was to evaluate the effect of prenatal administration of the antiandrogen flutamide (FLU) (10 mg/kg daily) to pregnant rats from gestational day 14th to 21st on the DA system development. We found that FLU reduced anogenital distance and induced a two-day delay in the completion of testis descend in the offspring. Malformation of penis, cryptorchidisim and atrophied seminal vesicle were also observed. Morphological studies in mesocorticolimbic DA areas revealed that FLU males presented a decrease on the number of MAP2 immunoreactive neurons in comparison with vehicle treated rats (5% ethanol-propylene glycol) suggesting that prenatal FLU reduced the dendritic arborization of mesencephalic structures, impairing normal connectivity between areas. This research demonstrates that the effects of prenatal androgen manipulation resemble PS impairment of the DA system suggesting that one of the possible mechanisms of action of prenatal insults is related to the alteration of the organizational role of androgens on brain development.

Cellular and Molecular Neurobiology
Poster Number 47 / Session 2

The neural network dynamics underlying the Motion After-effect in zebrafish larva

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An illusion is a perceptual misinterpretation of a real external sensory experience that may induce sensory perception in complete absence of any environmental stimulation.
To better understand what are the neural network mechanisms underlying sensory illusions we are using the motion after-effect (MAE), in which exposure to coherent continuous motion for a certain period of time induces motion perception in the opposite direction following the end of the moving stimulus.
Even thought this effect has been intensely study at the behavioral and single-cell physiology levels using different experimental models, the neural network representation at different sensory processing brain regions remains elusive.
For this purpose we are using the zebrafish larva as the experimental model, which allows monitoring the dynamics of large neural networks from large portion of the nervous system in a behaving organism.
After behaviorally validating the existence of a robust motion after-effect visual illusion when presenting to zebrafish larvae coherent continuous moving visual stimuli, we performed similar experiments in intact transgenic larvae expressing a genetically encoded calcium indicator (GCaMP3) under a two-photon scanning microscope.
We have found that neurons, within the larval optic tectum, that stand as a neuronal correlate of the behavioral illusory response implying that this ensemble of neurons may be involved in the perception of the MAE visual illusion.

Cellular and Molecular Neurobiology
Poster Number 48 / Session 3

TGF-beta in cell fate decision of adult neural stem cells from the SVZ

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Adult NSC (aNSC) are able to differentiate into neurons, astrocytes and oligodendrocytes throughout life. Notch and transforming growth factor beta (TGF-beta) signaling pathways play critical roles in the control of cell fate. Previously it was demonstrated that TGF-beta is pro-neurogenic on hippocampal aNSC and it was reported that might interact with Notch pathway in different cellular types. Therefore the objective of our work is to study the effect of this cytokine on the generation of specific cell types from aNSC of the subventricular zone (SVZ) and its interaction with the Notch pathway. The addition of TGF-beta on aNSC cultures obtained from the SVZ of adult rats results in a 17.5% increase of the TujI positive population, whereas there were no changes in Nestin and GFAP positive population. This pro-neurogenic effect was also observed in vivo 21 days after the injection of an adenoviral vector expressing TGF-beta in the SVZ of adult Wistar rats. To study the participation of Notch pathway on this effect we performed real time PCR for Notch activation pathway reporter's gens as Hes1 and Hey1. The presence of TGF-beta produced an increment in the Hes1 expression showing the activation of Notch pathway. Moreover, Hes1 expression increase was blocked by a gamma-secretase inhibitor. These data show that TGF-beta modulates the phenotype fate decision and preliminary results suggest that might also alters Notch pathway activation on these cultures.

Cellular and Molecular Neurobiology
Poster Number 49/ Session 1

Reactive gliosis and abnormal hippocampal neurogenesis in TDP-43-ΔNLS transgenic mice

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Recent studies demonstrated that Tar-DNA Binding Protein 43 (TDP-43) is a major disease protein in a group of neurodegenerative disorders now collectively referred to as TDP-43 proteinopathies. In these conditions, TDP-43 is redistributed from its normal nuclear localization to form cytoplasmic insoluble aggregates. In order to study TDP-43 pathophysiology, we are using novel transgenic mice with cytoplasmic inducible neuronal expression of human TDP-43 (hTDP-43-ΔNLS). We are currently assessing the development of inflammatory processes at different time points after transgene induction (TI) in specific brain areas of these mice. Double immunofluorescence (IF) with CD11b/ human (h) TDP-43 antibodies revealed activated microglia in the dentate gyrus (DG) of the hippocampus as early as 2 weeks after TI. At 4 weeks, there is an increase in microgliosis in DG and cortex, which later decreases throughout the neurodegeneration process. Astrogliosis was measured using double IF for GFAP/hTDP-43. In addition, recent evidence suggests that TDP-43 might transcriptionally regulate cell-cycle genes. We are evaluating adult neurogenesis in transgenic mice 1 month after TI by double IF with BrdU/ hTDP-43 and DCX/hTDP-43 antibodies. We aim to determine the time course of gliosis and reveal how neurodegeneration and neurogenesis are affected by TDP-43 in the context of inflammatory processes, topics that are vital to develop new and more effective therapies for these disorders.

Cellular and Molecular Neurobiology
Poster Number 50 / Session 2

Early neuroglial and cognitive impairment before amyloid deposition in young PDAPP-J20 transgenic mice, model of Alzheimer's disease

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The Alzheimer's disease (AD) is the most common form of dementia and is characterized in late stages by widespread amyloid deposition and neurodegeneration in the hippocampus but less is known about early brain and behavioral alterations. We evaluated neuroglial alterations in PDAPP-J20 mice (Tg), model of AD, at 5 months of age, an early stage when no amyloid plaques are present. The hippocampus of Tg mice showed a significant decrease in the number of neurons in the dentate gyrus and CA1 subfield. Additionally, mature granular neurons exhibited signs of cell atrophy. Neurogenic capability was also affected in Tg mice: the number of newborn DCX+ granule cells was reduced, along with differed maturation. In stratum radiatum under CA1, young Tg mice showed a diminution in the number of astrocytes compared to control group, analyzed by confocal microscopy and 3D reconstruction. Astroglia was morphologically altered presenting a decline in surface/volume ratio, analyzed by confocal microscopy and 3D reconstruction. Glial changes could reflect less support to neurons. These morphostructural alterations were associated with cognitive impairment at this initial stage of AD. The performance in the novel object location recognition test suggested that the spatial memory of Tg mice was affected. In summary, these results focalize in early neuronal, astroglial and cognitive alterations in AD, which can be proposed in the future as potential therapeutic and diagnostic targets.

Cellular and Molecular Neurobiology
Poster Number 51 / Session 3

Parkinson´s in a dish: A model to study Alpha-Synuclein overexpression on mitochondrial function using human neurons

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The main pathological feature of Parkinson's disease consists in a progressive damage of dopaminergic neurons, caused —among many others— by alfa-synuclein (aSyn) gene duplication or point substitutions: A30P, A53T and E46K. Growing evidence links mitochondrial disfunction and oxidative stress with Parkinson's neuronal loss, however, aSyn direct or indirect interactions with mitochondria remains unknown. As Parkinson's disease modeling in animals prove difficult, stem cells research development has opened a promising field to study human diseases in human cells. In the present work we analyse the effects of wt or mutant forms (A30P and A53T) of aSyn overexpression in human embryonic stem cells derived neurons, focusing on mitochondrial homeostasis and dynamics. To validate the differentiation, a complete characterization with neuronal markers was performed by immunofluorescence and qPCR. Also, neuronal identity was confirmed by electrophysiological recordings. Mitochondrial dynamics were analysed in neurons transfected with plv-vector driving the expression of wt or mutant aSyn. Results revealed two significant changes: A53T increases mitochondrial density in the axon while decreases its size, and aSyn wt increases mitochondrial travelled distance. Deletereous effects were also studied, measuring survival rate over time.
In conclusion our results suggest a novel link between aSyn and mitochondrial homeostasis, which opens new avenues of research.

Cellular and Molecular Neurobiology
Poster Number 52 / Session 1

Uses and limitations of BrdU technique for the study of olfactory neurogenesis in amphibians

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The 5-bromo-2'-deoxyuridine (BrdU), is a thymidine analogue that incorporates into the DNA of dividing cells during the S-phase of the cell cycle. This analogue is widely used for the study of mitosis and cell lineage in vitro and in vivo. However, some reports questioned the validity of the use of BrdU in biological systems where this molecule shows cellular toxicity. In the present work we examined the validity of the BrdU incorporation technique for studying cell proliferation and differentiation in the olfactory epithelium (OE) in an amphibian model. Using 10 mM of BrdU, we found an increase in the number of apoptotic cells and an alteration of redox balance within the EO. We also observed a variation in the expression of different cellular markers in both olfactory receptor neurons (ORNs) and supporting cells (SCs). Moreover, the histochemical analysis showed alterations in the secretory vesicles of substentacular cells. The use of lower concentrations of BrdU (0,1 mM and 1 mM), showed that: 1) 0,1 mM was not enough to be detected by immunohistochemistry and 2) 1 mM reduced the adverse effects caused by higher concentrations, however, we observed alterations in the pattern of differentiation of the NRO. We conclude that BrdU can be successfully used as a marker of cell proliferation in the EO, but it is not appropriate for studying cell lineage because it have toxic effects on cells where is incorporated, as well as in neighboring cells.

Cellular and Molecular Neurobiology
Poster Number 53 / Session 2

A search for proteins restoring plasticity in the adult mouse visual cortex

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The scarce recovery of the adult nervous system following injuries or diseases is largely due to the low level in its plastic potential, the ability to re-organize its connections as a function of experience. Recently, some strategies that restore high levels of plasticity in the adult and thus improve the likelihood of recovery of certain functions have been identified. Pioneer studies in the rodent primary visual cortex (VC1) have shown that chronic treatment with the anti-depressant fluoxetine enhances plasticity in the adult and induces recovery of vision in amblyopic animals. However, the mechanisms underlying the restoration of plasticity in the adult are still largely unknown. The present work aims to contribute to the characterization of these mechanisms at molecular level. In particular, we employ a proteomic assay using two-dimensional gel electrophoresis followed by mass spectrometry on samples of VC1 adult C57B6 mice treated with fluoxetine (plasticity restored, 15mg/Kg/day, 4 weeks from P70 to P98) and adult controls (low plasticity, P98). Preliminary results allowed us to identify 22 differentially expressed proteins: 11 upregulated by fluoxetine and 11 downregulated. These proteins are involved in various biological processes, as the control of the cellular redox state, the regulation of neuronal structure, and the cellular metabolism. We plan to confirm the role of some of these proteins in restoring adult cortical plasticity induced by fluoxetine in vivo.

Cellular and Molecular Neurobiology
Poster Number 54 / Session 3

Delayed maturation of granule cells generated in the aging hippocampus is prevented by running

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Neural progenitor cells of the adult dentate gyrus can differentiate and develop into fully functional neurons. Adult neurogenesis is tightly regulated by several physiological conditions. For instance, we have recently demonstrated that the timing of neuronal maturation is regulated by the activity of the surrounding networks. Since aging is one important factor associated to decreased rates of neuronal production, in the present work we investigated whether maturation of adult-born neurons was also affected by age. To approach this question we used retroviral labeling of adult-born neurons to compare granule cells developing in 2-, 5- and 8-month old mice (work in progress). We have analyzed the morphology and expression of neuronal markers at different stages of neuronal development (dpi; days post-infection). Fourteen and 21 dpi neurons in 5-month-old mice displayed immature features when compared to neurons of the same age in 2-month-old mice; however, similar levels of maturity were observed by 28 dpi. Such delayed maturation in the aged hippocampus seems to correlate to reduced levels of network activity (measured by ARC expression in the dentate gyrus). Interestingly, the observed delay was reverted by housing mice with a running wheel. We are currently investigating the mechanisms underlying the age-dependent delay in neuronal maturation.

Cellular and Molecular Neurobiology
Poster Number 55 / Session 1

Excitotoxic lesion by hypoxia-ischemia alters expression and distribution of AP-2 coat proteins and expression of NMDA-R in certain areas of rat brain

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Introduction: AP-2 is a protein adaptor complex involved in the clathrin-mediated endocytosis, that interacts with motifs of the cytoplasmic domain of glutamate receptors, as a step in formation of clathrin coated vesicles. These receptors are known to be important players in the excitotoxic lesions and in neurodegenerative diseases.
Aims: As the NMDA receptors (NMDA-R) are recognized by AP-2, and assuming that membrane-bound AP-2 is an index of endocytic activity, we studied the expression and distribution of AP-2 in areas of rat brain subjected to excitotoxic lesion by hypoxia-ischemia, and attempted to correlate with expression of NMDA-R. Methods: Seven days old rats (Wistar- Kyoto) received hypoxia-ischemia treatment by ligature of the left carotid artery followed by short exposure to 100% N2 .Brain tissues were obtained 72 h after lesion, and α-2 subunit of AP-2 was evaluated by WB in membranes and cytosols from hippocampus (HIP), striatum (ST) and motor cortex (MC). Expression of NMDA-R was also studied in the membranes of the areas under study.
Results: We observed that AP-2 bound to membranes tends to increase in the MC and HIP but not in the ST. In turn, expression of the NMDA-R was also increased in the injured tissues (bilaterally).
Conclusions: These results indicate that certain brain areas undergo modifications in the endocytic machinery due to excitotoxic lesion, altering possibly the distribution of NMDA-R and, consequently, the glutamatergic synapses.

Cellular and Molecular Neurobiology
Poster Number 56 / Session 2

Prostaglandins: their role in bone marrow mononuclear cell migration to the injured nerve

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We have previously described the reorganization of major myelin proteinsMBP and P_0 and axonal protein PGP 9.5 during sciatic nerve demyelination, as well as the migration of bone marrow mononuclear cells (BMMC) exclusively to the injured nerve.Once in the ipsilateral nerve, some BMMC colocalize with Schwann cell and nerve fiber markers. These cells accelerate the degeneration process and, as a consequence, promotethe onset of regeneration.In this context, the aim of the present work was to evaluate the signals that could stimulate the recruitment of BMMC to the demyelinated nerve.To that end, adult rats were submitted to sciatic nerve crush to promote demyelination and confocal microscopy was usedtodeterminewhether the inhibition of prostaglandin (PG) synthesis with indomethacin affects the migration of transplanted BMMC. In the light of results obtained, we also evaluated the expression of ciclooxigenases (Cox), the key enzymes in PG biosynthesis. Our findings show that, as soon as 24 h post injury, BMMC arrived at the edges of the ipsilateral nerve and, after 3 days, they became part of the nerve.The treatment with indomethacin inhibited the migration of BMMC, suggesting that PG aresomehow involved in the recruitment and migration of these cells. In support of these results, Cox-2expression was induced 2 hours after nerve injury and was still upregulated24 hours after nerve injury. Further experiments will be necessary to elucidate other possible biological signals involved in BMMC migration during the degeneration-regeneration process.

Cellular and Molecular Neurobiology
Poster Number 57 / Session 3

GM2-ganglioside accumulation mediates Endoplasmic Reticulum calcium depletion and PERK signalling activation

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The accumulation of misfolded proteins within the endoplasmic reticulum (ER) triggers a cellular process known as the Unfolded Protein Response (UPR), in which the cell attempts to restore ER homeostasis. If ER damage is persistent or excessive, an apoptotic response is initiated. It is well accepted that ER calcium depletion induces ER stress. PERK is an early ER stress sensor that attenuates protein synthesis. We demonstrated in Xenopus oocytes that Calcineurin (CN) associates with PERK, enhancing inhibition of protein translation and cell viability. But PERK signaling, including pro-apoptotic transcription factor CHOP, persists activated under prolonged stress. Chronic UPR is proposed to contribute to the pathology of many neurodegenerative diseases. GM2-gangliosidosis are characterized by a progressive neurodegeneration. However, the mechanisms that determine how GM2 accumulation triggers neuronal cell death remain unknown. Here, we report, by thin layer chromatography and immunocytochemistry approaches, that N2a neurons loaded with exogenous ganglioside accumulate GM2 at ER membranes. The abnormal GM2 build-up induces PERK activation, and provokes up-regulation of either CN or CHOP, at different time points. This stress also decreases the ER calcium content in Fura2-loaded cells. Moreover, calcium depletion, as well as Chop level increase induced by GM2 accumulation, was enhanced by MBCD, a pharmacological agent that augment ganglioside delivery to the ER

Cellular and Molecular Neurobiology
Poster Number 58 / Session 1

Prevention of glutamate overload toxicity by Oligodendrocytes: Effect of antibody-mediated activation of Myelin-Associated Glycoprotein

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Myelin-Associated Glycoprotein (MAG) is a glycoprotein selectively expressed at the periaxonal layer of myelin that mediates oligodendrocytes (OLs)-neuron interaction. Cross-linking of MAG at the cell membrane of OL (to mimic axonal ligands) by using an anti-MAG mAb (clone 513) can activate signalling pathways, but their physiological role remains unknown. Our data shows that 513-induced MAG activation can protect OL and nearby cells against excitotoxic insults in murine stroke models induced by NMDA and L-glutamate intra-striatal injection as well as L-glutamate treatment in cerebellar organotypic cultures. Increased extracellular glutamate depletes cells of cystine by blocking the gradient-driven glutamate/cystine antiporter system Xc- hence leading to diminished levels of antioxidant glutathione, triggering cell death by oxidative mechanisms. In an attempt to elucidate anti-MAG mAb protection mechanisms using primary OL culture, we observed that mAb 513 can increase OL intracellular levels of glutathione in a system Xc—dependent manner. Also 513 treatment prevented glutamate-induced glutathione depletion in OLs. Our results identify a novel role for MAG as a receptor involved in the modulation of glutathione levels in OLs. Overall these results highlight the important role of OLs in maintenance of glutamate homeostasis in white matter and at the same time opens a new opportunity for therapeutic intervention of diseases involving excitotoxicity.

Cellular and Molecular Neurobiology
Poster Number 59 / Session 2

Modulation of CaV2.1 channels by cholesterol levels

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Calcium channels show different compartmentalization on neuronal plasma membranes where they form clusters, involving both cytoskeletal elements and microdomains within the lipid bilayer. CaV2.1 channels are distributed in lipid microdomains.We showed an acute effect of pregabalin (PGB, a α2δ-binding drug) on the cellular function and distribution of CaV2.1 channels transfected in HEK293t. The system allowed us to visualize the internalization of subunits within cells after PGB treatment by means of fluorescence microscopy, while recording barium-mediated currents (IBa). We studied how the cytoskeleton and the lipid rafts organization might modulate the calcium channels. For this purpose, we treated transfected cells with methyl-cyclodextrin (MβCD, 5-10 min.), a cholesterol sequestering drug, and determined the internalization of the fluorescent subunits, and the distribution of microtubules.
MβCD (10 mM, 10-20min) increased α1 internalization (with a membrane/interior ratio 10% lower compared to untreated cells), similarly as after PGB treatment. However, it did not increase α2δ internalization. Acute MβCD reduced IBa. MβCD and PGB exerts an effect on the microtubule cytoarchitecture evidenced by a diffuse tubulin staining. The implications on the importance of this modulation lies on the fact that lipids change in the aged brain, and the fact that the different subunits might be internalised through different mechanisms (clathrin vs.caveolae-mediated mechanisms).

Cellular and Molecular Neurobiology
Poster Number 60 / Session 3

Analyzing the effect of APP in mitochondrial networks using neuronal-specific lentivirus

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Alzheimer Disease (AD) is characterized by progressive cognitive and memory deterioration due to neuronal degeneration. This last process is associated with senile plaques accumulation as a result of Amyloid-β (Aβ) aggregation and deposition. Aβ is generated by metabolic processing of the Amyloid-β Precursor Protein (APP). Inherited forms of AD are caused by APP mutations which alter APP processing and/or enhance Aβ aggregation. Experimental evidence also suggests that altered APP processing correlates with mitochondrial network dysfunctions (metabolic alterations, increased ROS levels and oxidative stress). Here we describe the use of lentiviral vectors with specific neuronal promoters and carrying different APP isoforms and mitochondrial-targeted YFP (to allows direct morphological assessment of the organelle) to address the role of APP in the neuronal mitochondrial network of hippocampal cultures. Using this experimental approach we analyzed mitochondrial structure as an indicator of cellular health, mitochondrial membrane potential to assess its metabolic state and levels of superoxide radical to sense oxidative stress. Data regarding the effect of APP and APP variants will be presented and discussed.

Cellular and Molecular Neurobiology
Poster Number 61 / Session 1

Is the mitochondrial network poised at criticality?

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Complex systems such as ecosystems, societies, brains and cells are the consequence of nonlinear interactions between their constitutive elements. It has been pointed out that complex behavior emerges when systems are poised at the critical point of a second-order phase transition, and if that is the case, no typical scale in which the system's properties can be described exists. Recently, it was found that the average abundances of metabolic species within cells follow a power-law distribution, suggesting that biological processes at the very cellular level could be described as critical. Following these reasoning, here we explore the possibility that the mitochondrial network in neurons is in some way poised at criticality, given that the length distribution follows a power law. Moreover, we evaluate if this distribution can be generalize for other cellular types (universality), and if, in fact, the absence of such a power law distribution can be correlated with pathology.

Chronobiology
Poster Number 62 / Session 2

Turn it off, turn me on: decreased motivation and interval timing under constant light

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Time perception in the second-to-minutes range, called interval timing, is crucial for multiple cognition processes such as learning, memory and decision making [1]. We have previously reported that learning to time is influenced by the circadian system [2]. In this sense, our previous results indicate that mice with circadian arrhythmicity -caused by constant light- were unable to perform interval timing. To investigate if this deficit could be related to abnormal locomotor activity or anxiety levels, we used both the open-field and elevated plus maze tests. Mice under constant light showed no significant differences in locomotion or anxiety levels. Additionally, we found normal long-term recognition memory in the novel object recognition (NOR) task, indicating that cognitive functions are not affected by constant light.

On the other hand, impaired interval timing may be related to motivational deficits [3]. We performed a progressive ratio (PR) task to assay motivational effects. Our results reveal that mice with circadian arrhythmicity displayed lower motivation compared to controls. This result correlates with a loss of striatal dopamine rhythmicity under constant light conditions, suggesting that dopamine might be a connection between the circadian system and interval timing, through motivational effects.

[1] Lustig et al., 2005, Memory, 13:441.
[2] Agostino et al.,2011, Brain Res, 1370:154.
[3] Galtress et al., 2012, Behav Processes, 90:142.

Chronobiology
Poster Number 63 / Session 3

Identification of relevant ion channels for controlling behavior in Drosophila melanogaster

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Circadian rhythms (circa: around, diem: day) are biological rhythms with a period of approximately 24h and have been described in every organism on Earth. The fruit fly Drosophila melanogaster has been a biological model crucial in the development of this field. In Drosophila the small lateral ventral neurons (sLNvs) command the behavioral rhythms under free running conditions through the release of the neuropeptide PIGMENT DISPERSING FACTOR (PDF).

The relationship between circadian rhythms and the function of the molecular clock in pacemaker neurons has been studied for some time. However, only recently we have started finding out about their physiological properties. The amount and type of ion channels present in the membrane of a neuron sets features such as action potential firing and excitability. In the present work we propose that the oscillation of particular voltage-gated ionic currents would establish the differential electrical properties of the LNvs between day and night, and this in turn would impact in the generation of the circadian locomotor behavior.

We have performed a behavioral genetic screen through the down regulation of candidate voltage-gated ion channels using RNAinterference specifically in LNvs. In this way we have been able to identify several ion channels that affect normal circadian locomotor behavior. Further immunohistochemical analysis of the PDF circuit indicates that some ion channels might exert their effect through the modulation of PDF.

Chronobiology
Poster Number 64 / Session 1

Matrix Metalloproteinases modulate PDF neuropeptide levels affecting circadian remodeling of adult oscillator terminals in Drosophila melanogaster

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The neuropeptide pigment dispersing factor (PDF) is expressed in specific neurons, the sLNvs, which are essential in the control of rest-activity cycles in Drosophila. A number of years ago we reported that the sLNvs undergo circadian remodeling of their axonal projections. We then proposed that such remodeling could provide an additional means of transmitting time of day information in addition to differential neurotransmitter release (as it has been reported for PDF). Axonal arborizations display higher complexity during the day and less so at night. In this work we show the relevance of matrix metalloproteinases (MMPs) in the control of this form of plasticity. It is known that flies express only two MMP's, called MMP1 and MMP2. Deregulation (either overexpression or silencing) of MMP's in adult flies impairs circadian remodeling. Surprisingly we found that only MMP1 affects PDF levels at the dorsal terminals, and more notably, down-regulation of PDF expression per se affects structural plasticity. We propose that MMP1 modulates either directly or indirectly PDF processing, which leads to daily axonal remodeling and normal circadian behavior. We are still studying the molecular mechanisms underlying this phenomenon.

Chronobiology
Poster Number 65 / Session 2

Boosting clock`s complexity: an inhibitory hand in the circadian pacemaker of *Drosophila*

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The internal time-keeping mechanism, the circadian clock, generates daily oscillations in physiology that enable the anticipation to reoccurring daily events. Among the 150 clock neurons in the Drosophila´s brain, the small ventral lateral neurons (sLNvs) constitute the major pacemaker since under constant conditions they guide the temporal organization of daily locomotor activity. In addition to PDF-(pigment dispersing factor)-filled vesicles, they contain small clear vesicles putatively packed with a fast neurotransmitter potentially involved in synchronizing the circadian network. We identify this neurotransmitter by evaluating flies' locomotor activity pattern after disrupting either membrane or vesicular neurotransmitter transporters function, specifically within PDF neurons. We found that downregulating glycine transporter expression increases period length in almost an hour without affecting rhythmicity. A decrease in intracellular glycine availability seems to underlie period lengthening as disrupting glycine synthesis has a similar effect. Daily oscillations in PDF levels at the sLNvs axonal termini are decreased under such conditions. The pursuit of glycinergic targets by immunohistochemistry revealed that PDF neurons express glycine receptor. Behaviorally, downregulating glycine receptor in PDF neurons decreases rhythmicity. Whether sLNvs glycinergic transmission entails cluster synchronization is still unknown. Current experiments will shed light on this issue.

Chronobiology
Poster Number 66 / Session 3

Neuromodulation of an electric behavior in two species of south american weakly electric fish

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South American weakly electric fish of the species Gymnotus omarorum and Brachyhypopomus gauderio display rate modulations of their electric behavior that are ultimately driven by a medullary pacemaker nucleus whose activity is modulated by environmental, sensory, and social cues. The basal rate of the electric organ discharge (EOD-BR) signals social hierarchy in both species and shows a species-specific nocturnal rise (NR) coincident with arousal and increase in locomotor activity. In B. gauderio (gregarious) the NR is persistent and modulated by the reproductive state and social context. In G. omarorum (solitary), the NR is transient and small in amplitude. As this NR of EOD-BR is relevant both as a social and circadian display, we aimed to assess the contribution of the actions of Arginine-vasotocin (AVT, social modulator) and melatonin (key hormone in circadian regulation) on it. We recorded the EOD of isolated adults during 5 days with a light-dark cycle 12:12. On the third day fish were either injected with a) AVT (1µg/g); b) Manning compound (AVT antagonist, 1µg/g); c) melatonin (200 □g/g); d)luzindole (melatonin antagonist, 0.1 □g/g); or e) saline. Our data suggest that AVTergic and melatoninergic systems are involved in the NR of EOD-BR in both species. Whether the melatoninergic system is commanding the AVTergic system or both are acting in parallel is a key point for a better understanding of the evolution of neuromodulation systems.

Cognition, Behavior and Memory
Poster Number 67 / Session 1

Organization of brain networks governed by long-range connections index autistic traits in the general population

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The dimensional approach to Autism Spectrum Disorder (ASD) considers ASD as the extreme of a dimension traversing through the entire population. We use electroencephalography (EEG) functional connectivity to explore its potential utility as a biomarker. We hypothesized that individual differences in autistic traits of typical subjects would involve a long-range connectivity diminution within the delta band.Resting state EEG functional connectivity was measured for 74 neurotypical subjects. All participants also provided a questionnaire (Social Responsiveness Score, SRS) by an informant who knows the participant in social settings. We conducted multivariate regression between SRS score and functional connectivity in all EEG frequency bands.Our results show a decay in functional connectivity mainly within delta and theta band (the lower part of the EEG spectrum) associated with increasing amount of autistic traits. When inspecting the impact of autistic traits on the global organization of functional network we found that optimal properties of the network are inversely related to the amount of autistic traits, suggesting that the autistic dimension, throughout the entire population, modulates the efficiency of functional brain networks.EEG functional connectivity at low frequencies and its associated network properties may be associated with some autistic traits in the general population.

Cognition, Behavior and Memory
Poster Number 68 / Session 2

Memory destabilization and retrieval dynamics of contextual fear memories: critical role of learning conditions

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The mismatch hypothesis suggests that the contrast between what is expected and what is experienced triggers memory destabilization and reconsolidation. Until recently, most studies addressing this problem focused on the manipulation of the retrieval phase without considering the original learning situation. Using contextual fear conditioning (CFC) in rats and the fast acting GABA-A receptor agonist Midazolam (MDZ), we studied if the dynamics of retrieval and destabilization can be determined by different learning conditions. Two learning protocols were used: 1 or 5 minutes of context exposure prior to shock administration. Our data clearly revealed that identical reactivation procedures induced different mnemonic processes, depending on the training protocol. A clear pattern emerged: an inverted U relationship between the amount of reactivation and trace destabilization, in which too little reactivation is not sufficient for destabilize the memory, a great amount of reactivation produces extinction and in between the memory becomes unstable (destabilization and reconsolidation occurs). Importantly, the inverted U pattern is determined by the original learning condition.

Cognition, Behavior and Memory
Poster Number 69/ Session 3

Short-term Suppression of TDP-43-NLS Overexpression Reverses Behavioral Deficits in a Frontotemporal Dementia Transgenic Mouse Model

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TDP-43 is a predominantly nuclear DNA/RNA binding protein that has been reported to regulate transcription, pre-mRNA splicing and stability. It has recently been identified as a pathological hallmark of the neurodegenerative disorders amyotrophic lateral sclerosis (ALS) and fronto-temporal lobar degeneration (FTLD). Using a transgenic (Tg) mouse model that conditionally overexpresses a cytoplasmically-localized form of human TDP-43 (TDP-43-ΔNLS) in the forebrain, we conducted a variety of behavioral tests to evaluate the effect of TDP-43 on motor, cognitive and social function. Our results indicate that TDP-43-ΔNLS transgenic mice develop motor abnormalities, including a dramatically altered rotarod performance, a spontaneous hyperlocomotor phenotype and pathological abnormal limb clasping as early as 2 weeks post-Tg induction. TDP-43-ΔNLS mice also showed altered social investigation behavior, a hallmark feature of FTLD patients. Furthermore we found significant deficits in cognitive function in novel object recognition, inhibitory avoidance and Y-maze tests at 1 month post-induction. Remarkably, we found that suppression of Tg expression for 2 weeks completely reversed the motor abnormalities. However, we found no differences in cortical neuronal loss compared to mice with continued Tg expression, suggesting that TDP-43-ΔNLS overexpression in young mice reversibly affects normal neuronal function, which might account for the behavioral deficits observed in these mice.

Cognition, Behavior and Memory
Poster Number 70 / Session 1

Measuring crab´s memory: improving conditioning

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Context-Signal Memory (CSM) of the crab Neohelice granulata has been exhaustively studied as a learning and memory model that allowed to unravel details from processes such as consolidation, reconsolidation, extinction and retrieval. However, a limiting feature of the experimental design has been the high number of animals needed to draw conclusions.
Using the traditional device, it was demonstrated that paired presentations of the context (CS) with the visual danger stimulus, VDS (US) increases the predictive value of the CS thus eliciting an anticipatory response. This new paradigm was named Contextual Pavlovian Conditioning (CPC) (Fustiñana et al., 2012).
Recently, we developed a new device to measure the crab´s escape response in order to reduce the number of individuals. For this purpose, the crab is hold from the dorsal carapace over a cylinder that rolls as the animal tries to move. A computer records distance and time, and controls stimulation.
Our challenge was to adapt CPC to the new device. Here, we present data showing that learning and memory retention can be clearly revealed in this new device using four times less animals than in the traditional one. Moreover, it allows more detailed measurements and a thorough description of the behavior.
This tool promises a whole new set of possibilities to venture into learning and memory mechanisms and, applying experimental approaches suited for reduced number of animals.

Cognition, Behavior and Memory
Poster Number 71 / Session 2

Untangling the auditory and visual effects acting on onomatopoeias

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One of the most natural and unexplored objects for studying the role of mimetic elements in language is the onomatopoeia, regarded as the process that transforms events of nature as collisions, bursts and strikes into words.
We asked our participants to produce onomatopoeic sounds from audiovisual movies of iteracting objects. Our analysis revealed that, as expected, onomatopoeic sounds correlate with the movies' sounds, but also showed consistent associations between the shape of the objects and the place of articulation on the vocal tract, and between the type of movement and the sound source of the vocal system.
This indicates that onomatopoeias result from a competition between direct acoustic imitation and cross-modal associations, contributing to a global view of word formation from mimetic forces.

Cognition, Behavior and Memory
Poster Number 72 / Session 3

NMDA receptor subunits transiently increase in the adult rat hippocampus after habituation to an open field

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NMDA receptor (NMDAR) subunits level change during development. Also, NMDAR synaptic expression is rapidly modified after synaptic plasticity induction in hippocampal slices from new-born rats. Recently we have shown that GluN1 and GluN2A subunits increase as revealed by western blot and/or immunofluoresce in adult rat hippocampus after 1) habituation to an open field (OF), 2) KCl depolarization of mature neurons culture and 3) LTP induction in slices. To explore possible underlying mechanisms, hippocampal slices were treated either with cycloheximide (a translation inhibitor) or actinomycin D (a transcription inhibitor) during electrophysiological assays. It was corroborated that translation was necessary for LTP induction and expression; the rise in GluN1 depends on transcription and translation, while the increase in GluN2A appears to mainly depend on translation. LTP effective induction was required for the subunits to increase. To explore the temporal course of these changes, rats were exposed to an OF for 5´ to analyse hippocampal –and cortex and amygdala- GluN1 and GluN2A levels. The increase of these subunits occurred in the hippocampus but not in the other regions was transient and returned to basal levels 4h after OF. Similar results were obtained in 22, 32 and 45 days old rats. We hypothesize that the increase is part of a general mechanism related to memory consolidation; hence, we are studying NMDAR subunit levels in other behavioural paradigms.

Cognition, Behavior and Memory
Poster Number 73 / Session 1

Evidence of behavioral tagging in humans. The effect of novelty on the formation and persistence of Long Term Memory

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In previous researches we have shown that rodents under weak training protocols (only induce short term memory) could consolidate a long term memory (LTM), provided that the training session occurred close to an unrelated novel experience. This process begins with the setting of a learning tag, established by the weak training and also requiring synthesis of Plasticity Related Proteins induced by the novelty. Hence, is this Behavioral Tagging (BT) mechanism also involved in humans LTM formation? In order to answer this question, we first focused on elementary school children. With them we intended to find out, if a novel or familiar event exerted a similar effect on LTM. Our results suggest that the learning task triggers a transient process, enabling the consolidation of that information by the effects of the novel experience. In the present work, we show an analogous promoting effect in high school students by using different kinds of learning and novelty events. We found memory improvements in the students group which experienced a novel lesson 1 hr before or after the graphical activity (Rey-Osterrieth) or a regular learning in the classroom. This was not appreciated when these were 4 hrs apart. Interestingly, our results show that the experience of educationally relevant novel events, improved LTM measure either 48 hrs or 45 days after learning. In conclusion, these experiments performed in students support the idea that BT might be acting in the formation of human memories.

Cognition, Behavior and Memory
Poster Number 74 / Session 2

Memory reactivation triggers different patterns and an increment of brain HSC/HSP70 expression in the crab Chasmagnathus

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In the crab Chasmagnathus memory model, animals associate the training context with a visual danger stimulus passing overhead. After a strong training (ST) crabs exhibit long-term memory that can be expressed for 5 days, but after a weak training (WT) memory is not expressed after 8 hours. However, in both protocols a brief exposure to the training context (reminder) triggers memory reactivation and reconsolidation. In this study we used Heat Shock Protein HSC/HSP70 as a marker of changes in metabolic activity. Although some of the neural substrates that support memory in crabs have been shown in optic ganglia, brain areas activated by retrieval processes are still unexplored. We evaluated the changes in levels of HSC/HSP70 protein expression in the brain after reminder sessions of ST and WT by western blot. We found a significant increment of protein expression in WT crabs, and a tendency in ST crabs. In addition, we evaluated changes in spatial patterns of HSC/HSP70 expression in brain induced by memory reactivation. Inmunohistochemistry showed an increase tendency of expression in different neuropils of WT crabs, being remarkable in the anteromedial neuropil. In further experiments we will test different pharmacological treatments to demonstrate the dissociation between mechanisms mediating memory reactivation and those underling the behavioral expression of memory.

Cognition, Behavior and Memory
Poster Number 75 / Session 3

Neurophysiological markers of asynchronies in a finger tapping task

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Sensorimotor synchronization (SMS) is a form of referential behavior, mostlyspecifically human, in which an action is coordinated in time with a predictable external stimulus. Music and dance are archetypical SMS behaviors; yet, the neural basesof the synchronization ability remain unknown, even in the simpler, paradigmatic task of finger tapping to a metronome. We make a step towards the identification of the neurophysiological markers of SMS by recording high-density EEG eventrelated potentials and the concurrent behavioral response-stimulus asynchronies (time difference between each response and the corresponding stimulus) during a paced finger-tapping task, both isochronous and with temporal perturbations. Using Principal Component Analysis, we found an asymmetry between the traces for advanced and delayed responses to the stimulus; the second principal component encodes the higherlevel percept of asynchrony 110 ms after the current stimulus for both types of tone sequences. Furthermore, its amplitude past 300 ms after the stimulus predicts the asynchrony magnitude at the next response. Our results suggest that the correction of a large asynchrony in a periodic task and the recovery of synchrony after a perturbation could be driven by similar neural processes, and that the neurophysiological processing of synchronization errors is performed within a fixed-duration interval after the stimulus.

Cognition, Behavior and Memory
Poster Number 76 / Session 1

Perinatal protein malnutrition impairs declarative long-term memory

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Protein malnutrition is a worldwide condition that affects the development of infants. Unlike undernutrition, malnutrition is also present in developed countries and is known to cause learning disabilities in malnourished children.
With the aim of further understanding the link between nourishment and cognition we established a model of protein malnutrition during development. CF-1 dams were fed either with normal protein (20% casein) or low protein (9% casein) diet during pregnancy and lactation. Malnourished mothers spent less time licking and grooming the pups, a sign of low maternal care. Mothers of the low protein group also exhibited traits of anxious behaviour when subjected to the elevated plus maze test. In order to further understand how maternal malnutrition affects emotional capabilities of the progeny, we performed the tail suspension and the cage escape tests in male and female mice. The first test revealed the presence of depression-like behaviour in the low protein group while the second suggested that they also where less motivated to explore the environment. Finally, offspring's cognitive abilities were tested in the Y-maze (spontaneous alternation and cued novel arm exploration) and with the novel object recognition test, where male mice from the low protein group had a lower performance in terms of short and long term memory.
The results obtained so far indicate that maternal malnutrition affects both cognitive and emotional abilities of the offspring.

Cognition, Behavior and Memory
Poster Number 77 / Session 2

Role of dopamine in corticostriatal postnatal maturation and related behaviors

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Attention deficit hyperactivity disorder (ADHD) is currently perceived as a neurodevelopmental condition related to an hypodopaminergic state and corticostriatal dysfunction. Neonatal dopamine depletion with 6-hydroxydopamine has been proposed as an ADHD mouse model because it mimics key hallmarks of the human disease, including hyperactivity and clinical response to psychostimulants. We have previously reported functional alterations that might underlie these abnormal behaviors: higher striatal spontaneous activity, higher susceptibility to undergo long term depression and lower corticostriatal synchronization and connectivity. We extended the analysis studying behavioral phenotypes on adulthood and morphology of striatal projection neurons. In adulthood, lesioned mice exhibited elevated vertical activity, deficits in the accelerating rotarod (a striatum dependent task) and lower interaction with salient stimuli and peers. In addition we used D1-TOM / D2-EGFP double transgenic mice to determine whether these functional changes have a morphological correlate in the direct and indirect pathways. We found a reduction in length and complexity of the dendritic tree in both D1- and D2-expressing striatal projection neurons. Preliminary results show no differences in spine density. We propose that decreased dopamine levels during development causes a functional and structural corticostriatal disconnection which may underlie hyperactivity and reduced interest in salient stimuli persisting into adulthood.

Cognition, Behavior and Memory
Poster Number 78 / Session 3

Repeated reactivation sessions induced a resistant fear memory to the disruptive effect of Midazolam on memory reconsolidation: Influence of D-Cycloserine

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The retrieval of a consolidated memory results into a labile phase, which is vulnerable to the interference by benzodiazepines. The aim of the present study was to assess MDZ vulnerability of contextual fear memories after retrieval in animals that had experienced multiple reactivation sessions. Male Wistar rats were subjected on day 1 to a contextual fear conditioning paradigm (3 shocks, 0.5 mA). On day 3 and day 5 one group of rats (3R) were re-exposed to the training context (A) for 3min. The control group (1R) remained in the home cage. Seven days after training, both groups were re-exposed to A for 3min. and immediately administered (i.p.) either with SAL or MDZ 3 mg/kg,. One day later, rats were tested in A. The results showed that MDZ does not affect reconsolidation only in 3R rats. In addition, we tested the influence of pre-reactivation D-cycloserine (DCS) on MDZ´s effect on fear memory reconsolidation.We then asked whether the process of retrieval induced-lability would mediate the resistance to disruption. To answer this, another group (2R-90s) were trained on day 1 and briefly (90 s) re-exposed to A on day 3 and day 5. The results showed that MDZ does not affect reconsolidation only in rats subjected to multiple reactivation sessions of 3 min. duration (3R). Our evidence showed that: a) Multiple reactivation-labilitation session prevents MDZ's disruptive effect on fear memory reconsolidation b) DCS prior to reactivation promotes retrieval-induced lability in such resistant memory trace and (c) retrieval-induced fragility enables such memory resistance upon reactivation.

Cognition, Behavior and Memory
Poster Number 79 / Session 1

Characterization of the effects of early social stimulation in a mouse model of autism

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Autism is a severe neurodevelopmental disorder characterized by poor social interaction and communication, and by stereotyped or restricted behaviors. Symptoms appear in early childhood and persist in adulthood. Several clinical studies suggest early social stimulation as the most effective treatment of autism.
We have previously shown that the prenatal exposure to valproic acid (VPA) results in reduced social interaction and other autism-related phenotypes in the adult offspring. In those experiments VPA-treated mice were weaned with other VPA mice.
Here, we compared VPA mice weaned with VPA mice (VPA-VPA mice) with VPA-Saline groups (VPA-Sal), containing 2-3 VPA-exposed mice per cage along with 2-3 Saline mice. This design allowed VPA and Sal mice to interact in the home cage from postnatal day (P)21 to P60. At P60, VPA-Sal mice showed higher levels of sociability than VPA-VPA, showing that this treatment can rescue at least some of the behavioral alterations observed in our model.
We will use this design to study what are the cellular and molecular changes that correlate with the autism-related phenotype and whether these or other pathways participate in the social rescue that we observe. To this aim, we are studying the inflammatory alterations, as we have previously found that VPA-treated mice have increased inflammatory responses in adulthood. In addition, we are characterizing the neuronal activation observed upon exposure to a novel object or to a social novelty.

Cognition, Behavior and Memory
Poster Number 80 / Session 2

Unconditioned sensitization and conditioned tolerance to the stimulating effect of ethanol in the infant rat

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Relatively high ethanol doses induce acute locomotor stimulating effects in preweanling rats, an effect associated with its rewarding properties. The goal of the present work was to explore how the ethanol-mediated locomotor response is modulated by the context and by the chronic experience with the drug. Subjects were trained with ethanol (0 or 2.5 g/kg) between postnatal days (PDs) 8 and 12. Training was carried out in the presence or absence of an odor cue. Three days later (on PD 15) subjects were evaluated in response to ethanol or water in the presence of the odor cue. Repeated exposure to ethanol induced conditioned tolerance or unconditioned sensitization. Tolerance to the locomotor stimulating effect of ethanol was observed when the odor cue was presented during training and testing. Locomotor sensitization occurred when rats were trained in absence of the odor cue, in a different context than the one employed at testing. These results represent the first evidence of conditioned tolerance and unconditioned sensitization to the locomotor activating effect of ethanol in this ontogenetic period.

Cognition, Behavior and Memory
Poster Number 81 / Session 3

Aversive memory reconsolidation in neonatal handled and separated rats

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Our aim was to study the effect of early life experiences on the ability to labilize aversive memories, in male rats. Litters were assigned to 3 treatments, from PDN1-10: intact - left undisturbed with their dams; handling - pups were placed inside an incubator at 32° C for 10 minutes, once a day; maternal separation – same procedure but for 3 hours. In adulthood, contextual fear conditioning was performed to determine changes in their aversive memory reactivation-reconsolidation process. In the training session, after 3 minutes of habituation, animals received three 0.8mA footshocks, followed by one more minute in the apparatus. 24 hours after, a 5-minute reactivation session was conducted, followed by immediate administration of either saline or midazolam 3 mg/kg. The test session consisted of re-exposure to the apparatus for 5 minutes. No significant differences were found in the reactivation session. In the test session, intact midazolam animals significantly decreased their freezing duration compared to saline-treated, but no statistically significant effect was observed in the other groups. In both sessions, handled animals exhibited less freezing. In this work, intact males responded to an amnesic agent administered during the reconsolidation window, while rats that suffered early life interventions may have had more difficulties labilizing aversive memories. It is also noteworthy that handled rats seem to have different strategies to cope with aversive environments.

Cognition, Behavior and Memory
Poster Number 82 / Session 1

Ultrasonic vocalizations in young rats are modulated by ethanol-related cues as a function of prenatal exposure to the drug

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Prenatal ethanol experience affects later recognition of ethanol-related chemosensory cues. Infant and adolescent rats emit higher levels of Ultra Sonic Vocalizations (USVs) during anxiogenic events.

In this study, we analyzed USV emissions as a function of differential ethanol prenatal experiences, in isolated subjects during infancy and adolescence. USV emissions were also confronted with ethanol-related or non-related odorants.

Pregnant females received 0 or 2 g/kg ethanol during gestational days 17-20. During postnatal day 16 (PD16), while isolated, pups were exposed to no particular odor, pine shaving´s odor or ethanol odor. Similarly, adolescents were tested in terms of USV emission while exposed to either no odor or ethanol odor. In both ages, pups that experienced alcohol in utero showed very high USV levels when exposed to no specific odor or pine shavings. Ethanol odor clearly inhibited this anxiogenic response apparently related with social isolation.

According to prior studies it appears that ethanol prenatal treatment increases stress responses via a hyperactivation of the HPA axis. Yet, this exacerbated response elicited by social isolation is clearly inhibited when the odorant perceived in utero is again presented.

Cognition, Behavior and Memory
Poster Number 83 / Session 2

Stress influences the hippocampal structural plasticity associated with fear extinction memory

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Fear extinction results in the suppression of the fear response once the conditional stimulus does not predict the threatening event anymore. Different anxiety disorders (e.g.: PTSD) have typical deficits in extinction memories formation and expression. Stress is known to be a possible factor causing such deficits. Thus, we planned to define whether acute stress may affect synaptic remodelling in the dorsal hippocampus (DH), possibly accounting for some of the effects of stress on extinction memory. Stressed animals were fear conditioned to context and later trained in an extinction paradigm (repeated context re-exposures without footshock). Animals were sacrificed for preparation1 day after conditioning (before extinction) or 1 day after extinction.

We confirmed that stress exposure induced a delay in extinction learning. Remarkably, a higher density of dendritic spines and particularly mature ones, was observed in the DH of non-stressed but conditioned animals at pre-extinction, reaching control values after the end of the extinction sessions. In contrast, stressed animals did not show such spines boost. Moreover, animals with intra-BLA Midazolam administration prior to stress showed structural changes similar to non-stressed animals.

In sum, here we show that stress impairs the structural plasticity in DH associated with extinction memory. We are currently extending our studies to other areas involved in extinction memories processing.

*equal contribution

Cognition, Behavior and Memory
Poster Number 84 / Session 3

Zif-268 gene induction in the lizard brain: involvement of proto-hippocampal areas with spatial novelty

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In the present study, behavioral alterations associated with the increase of Zif268 protein expression in telencephalic areas of the tropical lizard Tropidurus hispidus, corresponding to the mammal Hippocampus (HC), were investigated. Eleven male T. hispidus lizards were utilized. The animals were distributed in two different groups: a control group-CTR (n=5) and an exploration group-EXP (n=6). Animals from the EXP group were exposed to an enriched environment with many spatial clues unknown to them. CTR group animals remained in the environment to which they were previously habituated. After 90 min from the start of the new environment exposition, animals from both groups were submitted to intracardiac perfusion with PFA 4%, and the brains were removed, crioprotected, sectioned and submitted to imunohistochemichal analysis for Zif268. The lizards from the EXP group presented higher Zif268-positive cells (Mean ± S.E.M.) when compared to the controls in the medial (145,9 ± 11,3 and 80,4 ± 6,8, $p<0.05$), dorsomedial (140,7 ± 8,3 and 85,2 ± 7,4, $p<0.05$), and dorsal (160,9 ± 10,1 and 92,5 ± 9,3, $p<0.05$) cortices but not in the lateral cortex (125,9 ± 17,1 and 113,4 ± 12,4 $p = 0,58$). The data corroborate the notion that the reptilian hippocampus, as well as mammal HC, plays an important role in spatial exploration. Furthermore, this experiment is a evidence of plastic phenomena in T. hispidus cortex

Cognition, Behavior and Memory
Poster Number 85 / Session 1

Calcineurin Phosphatase as a negative regulator of fear memory: Control on nuclear factor-kappaB signaling

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Previous studies on neural plasticity support that synaptic strengthening is induced by altering the balance between protein kinases and protein phosphatases towards kinases activation. Conversely, synaptic depression is mediated by phosphatase activation. The phosphatase calcineurin (CaN) was particularly studied due to the fact that it is activated directly by Ca2+/Calmodulin signals and that it is highly present in synaptic spines. Some studies suggests its role as a constraint in memory formation, but there are few studies proposing which signaling pathways CaN indeed regulate. On the other hand, it is well known that the transcription factor NF-κB is necessary for memory formation. In the present work we studied the effect of CaN inhibition in hippocampus during fear conditioning consolidation and reconsolidation, and assessed whether NF-κB signaling pathway is regulated by this phosphatase. We found that hippocampal CaN inhibition by means of FK506 administration improved contextual fear memory and if NF-κB was also inhibited by sulfasalazine intrahippocampal administration, facilitation of memory was not observed, suggesting that CaN exerts its negative regulation via NF-κB pathway. Regarding reconsolidation, CaN inhibition before retrieval facilitates memory, and this facilitation is also dependent on NF-κB signaling. Our results propose a novel mechanism by which memories formation can be controlled by protein phosphatases.

Cognition, Behavior and Memory
Poster Number 86 / Session 2

Prior stress affects ZIF 268 expression after the retrieval of a contextual fear memory

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It is well known that a fully consolidated memory can enter into a labile state after retrieval, requiring an additional restabilization process known as reconsolidation. However, there are boundary conditions that limit the occurrence of the labilization/reconsolidation process, for instance, learning strength and memory age, among other factors. Previous studies in our laboratory have shown that a stressful experience prior to a contextual fear conditioning procedure generates a memory that is resistant to the disruptive effect of Midazolam (MDZ) on reconsolidation. The goal of this study was to evaluate the influence of a previous stress experience on the expression of the transcription factor zif 268 in the basolateral amygdala (BLA) after the retrieval of a fear memory. We observed that 90 minutes after reactivation, zif 268 is enhanced in BLA in unstressed animals. In contrast, this increase was not evident in animals that were stressed before fear conditioning. No differences were observed in non reactivated rats. This preliminary result indicates that such molecular event suggested to be involved in the labilization/reconsolidation process is absent in stressed rats. This evidence agrees with the lack of interference on fear memory reconsolidation following MDZ administration in stressed animals. Finally, we propose that the occurrence of a negative emotional state at the moment of learning limits the subsequent emergence of the labilization/reconsolidation process.

Cognition, Behavior and Memory
Poster Number 87 / Session 3

Nuclear Factor κB-dependent histone acetylation of Camk2d gene is specifically involved in memory persistence

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We have demonstrated that histone acetylation is a specific molecular signature of enduring memories consolidation. To gain insight into the specific gene expression effect of the induction of this epigenetic mechanism, we studied the role in this mechanism of Nuclear factor κB (NF-κB) transcription factor during novel object recognition (NOR) memory persistence. To address this aim, we used three different training protocols: one group of mice received a weak training which did not induce long-term memory (LTM); other group which received a standard training which lead to 24hs LTM, and the last group received a strong training which induced 7 weeks LTM. We found that only after strong training, NF-κB inhibition impaired memory persistence and prevented the induction of general H3 acetylation. To determine the histone acetylation level in specific genome locations, we studied the promoter regions of two particular genes which were associated with neural plasticity and memory: Zif268 and CaMKII. We found an important increase in H3 acetylation at a specific NF-κB-regulated promoter region of the Camk2d gene, which was reversed by NF-κB inhibition. This H3 acetylation increment led to δCaMKII mRNA induction 6h after strong training, but not after weaker training protocols. This result showed that δCaMKII expression was only induced during consolidation of enduring memory. Our work presents a molecular link between transcription factor activation, epigenetic mechanism, and late gene expression in the regulation of memory persistence.

Cognition, Behavior and Memory
Poster Number 88 / Session 1

Early neonatal stress lessens sensitivity to Ethanol-Induced motor sedation

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An early onset of alcohol consumption (Pilatti et al., 2013) and exposure to neonatal stress constitute vulnerability factors that promote problematic use of alcohol. A significant source of early stress comes are the alterations in quantity or quality of maternal care (Pautassi et al., 2008). The maternal separation paradigm (Plotsky and Meaney, 1993) is a model of early stress that has been shown to alter sensibility to the motivational (i.e., appetitive, aversive and negative reinforcing) effects of ethanol. These effects are important modulators of etanol-seeking and intake. Ethanol-induced motor activity has been used as a proxy for the appetitive effects of the drug. Alcohol induces biphasic motor effects, motor activation and depression, at low and high doses, respectively (Pautassi et al, 2009). In a previous Experiment of our lab we assessed etanol-induced motor activity in 15-day old infant rats that had been exposed to normal rearing conditions or that had experienced daily maternal separation [240 min per day] from postnatal day (PD) 1 to PD 14. Results indicated greater sensibility to etanol-induced activation (dose: 1.25 g/kg) in pups with history of maternal separation. The present study further analyzed behavioral activation induced by ethanol as a function of chronic maternal separation during PDs 1-14. On PD 15, animals were removed from the maternal cage and administered high-dose ethanol (2.5 g/kg). They were subsequently asssed in activity chambers during post-administration time 5-20 min. Data Analysis (ANOVA) indicated similar activating effects of 2.5 g/kg ethanol in control or maternally separated animals. Control animals, however, also exhibited a significant reduction in motor activity by the end of testing, when compared with vehicle-treated counterparts. This difference, indicative of ethanol-induced motor depression, was not observed in animals thah had been exposed to early neonatal stress. In other words, pups exposed to chronic maternal separation were insensitive to the sedative effects of ethe drug. Altogether, these results indicate that early neonatal stress alters the balance between the different motivational effects of ethanol. Specifically, stressed pups seems to be more sensitive to the behavioral activating effects of ethanol, but less sensitive to the motor depressing effects of ethanol.

Cognition, Behavior and Memory
Poster Number 89 / Session 2

Effects of being reared in overlapping litters on the maternal behavior of female rats

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Female pups born in overlapping litters (OL, reared by their mothers and juvenile siblings) receive a different pattern of maternal stimulation compared with control reared females (CL: reared by their mothers in a single litter). For example, mothers of OL lick less the new born pups compared to CL dams, however as juveniles also lick them, the overall amount of stimulation received by these animals is similar to that received by pups only reared by their mothers. Based on the Transgenerational transmission of Maternal Behavior hypothesis, we aimed to characterize the maternal behavior (MB) of adult OL females on their own postpartum period. Thus, we compared the MB of lactating rats that were reared under OL and CL conditions from day 1 to 7 postpartum. No differences were found between the behavior of both groups. These results suggest that even though OL females received less maternal stimulation from their mothers, the behavior displayed by juveniles seems to be sufficient, at least in its frequency, to compensate this deficit.

Cognition, Behavior and Memory
Poster Number 90 / Session 3

The effect of an aversive emotional context on the fate of a neutral declarative memory in humans

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Aversive emotional events could enhance consolidation of other learning situations occurring in the same spatial context and close temporal relationship. Our Laboratory has demonstrated the reconsolidation process of a neutral declarative memory (NDM) in humans. Little is known about the influence of aversive emotional context in the acquisition and fate of such memory type. To reach such goal we developed a new adaptation of the Trier Social Stress Test protocol using a virtual auditory communication (TSSTv). The original test is a widely used protocol to induce high social stress levels in humans. It consist in two phases of five minutes each, a) An oral exposition and b) An arithmetic task, during which a supposed group of experts observed and provided no feedback at all. Here, subjects that performed the task were told that they had to talk via the internet with a group of experts. A pitch modifier was used to allow the experimenter (who was in the next room) to have three different voices. Several physiological and psychological measures were used to assess the emotional arousal. A fake TSST (TSSTf), were the subjects completed the same task in a paper but without social interaction, was used to compare the effects. We found that the TSSTv compared to the TSSTf increases the salivary cortisol levels, electrodermal activity, heart rate, blood pressure and general anxiety state. Finally we explore the effects of the TSSTv in the acquisition and consolidation of the NDM.

A fear memory can be disrupted by the exposure to an appetitive stimulus after reactivation: Role of NR2b receptors in the Basolateral Amygdala

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To date, there is no experimental data regarding the possibility that a fear memory can be influenced by a rewarding experience after reactivation. To explore this, animals were habituated to voluntary sucrose consumption (SUC) and later on subjected to a contextual fear conditioning procedure. Reactivation conditions to destabilize the fear memory were determined by systemic administration of Midazolam, a GABA-A ligand agent. Various SUC concentrations (10, 20 and 30 %) were tested to determine which one induces the highest voluntary consumption. After establishing these parameters, a series of experiments explored if the original fear memory could be influenced by the appetitive stimulus after its reactivation. Experiment 1 confirmed this hypothesis: the fear memory was disrupted by the SUC experience only if such trace was destabilized after retrieval, as demonstrated in a 24 h post reactivation test. Experiment 2 revealed that this effect is absent if SAC consumption takes place outside the reconsolidation window (6 h after retrieval). Experiment 3 showed that this effect is dependent on SAC concentration and that SUC-induced memory disruption is persistent. Experiment 4 showed that intra-Basolateral Amygdala infusion of the NR2b antagonist Ifenprodil, prior to memory reactivation, blocked the impairing effects of SUC on fear memory. Our data suggests that an appetitive experience, following reactivation-induced destabilization, can interfere with a fear memory.

Cognition, Behavior and Memory
Poster Number 92 / Session 2

Pre-training treatment with scopolamine does not impair memory storage

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CF-1 male mice (25-30 g) were trained in an inhibitory avoidance task (IA) using a strong footshock (1.2 mA, 3 sec). They were tested for memory retention 48 hours after training, with latencies at the ceiling (300 sec), and tested several times 24 hours apart to develop extinction of the avoidance memory. Twenty four hours after it mice were tested again, and received a mild footshock (0.4 mA, 1 sec) when stepped in the dark compartment, which reinstate the avoidance memory. Another group of mice received a pre-training injection of scopolamine (SCP, 0.5 mg/kg) and were trained in the IA using the strong footshock. SCP impaired the avoidance memory. Mice were tested 24 hours apart, with progressively reduced latencies, suggesting that extinction was developing, despite the avoidance memory was poorly expressed. At the third retention test, mice received the mild footshock, and were tested again 24 hours after it. The mild footshock reinstate the avoidance memory, to a level similar to control mice. These results suggest that the pre-training administration of SCP did not impair storage of memory, but it remained poorly expressed. This memory developed extinction and was successfully reinstated using a mild footshock. Our results support the notion that SCP did not affect memory storage, but impaired memory expression.

Cognition, Behavior and Memory
Poster Number 93 / Session 3

Retrosplenial cortex and contextual fear conditioned memory

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We have recently developed a non-invasive protocol to induce acute degeneration of neurons in deeper layers of the granular subdivision of the retrosplenial cortex (RSG) of adult male rats. The protocol is based on the high vulnerability of layer IV RSG (RSG-IV) neurons to systemic applications of MK801, a highly specific non-competitive NMDA-antagonist. MK801-induced degeneration of RSG-IV neurons is sexually dimorphic and strongly modulated by gonadal hormones; therefore it is enhanced by orchiectomy and prevented by testosterone. Here we used different MK801-treatments to address the participation of RSG-IV neurons in contextual fear conditioned memory. Interestingly, we found MK801-treatments that induce loss of RSG-IV neurons significantly impair contextual fear conditioned memory. On the contrary, treatments with MK801 that do not promote degeneration of RSG-IV neurons have no effect contextual fear conditioned memory. Moreover, unconditioned fear response is not affected by MK801-treatments. Altogether, these observations support the participation of RSG-IV neurons in anatomo-functional circuits of contextual fear conditioned memory.

Cognition, Behavior and Memory
Poster Number 94 / Session 1

Stress exposure facilitates the emergence of fear memory and structural plasticity changes in the dorsal hippocampus

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A robust fear response is observed following the interaction of a trace memory induced by a weak fear conditioning procedure and the exposure to a stressful experience. Similarly, it is widely accepted that prior stressful experience promotes the formation of fear memory. This evidence highlights the importance of the emotional state previous to the encoding process or to the retrieval experience on the fear output. The question that arises is whether structural plasticity in dorsal hippocampus (DH), a key brain area for contextual fear memory, accompanies such behavioral manifestation? To this purpose, we assessed structural plasticity changes in the DH in animals stressed and later fear conditioned or, vice versa fear conditioned and later stressed. The behavioral and imaging analysis were performed 1 day after the last manipulation. Behaviorally, we observed that a single stressful exposure either prior or after fear encoding, induced a higher fear response. In a similar way, animals presented a higher density of total dendritic spines and particularly mature spines, in stressed animals prior or after encoding in comparison to non-stressed animals. In conclusion, the structural remodeling in DH accompanied the facilitated fear memory following a combination of fear conditioning and stressful stimulation.

Cognition, Behavior and Memory
Poster Number 95 / Session 2

Gonadimectomized individuals exhibit territorial agression in the weakly electric fish Gymnotus omarorum

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The agonistic behavior arises in the competition between co-specific individuals for the access to limited resources. In teleosts, as in most vertebrates, it has been demonstrated that gonadal androgenic hormones control reproductive aggression. The existence of non-breeding aggression, when gonads are regressed and low levels of androgenic hormones are expected, challenges this traditional paradigm and promotes the search of alternative control mechanisms yet unexplored among teleosts. Gymnotus omarorum (solitary, seasonal breeder) is a highly aggressive electric fish that defends its territory all year round. Interestingly, during the non-breeding season, G. omarorum exhibits non-sex biased territorial aggression. To study if agonistic behavior depends on gonadal steroid hormones levels, we contrasted dyadic contests between gonadectomized males (n=6) with contests between surgical sham males (n=6) in a plain arena of equally sized compartments with 5-20% weight asymmetry between contenders. All gonadectomized males exhibited agonistic behavior, showed similar locomotor and electric displays as sham males, and established the predicted dominance relationships according to their weight asymmetry. Partially supported by PEDECIBA & ANII_FCE_1_2011_6180.

Cognition, Behavior and Memory
Poster Number 96 / Session 3

How does 'every' + 'thing' become 'everything'? An electrophysiological study of word learning in Dutch

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The general aim of this work is to compare the processing of novel compound words with that of words already established in the mental lexicon. During a first session, adult Dutch subjects learn a series of novel compound words and immediately after they perform a morphological priming task involving speech production. In this procedure, the targets are pictures (e.g., an apple) and the primes are compound words morphologically related to the target, either Familiar (e.g. appelmoes, 'applesauce') or Novel (e.g. appelgezicht, 'apple-face'). A second session took place two days after the first one, where they perform the same priming task. Target's naming latencies and event-related potentials (ERPs) data were collected in both sessions. Our results show that Novel compounds have initially a stronger priming effect (i.e., reduced naming latencies) than Familiar compounds, respect to an Unrelated condition, while this difference is reduced 48h later. ERPs reveal a decrease in the N400 amplitude for the Novel condition respect to the Familiar and Unrelated. This effect is expressed in the centroparietal region, only during Session 2. Our results suggest that the novel compounds would be initially processed as separate constituents, while the change through sessions could reflect a consequence of the memory consolidation process that may help to assembly two initially separate words into a single unit.

Cognition, Behavior and Memory
Poster Number 97 / Session 1

Interaction among appetitive and aversive pathways during learning and memory formation in honey bees

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How appetitive and aversive stimuli are encoded in the brain to induce learning and memory is a relevant question in neuroscience. Insect are useful models to tackle this issue since both kinds of stimuli can be delivered while animals are prepared for neural recordings. Networks and transmitters involved in appetitive and aversive pathways have started to be revealed. In honey bees it was demonstrated that octopamine mediates the appetitive stimuli while dopamine (DA) mediate the aversive stimuli. We have postulated that appetitive and aversive pathways must work coordinated ensuring adaptive behavior. Accordingly, we found that DA, so far only involved in aversive learning, interferes with appetitive memory while a DA receptor antagonist facilitates appetitive memory. It is not known yet at what level, from sensory processing to motor output, this interaction takes place. We are performing calcium imaging to study how DA modulates neural signals in response to sugar and odors. As a first progress we found that DA increases the neural signals evoked by odor in the antennal lobe (AL), the first relay in odor processing. This effect could be related with more sensitivity to odors that predict aversive stimuli. We postulate that DA should decrease the signal evoked by sucrose, providing a neural substrate for the interference of appetitive memory observed behaviorally.

Cognition, Behavior and Memory
Poster Number 98 / Session 2

The Honey bee as a model to study the interaction between the nervous and the immune system

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Proper response to infections is a critical issue for all animals. During last years, it has been established that although the immune system is the principal responsible for this task, the nervous system has a relevant role too. How these two systems interact is an important question in the field of immunology and neurosciences.
In this work, we demonstrated that the administration of an inflammatory molecule (bacterial lipopolysaccharides, LPS) into the thorax of bees causes a reduction in the locomotor activity from 50 min until, at least, 130 min after the injection. In addition, honey bees showed a loss of appetite both 60 and 90 min after the administration of LPS. 24 hours after injection animals recovered the appetite, confirming an acute modulation of behavior during inflammation. These results show that honey bees exhibit a sickness behavior, and allow us to use it as model to study how the immune and nervous system interact.
We will analyze two molecular pathways that we consider candidates for the regulation of the honey bee's behavior. We will examine the role of eicosanoids, reported as principal mediators of the immune response in insects. We propose also that there could exist an octopaminergic pathway activated in response to inflammation. The role of octopamine as neurohormone and neurotransmitter leads us to propose this amine as a key factor in the interaction of the nervous and the immune system.
Thus, further studies performed in honey bees could help us to increase the knowledge about the interaction between the nervous and the immune system.

Cognition, Behavior and Memory
Poster Number 99 / Session 3

Instrumental successive negative contrast in rats: preliminar studies on the role of prefrontal cortex

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When animals trained to receive a large reward experience a surprising decrease in reward magnitude, their performance deteriorates below the level of a control group always exposed to the small reward magnitude. This phenomenon, called successive negative contrast (SNC) has been found in both consummatory (cSNC) and instrumental (iSNC) procedures. There is behavioral and neural evidence that their underlying mechanisms are different. However, whereas there is evidence that prefrontal cortex areas, such as the anterior cingulated and the insular cortex, are involved in cSNC, no such cortical involvement has been reported for iSNC. We present results of a behavioral procedure developed to study the role of prefrontal cortex on iSNC via lesion and cell activity procedures. Two groups of rats received one trial per day in a runway situation rewarded with 32 pellets for either 12 or 24 daily trials. Thereafter, they were downshifted to 4 pellets for an additional 10 trials. Their runway performance deteriorated relative to a group that always received 4 pellets. Advantages of this procedure will be discussed in relation to ongoing experiments that explore the role of prefrontal areas in iSNC.

Cognition, Behavior and Memory
Poster Number 100 / Session 1

Dopamine in the dorsal hippocampus negatively modulates the persistence of cocaine-related memories

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One of the hallmarks of drug addiction is its persistence over time. Drug use and abuse depends on associations between environmental stimuli and drug effects. Although much effort has been done to elucidate the mechanisms involved in establishing drug-associated memories, how they persist over time remains unknown. Combining pharmacological and biochemical tools with behavioral assays, we manipulate the persistence of cocaine-conditioned place preference (CPP) memory. A weak CPP training resulted in an increased release of dopamine (DA) in the dorsal hippocampus late after training. Blocking hippocampal D1-like receptors (D1R) around the same time period promotes the duration of a short-lasting cocaine-associated memory. Conversely, the maintenance of long-lasting cocaine CPP memory was selectively abolished by intrahippocampal infusions of D1R agonist SKF 38393 or of a specific agonist of the D1R coupled to phospholipase C cascade, indicating that dopamine inputs to the hippocampus negatively controls the persistence of cocaine-associated memory storage.

Cognition, Behavior and Memory
Poster Number 101 / Session 2

Hippocampal M1 and M2 muscarinic acetylcholine receptors modulate memory reconsolidation of an inhibitory avoidance task in mice

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Previous experiments from our laboratory demonstrated that hippocampal muscarinic acetylcholine receptors (mAChRs) play a critical role in reconsolidation of an inhibitory avoidance response in mice. However, the specific type of mAChR involved in this process is still unknown. To further investigate it, we trained CF-1 male mice in an inhibitory avoidance (IA) task using either a mild or a high footshock. A retention test was given 48 hours later. Immediately after it, mice were given intra-dorsal hippocampus infusions of oxotremorine (OXO, a muscarinic acetylcholine receptor agonist, 1–10 µg/hip), scopolamine (SCO, a muscarinic acetylcholine receptor antagonist, 1–10 µg/hip), pirenzepine (a specific M1 muscarinic acetylcholine receptor antagonist, 1-10 µg/hip), solifenacin (a specific M3 muscarinic acetylcholine receptor antagonist, 1.5-15 µg/hip) or AF-DX116 (a specific M2 muscarinic acetylcholine receptor antagonist, 1-7 µg/hip). Memory retention was tested again 24 h later. Pirenzepine impaired retention performances regardless of footshock intensity. AF-DX116 impaired retention performances in mice trained with a high footshock, while enhanced retention performances in mice trained with a mild footshock. These effects were dose- and time-dependent. There was no effect of solifenacin on retention performances, at least, at the administered doses. Our results suggest that specific hippocampal mAChR M1 and M2 would be essential for the modulation of memory reconsolidation processes of an IA task in mice.

Cognition, Behavior and Memory
Poster Number 102 / Session 3

Spatial learning in the plus-maze discriminative avoidance task: role of proximal and distal cues and CA1 activity.

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Previous studies have demonstrated that an adequate performance in the plus-maze discriminative avoidance task (PMDAT, a task used to investigate memory and anxiety interactions in rodents) depends on the activity of the basolateral amygdala and an optimal anxiety level. However, the role of hippocampal-dependent learning in this task remains to be studied. PMDAT is performed in an elevated plus-maze, with two open and two enclosed arms. One of which presenting aversive stimuli (light and noise) during the training, but not the test session. Experiment I aimed to assess the role of proximal and distal cues in learning the task. Rats were submitted to a standard training session and tested in the presence (+) or absence (-) of proximal (Prox) and distal (Dist) cues (groups: Prox+/Dist+, Prox+/Dist-, Prox-/Dist+ and Prox-/Dist-). Analysis of the time in aversive arm versus non-aversive arm revealed that only Prox+/Dist+ and Prox+/Dist- discriminated the aversive arm. Experiment II aimed to assess the role of dorsal hippocampus (subarea CA1) activity in learning the task. Temporary bilateral inactivation of CA1 was conducted with muscimol (0.05 μg, 0.1 μg, and 0.2 μg) prior to the training session. Muscimol impaired the performance in a dose dependent manner, increasing aversive arm exploration in the test. In conclusion, proximal cues are more relevant than distal cues to learning the PMDAT. In addition, the results indicate that CA1 plays a role in learning this task.

Cognition, Behavior and Memory
Poster Number 103 / Session 1

The study of the strengthening function of the reconsolidation process and the effect of the temporal mismatch in the reminder structure in the crab Neohelice granulata

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After being consolidated through the presentation of a specific reminder, reactivated old memories become labile and again susceptible to amnesic agents. Such vulnerability diminishes with the progress of time and implies a re-stabilization phase, usually referred to as reconsolidation. This process is only triggered under certain circumstances. The discrepancy between actual and past events (mismatch), is the key factor of this process. One of the biological roles described for the reconsolidation implies that labilization-reconsolidation process strengthens the original memory.

Our laboratory has demonstrated in crabs and humans that the reconsolidation is triggered when the reminder includes a mismatch. Moreover we have also demonstrated the strengthening function for a declarative memory in humans. In this framework, the goal of this research consists: 1) To study the strengthening by repeated labilization-reconsolidation process of the associative contextual memory in the crab Neohelice granulata. To reach such objective we will use the Contextual Pavlovian Conditioning protocol (CPC). Experiments will be perform combining pharmacologic-behavioral variables such as type of training protocols (weak, medium and strong), number of re-exposure to the CS or intersession interval. 2) To analyze the possibility of triggering reconsolidation by a temporal mismatch. Experiments will include changing of the temporal relation between the CS and US during the reminder presentation.

Cognition, Behavior and Memory
Poster Number 104 / Session 2

Stress management in children: a pilot study in 7-9 year olds

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At present, school-age children suffer high levels of chronic stress which could produce potentially long lasting effects. The aim of this pilot study was to evaluate the effects of mind-body integration practices and cooperative activities on stress levels and social interaction in 7-9 year old children. We performed an intervention program once a week during two months in which children carried out mind-body integration practices and cooperative activities. Our findings showed that these practices reduced cortisol levels and increased social connectedness. Moreover, we found that most of the children used the learned mind-body integration practices in stressful situations in their homes, even five months after the intervention. Our results demonstrated the positive impact of these helpful tools and the great plasticity of children's behavior, which enabled them to incorporate healthy habits. Overall, the intervention enhanced health at an individual level and favored social network diversity at a group level. Our research illustrates how children can incorporate techniques that help them cope with stressful moments and reveals the effectiveness of this experience in reducing cortisol levels. The present study contributes to the understanding of how mind-body integration practices and social connectedness can be helpful in reducing chronic stress, a topic which has, to our knowledge, been little developed in children.

Cognition, Behavior and Memory
Poster Number 105 / Session 3

Possible mechanisms involved in the impairment induced by IL-1β on memory reconsolidation and its modulation by α-MSH

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Pro-inflammatory cytokines and their receptors are present in the brain, specifically in the areas that are known to be involved in memory formation, such as the hippocampus. In addition, increased levels of these cytokines can produce alterations in cognitive processes. Previous studies of our group have demonstrated that the intrahippocampal administration of IL-1β impairs reconsolidation of contextual fear memory. This effect was reversed by the melanocortin alpha-melanocyte-stimulating hormone (-MSH), through activation of MC4-R. The mechanisms underlying the effect of IL-1β on memory reconsolidation have not yet been established. We determined a significant increase in ERK phosphorylation in dorsal hippocampus after contextual fear memory reactivation. However, treatment with IL-1β inhibited the increase. The intrahippocampal administration of α-MSH can reverse the decrease in ERK phosphorylation induced by IL-1β. Our results establish a possible mechanism involved in the detrimental effect of IL-1β on memory reconsolidation and also that α-MSH may exert a beneficial modulatory role in preventing IL-1β effects.

Cognition, Behavior and Memory
Poster Number 106 / Session 1

Sex differences in juveniles expression of maternal behavior in a model of overlapping litter in Rattus norvegicus

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In rats, mating at the postpartum estrus and delaying the weaning of the juveniles result in the overlapping of two different-age litters. Under this condition, juveniles express some care-taking towards their young siblings suggesting that the expression of maternal behavior is facilitated. Therefore, we hypothesize that juveniles raised in overlapping-litters would exhibit a full repertoire of maternal behavior when tested in the absence of their mother. To probe this hypothesis, from postnatal day 2 to 6, male and female juveniles of overlapping litters were exposed to their newborn siblings on the nest cage in the absence of the mother and the maternal behavior was registered. We found that only male juveniles exhibited a complete repertoire of maternal behavior (5/9 male vs. 0/9 female). Thus, male juveniles displayed more corporal licking than females and retrieved the pups. Interestingly, the retrieving behavior was not directed to the nest site but to one of the pups. Therefore, we can conclude that the expression of maternal behavior is sexually different in juveniles of overlapping-litters, with males being more likely to show it. Moreover, the presence of the mother in the overlapping-litters seems to be preventing the expression of a full maternal behavior.

Cognition, Behavior and Memory
Poster Number 107 / Session 2

Visual-memory strategies employed by children of the autistic spectrum

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Children in the autistic spectrum display anomalous capacities in memory and sensory tasks. Here we compared the visual memory strategies of children in the spectrum and a control group. We aimed at determining whether children in the spectrum are impaired in the ability to parse a continuous set of stimuli into discrete categories, and to perform subsequent mental operations (including storage in memory) with only the category label, ignoring additional stimulus details. To this end, we developed a computer game where players were required to remember the sizes of a set of geometric figures. The responses of the players allowed us to evaluate whether figures were remembered using a photographic strategy (that is, by storing the images with no further processing) or whether only some specific features were remembered, as the category of the sizes (big, medium or small) or the comparison between the relative sizes of different figures (figure A is larger than figure B). To decide among these alternatives we proposed several playing strategies that gradually ranged between a purely photographic strategy and others that had varying degree of categorical elements. Using statistical techniques we evaluated the likelihood of each proposal by quantifying the probability of obtaining the measured responses conditional to a specific strategy. The analysis demonstrated that a subset of control subjects employed strategies with categorical elements, absent in the autistic population.

Cognition, Behavior and Memory
Poster Number 108 / Session 3

Reducing mother-pups' interaction shifts the preference of postpartum estrous rats from pups to male without affecting the execution of maternal and sexual behaviors

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During the postpartum estrus (PPE), maternal and sexual motivated rats prefer the pups in a pups-male choice test. However, by decreasing maternal motivation -reducing mother-pups' interaction period- PPE rats shift their preference from pups to the male. We propose that females' choice will be reflected in the execution of maternal and sexual behaviors. To probe this hypothesis, PPE rats that experienced 10 (INT10h) or 2 (INT2h) hours of interaction with their litter, were tested in a Y-maze with three-choice chambers: two with reinforcing stimuli (pups or male) and one neutral (empty). Afterwards, maternal behavior was assessed in their home cage and sexual behavior was registered in a sexual arena. As expected, INT10h-PPE rats prefer the pups, while INT2h-PPE rats exhibited a marked preference for the male. However, INT10h and INT2h groups did not differ in the latencies to execute active maternal components, in their total frequency or in the time they spend with pups. Independently of pups vs. male choice, the motivational components of female' sexual behavior did not differ between groups. Present results indicate that during the PPE a reduction of maternal motivation sufficient to allow the expression of sexual motivation in a challenge situation –pups vs. male- is not necessarily reflect in a differential performance of maternal or sexual behaviors when females are confronted to one of the incentive stimuli.

Cognition, Behavior and Memory
Poster Number 109 / Session 1

Neuronal plasticity in the Lateral Protocerebrum of Neohelice reflects long-term memory persistence independently of its expression

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Results from our group have shown that behavioral expression is not necessary for memory reactivation and labilization. In this view, memory persistence (evaluated by the capacity of memory to be reactivated and become labile) should be considered a memory attribute independent of memory expression. Here, we use in vivo imaging to analyze neural activity in the Lateral Protocerebrum (LP) of the crab Neohelice granulata during and after two different trainings that induce: a) long-term memory that is behavioral expressed, or b) long-term memory that is not expressed but evident because it is reactivatable. In addition, we evaluate the effects of amnesic agents that interfere with memory persistence or with memory expression. The results show that, after training, there is a reduction in the neuronal activity in the LP specifically elicited by the training stimulus. This reduction was observed after training protocols that induce memory persistence independently of its long-term expression. Treatments proposed to interfere with memory persistence (NMDA receptor antagonist MK801 1ug/g and muscarinic cholinergic antagonist Scopolamine 5ug/g) block the changes induced by training. These findings add system level support to the hypothesis that expression and persistence are different memory attributes, showing that neuronal plasticity in the LP induced by trainings reflects long-term memory persistence but not its behavioral expression.

Cognition, Behavior and Memory
Poster Number 110 / Session 2

Actin Cytoskeleton Dinamics in Fear Memory Reconsolidation

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In its initial state memory is unstable and becomes enduring and stable by the process of consolidation. In contextual fear conditioning, once fear memory is consolidated a brief re-exposure to the training context induces memory reconsolidation. During reconsolidation, memory is stabilized as in the initial consolidation. Dendritic spines are small actin-rich protrusions from neuronal dendrites that form the postsynaptic part of most excitatory synapses and are major sites of information processing and storage in the brain. Changes in the shape and in the density of dendritic spines are correlated with the strength of excitatory synaptic connections and heavily depend on remodeling of its underlying actin cytoskeleton. Some evidence suggests that the regulation morphology and density of dendritic spines plays a key role in memory consolidation. However, the regulation of spine dynamics in reconsolidation is unknown. We project to study the actin dynamic between the monomer form, G-actin, and the actin filaments, F-actin, in the hippocampus during memory reconsolidation. We aim to study the role of ADF/cofilin inducing the formation of G-actin and LIMK kinase in the formation of F-actin. Besides we are studying the effect on memory reconsolidation of drugs such as latunculin A that inhibits the formation of F-actin. These studies may help us understand the nature of reconsolidation at the molecular level.

Cognition, Behavior and Memory
Poster Number 111 / Session 3

Midazolam modifies the active defensive behaviors induced by the reexposure to an aversive conditioned stimulus

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Fear conditioning (FC) is a paradigm extensively used to study aversive memories. Although freezing has been the main behavioral response assessed for memory retention, decreased freezing does not necessarily indicate fear reduction. Using an olfactory FC test it is possible to access passive and active behaviors to investigate the coping strategies in rodents after the retrieval of a conditioned olfactory cue. Hooded rats were submitted to an olfactory FC procedure in a conditioning box A (5-footshock trial + CS-eugenol odor). One day later they were reexposed to the CS during 1 min in a box B, and Midazolam (MDZ; 3mg/kg) or saline were applied immediately after the session. On the next day, active behaviors were evaluated in Box C containing an open and an enclosed compartment (EC). MDZ-treated rats showed reduced defensive behavior represented by an increased approach to the odor source (p=0.036), reduced time spent in EC (p=0.010) and increased head-out behavior (p=0.031), when compared to saline-treated group. On day 4 rats returned to box A for contextual freezing (CF) measurement where MDZ-treated rats showed a significant reduced CF (p=0.001). These results suggest that brief exposure to the CS-odor was able to generate coping behavioral strategies to the olfactory cue, and MDZ was able to modify these strategies and the CS-induced freezing.

Cognition, Behavior and Memory
Poster Number 112 / Session 1

Caracterization of cognitive impairment in two age groups of aging rats on barnes maze and its morfological correlation in dorsal hippocampus

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Aging is the primary risk factor associated with the increment of neurodegenerative diseases. The hippocampus, a medial temporal lobe structure necessary for the formation of spatial memory, is particularly affected during both normal and pathologic aging. Human and animal studies have demonstrated age-related declines in learning and memory abilities. In previous studies, we observed a significant age-related increase in dopaminergic neuron loss in the hypothalamus and the substantia nigra in the Sprague–Dawley female rat (SDfr) which becomes more conspicuous at extreme ages.

In the present work we extended the studies in the SDfr, focusing on determining the extent of spatial memory impairment in 26 months (OLD) and 29-32 months old (SEN) as well as the histopatholical changes in their dorsal hippocampus, comparing them with their young counterparts (4-6 months old). Age changes in spatial memory performance were assessed with the Barnes maze. The results revealed differences between OLD and SEN rats in acquisition and spatial memory retention. Morphological analysis of dorsal hippocampus showed a huge decrease (94-97 %) in DOUBLECORTIN neuron number in the dentate gyrus in both aging groups and a 40% reduction in VIMENTIN glial cell number in the hilus only in the SEN group. We conclude that SEN rats present a higher degree of cognitive impairment than OLD rats on the Barnes maze. Cognitive deficits in SDfr could be associated with a dramatic reduction in neurogenesis.

Cognition, Behavior and Memory
Poster Number 113 / Session 2

Prenatal Stress Modifies Long-Term Memory and Neuronal Activity in the Prefrontal Cortex

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Prenatal stress is a risk factor for the development of psychiatric disorders in adulthood, which are characterized by increased behavioral perseverance and alterations of the functional connectivity between the prefrontal cortex (PFC) to others structures. The goal of this study was to address the impact of prenatal stress on the functional connectivity between the PFC and hippocampus (HPC), and its relationship with memory consolidation, a cognitive function dependent on the interplay between these structures. To this aim, pregnant mice were subject to restraint stress during the last week of pregnancy, and we assessed short- and long-term spatial memory under an aversive context in the adult offspring. One day after memory evaluation, we examined spontaneous neuronal activity in the PFC and HPC using in vivo extracellular recordings.
Prenatal stress did not affect short-term memory, and after short-term memory testing we did not find changes between groups in neuronal activity, neither in the PFC or HPC. In contrast, prenatal stress produced a persistance of long-term aversive memories that in control animals was extinguished. After long-term memory testing, prenatal stress decreased firing rate in the PFC respect to control animals. This finding was associated to a reduced proportion of PFC neurons cross-correlated with sharp-wave ripples in the HPC. Our data suggest that prenatal stress affects the functional connectivity related to memory consolidation

Cognition, Behavior and Memory
Poster Number 114 / Session 3

Memory rectivation beyond expression: Increments of HSP70 triggered by memory reactivation in the protocerebrum of Chasmagnathus

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The reconsolidation hypothesis has challenged the traditional view of consolidation, including the notion that new memories are fixed and established. Previous studies of the lab support the idea that there is dissociation between the mechanisms that mediate memory reactivation and the ones that mediate behavioral expression of memory. Our group has shown, in the Lateral Protocerebrum (LP) in Chasmagnathus , neural changes induced by different training protocols correlate with memory persistence (evaluated as the capacity of memory to be reactivated and become labile) but not with the long-term expression of the reactivated memory. The central hypothesis of this Master´s Thesis project is that memory reactivation induces neuronal activity patterns in LP regardless memory expression. The goal is to show that memory built up after a weak training protocol can be reactivated even when long-term memory (LTM) formed by this training remains unexpressed. Using HSP 70 as a neuronal activity marker in LP we are evaluating whether unexpressed memories are reactivated, which will add evidence to the view that reactivation occurs independently of the expression of memory. Preliminary results show that memory reactivation of a consolidated but unexpressed memory induces, in small neuropils of the LP, an increase in HSP70 immunoreactivity.

Cognition, Behavior and Memory
Poster Number 115 / Session 1

Postnatal stress, alcohol intake and anxiety in rats

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Adverse events early in life have been linked to a maladaptive stress response in adulthood that can predispose individuals to psychiatric and physiological disorders. Postnatal stress (PS) shows a variety of long-term neurochemical, hormonal and behavioural changes. The main physiological change is the release of glucocorticoids through activation of the hypothalamic-pituitary-adrenal (HPA) axis. We evaluated the consequences of chronic PS on alcohol intake, corticosterone (C) levels and anxiety. In PS, from postnatal day 2 the pups were separated from their mothers and exposed to cold for 1h during 20 days. Then animals were exposed to a voluntary ethanol (6%) intake for 7 days, 30 days of washout and then a second 7-day exposure to a voluntary intake. We measured the volume of intake, C plasmatic levels and anxiety with 3 different tests: elevated plus maze, open field, light-dark transition. Stressed groups significantly increased ethanol intake and showed decreased anxiety levels. We observed hormonal changes in all treatments, C ranged in all groups, showing an alteration in the hormonal stress response.

These results suggest that an exposure to PS increases alcohol intake and alters the HPA axis, which could be relevant to behaviour in anxiety tests. Unlike the anxiogenic effects of stress in adult animals, when the stressor appears early in life we observed decreased anxiety in adulthood. These results and the decrease in C levels indicate an attenuate response to stressful and anxiogenic stimuli.

Cognition, Behavior and Memory
Poster Number 116 / Session 2

Dissociation between the mechanisms mediating memory reactivation and that underling the behavioral expression of a declaratives memory

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The reconsolidation hypothesis has challenged the traditional view of consolidation, including the notion that consolidated memories are fixed and established. Our previous reconsolidation's studies in crabs and humans support the idea that there is dissociation between the mechanisms mediating memory reactivation and that underling the behavioral expression of memory. Recently, the lab have been demonstrated that both a mild stressor, cold pressor stress (CPS), and glucose can enhance declarative memory (association between five cue-syllables and their respective response-syllables) during reconsolidation, showing that the period in which this declarative memory can be reactivated and become labile largely exceeds the period in which that memory is expressed, proving evidence that conscious access is not needed for reconsolidation. The central goal of this project is to show that memory reactivation can occur regardless memory expression is interfered at retrievals sessions. Here, we expected that CPS administration both interfere with memory expression and positive modulated the reactivated memory during reconsolidation. Although very poor memory performance (expression) is expected at reactivation sessions, CPS will be still able to enhance reconsolidation, improving the long-term expression of the reactivated memory. This improving effect in memory expression is expected to be specific on the reconsolidation process.

Cognition, Behavior and Memory
Poster Number 117 / Session 3

Participation of p21-activated kinase in aversive memory processes in rats

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Several studies have shown the involvement of p21-activated kinase (PAK) in the dynamics of cellular cytoskeleton, resulting in cognitive and mnemonic changes. The aim of this work was to verify the role of group I PAK in aversive memory, set through the contextual fear conditioning (CFC) task in rats treated with an inhibitor of group I PAK, IPA-3 (0.5, 1.0 or 2.0 mM). The inhibitor was infused in the CA1 region of the hippocampus while control groups received saline or vehicle (DMSO 3%). Treatments were performed 15 min before, or 15 min, 3, 6 or 12 h after the training session (TrS) in the CFC. Test sessions (TS) were carried out 90 min after training in the groups treated 15 min prior to TrS and 15 min after TrS in an attempt to verify the participation of group I PAK in short-term memory (STM). Further TS were carried out 24 h after TrS in order to evaluate the treatments against long-term memory (LTM) parameters. Groups treated with IPA-3 at three concentrations, 12 h after TrS, were also tested 7 days afterwards to evaluate memory persistence. The inhibition of I PAK hindered the consolidation as well as the persistence of memory. No effects were observed on STM, neither on the acquisition nor on the retrieval of LTM. These findings suggest that group I PAK plays an important role in consolidation and persistence of memory, since the inhibition of PAK in the CA1 region of hippocampus yielded an amnesic effect in rats subjected to contextual fear conditioning task.

Cognition, Behavior and Memory
Poster Number 118 / Session 1

Reactivation-extinction: role of trace destabilization to attenuate spontaneous recovery and reacquisition

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Monfils et al (2009) developed a drug-free behavioural paradigm combining reconsolidation and extinction to attenuate conditioned fear and avoid its reemergence, a typical pattern of traditional extinction procedures. However, many studies failed to replicate that result, while others succeeded. This could be due to assume that any reactivation can destabilize a memory. Using contextual fear in rats, we tested that hypothesis. In Experiment 1, using the benzodiacepine Midazolam (MDZ), we found that 4 min., but not 1 min., reactivations were required to induce memory destabilization. In Experiment 2 we found that a 15 min. reactivation induced extinction and spontaneous recovery a week later. Hence, we determined how to merely reactivate (1 min.), destabilize (4 min.) or extinguish (15 min.) the memory. Experiment 3 revealed that reactivation followed 30 min. later by extinction diminished the fear response, but spontaneous recovery occurred. When memory destabilization preceded extinction, spontaneous recovery did not occur. Experiment 4 determined that this effect was absent when memory destabilization and extinction were separated by 6 hs. Finally, Experiments 5 and 6 demonstrated that memory destabilization followed by extinction attenuates reacquisition when compared to pure extinction, mere reactivation followed by extinction or control conditions. Our data suggests that memory destabilization must occur prior to extinction in order to attenuate fear recovery.

Cognition, Behavior and Memory
Poster Number 119 / Session 2

The presentation of post-retrieval positive images modify an aversive autobiographical memory in humans

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Memory traces can become labile upon retrieval and must be restabilized. It is widely established that, the disruption of this reconsolidation process can abolish a previously consolidated memory. The aim of the present study was to selectively modify an existing autobiographical memory by using a noninvasive interference after retrieval. Healthy participants (18 to 35 years old; 17 men, 17 women) were used in this study. Participants were tested on 3 consecutive days: Day 1, autobiographical memories were reactivated by means of the autobiographical memory cueing test, participants were presented with 2 negative (sad, angry) adjectives and were instructed to remember in as much detail as possible. After 10 minutes, the interference images (IAPS- positive or neutral) was presented. On Day 2, (7 days after day 1), memories were again retrieved. Day 3: (30 days after day 1), an additional test was performed as on Day 2. The following groups were defined: SAD/POSITIVE; ANGRY/POSITIVE; SAD/NEUTRAL and ANGRY/NEUTRAL. Results: the positive interference reduced the amount of content details of memories during successive retrievals only in women, whereas the neutral images increased the amount of details. Here, we show that a positive emotional induction after the reactivation of personal experiences impairs the original autobiographical memory, suggesting a potential reconsolidation interference on aversive autobiographical memories.

Cognition, Behavior and Memory
Poster Number 120 / Session 3

Ontogenetic analysis of the NR2B-receptor dynamics during acquisition of contextual fear learning in preweanling and weanling rats

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The capability to acquire contextual fear learning emerges around weanling in rats, and is NMDA-type glutamate receptors (NMDAr) dependent. Contextual learning deficits in preweanling rats have been associated with functional immaturity of the hippocampus (HPC).A recent study of our lab using the Context Preexposure Facilitation Effect procedure (CPFE), a HPC-dependent task, demonstrated evidences of contextual fear conditioning in preweanling rats. Moreover, we found that contextual fear memory is NMDAr-dependent at both ages, evidenced by the inhibition of these receptors during the pre-exposure phase of the CPFE. NR2B is an NMDAr subunit that is involved in the transport of NMDAr to synapses improving learning and memory function. The aim of the present study was to evaluate the dynamics of NR2B receptor during the acquisition of contextual fear learning in preweanling and weanling rats. We tested the temporal expression of NR2BY1472 (a phosphorylated state of NR2B subunit that promotes surface expression of NMDAr) after 10 min. of pre-exposure treatment, in the dorsal HPC of animals from both ages. Our results showed the same pattern of temporal expression of NR2BY1472 in weanling and preweanling rats. These results suggest that preweanling rats are capable of acquiring contextual learning through a comparable mechanism than weanling rats. These findings may have important implications for the ontogenetic analysis of the neurobiology of contextual fear conditioning.

Cognition, Behavior and Memory
Poster Number 121 / Session 1

Research Project: Role of 5-HT2A receptors in cognitive flexibility and memory interference during a spatial working memory task.

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Our ability to adjust our behavior to dynamic changes in the environment is called "cognitive flexibility" and it is part of the repertoire of executive functions. Memory interference is the result of competing memory traces. Both mechanisms are postulated to depend on the activity of the Prefrontal Cortex.
Clinical and pre clinical data support a role of the serotonergic system (5-HTS) in cognitive flexibility and memory interference. The 5-HT2a receptor (5-HT2AR) it is one of the most important post-synaptic receptors of the 5-HTS and highly expressed in cortical regions and the limbic system. One of the main problems addressing the role of 5-HT2AR in cognitive functions is the lack of specific drugs. We are using a genetically modified mouse model to study the role of the 5-HT2AR in a spontaneous alternation task. Spontaneous alternation paradigms model the natural tendency of rodents to flexibly shift between different spatial options and it is a good paradigm to simultaneously address behavioral flexibility and proactive memory interference. 5-HT2AR knock-out mice (htr2a -/-) show a deficit in working memory (without preservative responses) when measured with the Y maze spontaneous alternation task. Immunohistochemical analysis of various regions after completion of the behavioral task showed increased expression of c-fos in htr2a-/- mice compared with controls suggesting that lack of 5-HT2A protein alter brain reactivity during a particular class of working memory task.

Effect of open field exploration on frustration´s memory: Implications of the adrenergic system

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When the subjects are exposed to a novel situation pre training or pre testing in a specific learning situation, its retrieval is modulated(Izquierdo & McGaugh,1985,1987).This phenomenon involves a complex series of neurobiological and psychological mechanisms(Thiel,Huston & Schwarting,1998).On the other hand,animals´ behavior depends on their previous experience with different reward values.One way to study this phenomenon is with the incentive downshift paradigm through the consummatory Successive Negative Contrast.Thus, the aim of this work is to evaluate if the presentation of an open field exposure disturbs the incentive downshift and the role of the noradrenergic system in this phenomenon. For that purpose we submitted male rats to a 32% sucrose solution and then it was change it to a 4% one.Previously to the first or second contact with the downshifted sucrose solution the animals explored an open field.The exposition to the field interfered with the aversive memory of the event.Through the propranolol´s administration(an antagonist of the β-adrenergic system)or a vehicle substance to the animals, given in trials 1 or 2 of the devaluation phase, it was founded that this drug blocked the effect of open field. In a theoretical level we want to understand the neurobiological processes involved in emotional memory.The implications for the applied science are to provide research to achieve better interventions for subjects who are vulnerable to loss situations o deceptions.

Cognition, Behavior and Memory
Poster Number 123 / Session 3

Interfering with PSD-95 signaling complex affects memory consolidation

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PDZ domains are present in several diverse proteins, including PSD-95 where it was first described. These domains are protein-protein interaction domains that anchor membrane proteins and hold together signaling complexes. NF-kappa B is a transcription factor whose role in memory consolidation was first described by our lab and widely reported thereafter. Previously in our lab, we observed that NF-kappa B was strongly bound to the membranes of synaptosomes. Additionally, consolidation of inhibitory avoidance memories in mice leads to NF-kappa B activation at synaptosomes and increased attachment to membrane of these structures. Our research suggested the possibility that NF-kappa B interacts with PSD-95 and is anchored to the membrane to perform a non-canonical function. AT010 is a stable, cell-permeable peptide that was designed to bind to the PDZ domains 1 and 2 of PSD-95 with high affinity. We hypothesized AT010 might modulate the interaction between NF-kappa B and other proteins. In this work we show evidence of NF-kappa B and PDS-95 interaction and we show that intra-hippocampal injection of AT010 reversibly interferes with memory consolidation of the inhibitory avoidance paradigm in mice Exploratory toxicity studies of intravenous injections of AT010 showed no signs of toxicity.

Cognition, Behavior and Memory
Poster Number 124 / Session 1

New insight into long-term memory induction by spaced learning sessions

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Learning disability is a common cognitive alteration in a group of disorders, in which a higher activity of the Ras/mitogen-activated protein kinase (MAPK) is a hallmark. This group of genetic disorders, including Noonan syndrome, are caused by mutations in genes encoding for components of the Ras/MAPK signaling pathway.
Recently, we found that different csw gain-of-function alleles, including the cswN308D which models the commonest Noonan syndrome mutation, show a specific impairment of long-term memory (LTM) induction through spaced training. Importantly, by analyzing ectopic wing vein phenotypes in Drosophila, was previously identified that several genes, including Ras85D, Notch and Stat92E, interact genetically with the cswN308D allele.
Here we present preliminary studies on the effects of enhancing or suppressing the activity of genes that interact genetically with the allele cswN308D on learning and LTM in a Drosophila model system.
These studies showed that by suppressing or enhancing the activity of Ras, Notch or STAT in mushroom bodies, a brain region essential for learning and memory in Drosophila, learning was not affected. However, suppressing Ras, Notch or STAT activity impaired LTM. The enhancement of these gene functions produced an enhancement of LTM induction as well, but only through Notch or Stat92E, whereas Ras did not affect memory. These observations provide new insight on the role of Notch and Stat92E in LTM induction by spaced training sessions.

Cognition, Behavior and Memory
Poster Number 125 / Session 2

Open field exposure “prevents” amnesia caused by blockade of either NMDA glutamate receptors or cholinergic muscarinic receptors in the juvenile and adult rat

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Muscarinic receptors (MAChR) or NMDA receptors (NMDAR) antagonism produced amnesia of an inhibitory avoidance (IA) to a mild footshock in the rat. We studied a previous open field (OF) exposure effect on adult and juvenile rats´ performance in IA, when either MAChR or NMDAR were blocked. Adult rats were to 1 or 2 OF sessions and trained in IA; the muscarinic antagonist scopolamine was immediately injected intrahippocampus (IH) and the IA long term memory (LTM) was assessed 24 h later: They expressed an IA LTM, while those not exposed to the OF were amnesic. Both adult and juvenile rats previously exposed to the OF showed an IA LTM, even though they received an intraperitoneal (IP) injection of scopolamine before IA training. It was reported an increase in hippocampal ACh release during and after OF exploration and reexposure. This increase could contribute to "prepare the substrate" (metaplasticity?) for synaptic plasticity, which would result in IA LTM.

The blockade of hippocampal NMDAR channel with MK-801 during IA consolidation, though not during its acquisition in adult rats, caused amnesia, which was prevented by 2 OF sessions before IA training. Instead, IP MK-801 before IA training was amnesic in juvenile rats and this amnesia was also prevented by previous OF exposure. Based on these results and on recent findings of our lab (see Baez et al, SAN, 2013), we hypothesize that the OF substantially modifies NMDARs, facilitating synaptic plasticity and memory formation.

Cognition, Behavior and Memory
Poster Number 126 / Session 3

Enriched enviroment (EE): immediate and long term effects on spatial memory

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Environmental factors seem to play an important role in terms of mental and functional/behavioral plasticity, either in humans as in other animals. The application of different methods in terms of environmental enrichment beget physiological and behavioral effects in long term. This study were verified the immediate and long term effects of environmental conditions through the application of environmental enrichment (EE) on the spatial memory of rats. At the 70th day of its lives, they were tested of Morris' Labyrinth (ML) and were observed that the group subjected to EE had a better performance to locate the submerged platform in the ML than the group not subjected to EE. After completing 120 days of life, without begin subjected to EE, the both groups were again tested on the ML and, was featured that, whilst the mean time of the group not subjected to EE was two times the time of the group subjected to EE, this difference was not statistically significant. The data indicates that EE favors the performance in terms of spatial memory, effect that, despite not being submitted to EE, lasts for long terms.

Cognition, Behavior and Memory
Poster Number 127 / Session 1

Practice in Native Sensorimotor Coordinates Interferes Anterogradely With Learning During Visuomotor Adaptation

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Motor adaptation is a type of motor learning that allows maintaining accurate movements in the presence of environmental or internal perturbations by creating new sensorimotor maps. A typical experiment involves a session of familiarization during which subjects move to a visual target in native -unperturbed- sensorimotor coordinates (null trials), followed by an adaptation session to a visual perturbation. Often, null trials are used in savings protocols for equating the initial error levels across adaptation and re-adaptation sessions, necessary for determining an improvement in the adaptation slope (savings). Recently we have shown that a relatively small set number of null trials (176) can interfere with memory retrieval, thereby reducing the amount of savings. Here, we aimed to investigate if, like perturbations, null trials can directly interfere with new learning. To test this hypothesis we trained two groups of naïve subjects on a visuomotor adapation task to an optical rotation of -40º (for 6 blocks of 88 trials per block). The experimental group previously performed a similar number of null-trials (7 blocks), whereas the control group performed only one block. These practice sessions were separated by 15 minutes. We found a decrease in the speed of learning in the Experimental relative to the Control group (Time-by-Group interaction; p=0.04). Our results support the idea that null trials form a memory that can interfere with memory retrieval and new learning.

Cognition, Behavior and Memory
Poster Number 128 / Session 2

Reversible amnesia induced by crowding, a naturalistic stressor

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After reversible amnesia, not expressed memories can be updated during reconsolidation. Because memories should be reactivated to reconsolidate, lack of expression can not be explained as a deficit in accessibility but in expression of reactivated traces. Searching for an adaptive value for mechanisms that allows the consolidation of accessible but inexpressible memory traces, we are studying the effects on memory consolidation of a naturalistic stressor: crowding.
In the Context-Signal Memory model in Chasmagnathus, a Visual Danger Stimulus (VDS) is associated with the training context. The constraints of a reminder to induce reconsolidation were well described in this model: a short non-reinforced re-exposure to the training context labilizes the memory, while presentation of the VDS after the same re-exposure time impedes the labilization of memory.
We found that four hours of crowding can block the expression of acquired performance in the long-term if the stressor is applied immediately after training but not before. Memory expression can be rescued after induced amnesia by a non-reinforced exposure to the training context, but not when the VDS is presented. Also, this effect is only seen in the long-term but not immediately after the induction of reconsolidation. These results support the idea that experiences close to learning can modulate how memories are going to be expressed in the future. However, unexpressed experiences must remain available for future evaluation.

Cognition, Behavior and Memory
Poster Number 129 / Session 3

Long term recovery from behavioral alterations induced by exposure to moderate noise levels

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Previous findings of our laboratory demonstrated that noise-exposed developing rats undergo extra-auditory behavioral alterations, mainly related to the hippocampus (HC) when evaluated 30 days after exposure. The aim of this work was to reveal if these changes persist until adulthood (90-days-old rats).
Male Wistar rats were exposed to white noise (95–97 dB SPL, 2 h daily) either for 1 day (acute noise exposure, ANE) or between postnatal days 15-30 (sub-acute noise exposure, SANE). 90-days-old animals were subjected to open field test (OF) to evaluate habituation memory, object recognition task (OR) to evaluate recognition memory and inhibitory avoidance device (IA) to evaluate associative memory, at short (ST, 1h intertrial) and long term (LT, 24h intertrial).
Results showed that exposure to moderate noise levels induced impairments in memory habituation of 30-days-old animals only at LT, which disappeared at 90 days. In addition, a deficit in ST and LT object recognition memory was observed a 30 days, that returned to control values at 90 days. Finally, SANE produced impairments in the performance in the IA test in 30-days-old animals at ST and LT, which were completely restored at 90 days.
These data suggest that exposure of developing rats to noise levels of moderate intensity (95–97 dB SPL) is able to trigger changes in memory processes depending on the HC that seem to be temporary.

Cognition, Behavior and Memory
Poster Number 130 / Session 1

Long-term memory formation of object in context task requires medial prefrontal cortex activity and it is interfered by another object in context experience

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Recognition memory refers to the ability to identify an object or a situation and judge if it was previously experienced or not. In particular, the recognition of an item in connection with a context (what-where) constitutes an important element of episodic memory, which also implies remembering about what-when.
Here, we reveal that the acquisition of information about object-context association put in risk the long-term memory (LTM) expression for a previously learned associate object-context pair. Also, we investigated the effective temporal window of that interference, the required features of the interpolated material to be effective, as well as the brain regions involved in the phenomenon.
Our results show that LTM formation for a novel object associated with a context (but not the object recognition LTM) can be impaired if rats are subsequently exposure to a different object in context experience. Thus, the second learning experience can exert retrograde interference over the first one, in a limited temporal window. Finally, our results strongly suggest that the medial prefrontal cortex and dorsal hippocampus are important brain regions involved in the processing of both pairs of association and when both of them are being consolidated at overlapping time course, a competition occurs and only one of them could be store.

Cognition, Behavior and Memory
Poster Number 131 / Session 2

Nuclear Factor kappa B transcription factor regulates zif268 expression during object recognition memory formation in mice

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Nuclear factor kappa B (NF-kB) is a transcription factor that plays a key role in the activity-dependent neural plasticity involved in memory formation. In this work, we studied the role of NF-kB in the downstream regulation of the gene zif268 during novel object recognition (NOR) memory consolidation in mice. zif268 is an immediate early gene involved in different types of memory formation that codes for the regulatory transcription factor ZIF268. Several studies use its expression as a marker of learning-induced activity in the brain. We found that ZIF268 protein levels in the mice hippocampus were increased forty five minutes after training in a NOR task, and returned to baseline levels three hours later. This increase was significantly reduced when an NF-kB inhibitor was injected locally immediately after training. Furthermore, inhibiting NF-kB activation or zif268 mRNA translation in the hippocampus lead to low levels of NOR performance, suggesting not only that both transcription factors are necessary for NOR memory formation but also that the hippocampus is a key structure involved in this process. Overall in this study we demonstrate the first evidence that NF-kB upregulates ZIF268 protein levels during NOR memory consolidation and we show that both proteins are involved in the formation of the object recognition memory trace. Ongoing experiments performing ChIP assays are aimed at evaluating if the upregulation by NF-kB is taking place directly on zif268 promoter.

Cognition, Behavior and Memory
Poster Number 132 / Session 3

Characterization of territoriality in a natural population of the electric fish, Gymnotus omarorum

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Non breeding territorial aggression is an uncommon feature whose underliyng mechanisms are under ongoing research in birds and mammals. The electric fish Gymnotus omarorum is a teleost species that displays non-breeding territorial aggression irrespective of sex, and thus constitutes an interesting model system to study the neuro-endocrine mechanisms of territoriality. With the aim of exploring the environmental and physiological drivers of territory value and individual spacing, we studied a natural population of G. omarorum during the non-breeding season. We carried out diurnal electrical census of 7 homogeneous sites in the littoral area of Lag. del Sauce, Uruguay; and performed ecological, morphological, and electrophysiological assays in 60 individuals. We also correlated plasmatic levels of steroid hormones with territory size, morphometric and physiological traits and environmental parameters. In a first attempt to characterize the species' habitat, we found that oxygen concentration and aquatic vegetation density are variables influencing spatial distribution of G. omarorum. In particular, oxygen saturation had a positive relationship with the territory size, stressing the importance of this parameter as indicator of territory value. A positive relationship between body size and territory size was found, while other variables such as in situ discharge frequency (indicator of social hierarchy) did not show significant correlation with territory size nor body size.

Cognition, Behavior and Memory
Poster Number 133 / Session 1

Can the mother's responses to aversive stimuli affect rat pups' fear expression?

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Rat pups do not show fear responses toward unfamiliar proestrous females (UPF). However, in the context of the home-cage, UPF represent an aversive stimulus for the mother that promote maternal aggression and alters maternal behavior. Since alterations of maternal behavior by the repeated exposure to an intruder promote pups' fear responses, we hypothesized that UPF can be conditioned as an aversive stimulus and exert fear responses in 8-day-old pups. To this aim, firstly we exposed mother-litters dyads in their home-cage to UPF inside a cage or an empty cage from postnatal days (PPD) 1-4. Then, 8-day-old pups from each sex and each experimental condition were exposed to an anesthetized UPF and the fear responses were registered. Only female pups expressed fear responses toward the anesthetized UPF (diminished ultrasonic vocalizations and increased immobility time). Secondly, to assess if fear responses toward the UPF were the result of a fear memory, UPF pre-exposed female pups were confronted to an anesthetized UPF on PPD8 and then injected with cycloheximide (CHX: 0.0, 0.2 mg/kg, sc.), a protein synthesis inhibitor that blocked the reconsolidation process. 24hs later they were re-exposed to an UPF and the fear responses were registered. CHX suppressed the expression of fear PPD9. These results suggest that pups can learn and avoid an aversive stimulus, probably as a consequence of changes in maternal behavior, and that these processes differ between sexes.

Computational Neuroscience
Poster Number 134 / Session 2

Development of a heterogeneous semi-dedicated low-cost cluster for modelling in neuroscience

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Developments of mathematical and computational models are required to study neuronal dynamics. According to the level of biological plausibility, these models can be very complex and, therefore, require a high computational capacity. This problem has been solved by using a computational cluster: the Cluster-Gemini (28 cores) which uses the computational resources originated during non-activity periods. The main advantage of a partially dedicated cluster is the use of pre-existing and recycled resources which in turn induce lower costs. The main aim of the proposed project is to generate computational support to the Laboratory for Biological and Artificial Learning (LBAL) of the Hospital Italiano of Buenos Aires in its research projects. We used Linux Centos 6.3, under the RocksCluster distribution as operative system. Thus, with Gemini we have simulated 200 photoreceptors, using 27 non-linear differential equations per each one, with a Runge-Kutta algorithm of fourth order in Matlab™ (Toolbox ODE 45). The results demonstrated that the period of time required for processing the data was 10 times less using the cluster than using a standard desktop. Nowadays, we are employing Gemini to simulate two layers of the entorhinal cortex of rodent with the Neuron software. We may conclude that, using this computational tool, we can develop new mathematical models that will help to understand the functional mechanisms of different brain areas.

Computational Neuroscience
Poster Number 135 / Session 3

Modeling the regulation of collective foraging in the honey bee Apis mellifera: a role for socially acquired memories

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Social insects colonies are complex systems with thousands of individuals organized in groups of differentiated behavior (division of labor), coordinated without centralized control by the transfer of information. It has been proposed theoretical approaches in order to understand how behaviors and social interactions are integrated giving place to collective phenomena. However, only recently and just a few works consider the role of learning and memory in these systems. Individuals perform different tasks as they age and foraging is among the last tasks that individuals carry out. Young individuals far from the nest entrance can access to chemosensory information about resources currently incoming, such as food odor, by extensive social interactions, like mouth-to-mouth contacts (trophallaxis). Experimental data show that individuals use long term associative memories of these experiences in earlier tasks for decision making when performing foraging tasks. Our model examines how this early experiences influence foraging behavior in an Apis mellifera colony. The use of this information biasing the behavior of individuals shows, in agreement with available data, that both in short and long term, individuals collecting known resources have more followers and receivers, with positive feedback of probability of recruitment displays , an issue that interferes with recruitment to new discovered food sources.

Computational Neuroscience
Poster Number 136 / Session 1

Mathematical model of the retinal physiology: the base for an artificial vision system

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The camera was the first artificial vision system that the human being designed. It consists of a system of lenses and a film where the light projects and forms an image through chemical processes. Time went by and the camera developed into the actual digital camera, which has the same system of lenses but a new system of array arranged diodes where the image is digitalized. Nature created a different and complex biological vision system to sense the outside world which outperforms the better digital camera on the actual market. To have a better comprehension of how the biological vision systems sample the outside world, we have to perform a deep understanding of the cells that compose the retina in order to figure out, in a more detailed way, how the living beings see. The current study presents the mathematical model of the cells that form the architecture of the retina; the first stage on visual processing systems. The conductance of each ion through the membrane of each cell is modeled with the Hodgkin and Huxley model in order to deeply understand how different cells work. The simulation in solitary of each cell is first performed with the aim to corroborate the behavior with electrophysiological registries; then a more elaborated model of the general architecture is carried out.

Computational Neuroscience
Poster Number 137 / Session 2

Photoreceptor absorption curves account for human chromatic discrimination ability

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Photoreceptors constitute the first stage in the processing of color information; many more stages are required before a human subject can consciously report whether two stimuli are perceived as chromatically equal or not. Therefore, although photoreceptor absorption curves are expected to condition conscious discriminability, there is no reason to believe that they should suffice to explain it. However, using information-theoretical tools, here we demonstrate that photoreceptor absorption properties predict the wavelength dependence of human color discrimination ability. The bottleneck in chromatic information transmission, therefore, seems to be determined by photoreceptor absorption characteristics. Subsequent encoding stages preserve the wavelength dependence of chromatic discriminability at the photoreceptor level. Our methodology also allows us to predict the discrimination ability of subjects with unusual cone distributions, as those observed in daltonism and tetrachromacy.

Computational Neuroscience
Poster Number 138 / Session 3

Computational Models and Theory Information Approach to Characterize a Dynamical Neural Network

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We consider a network of cortical neurons with axonal conduction delays and spike-timing-dependent plasticity, which is representative of a cortical hypercolumn. Each neuron is randomly interconnected to other neurons. The network model is based on the Simple Model of Spiking Neurons, by E. Izhikevich. This model reproduces spiking and bursting behavior of known types of cortical neurons and combines the biologically plausibility of Hodgkin-Huxley-type dynamics and the computational efficiency of integrate-and-fire neurons.
In our current work we use an information theory approach based on causal quantifiers (permutation entropy and statistical complexity) to characterize the dynamics of neural activity of a simulated population of neurons. We investigate the ordinal patterns of complex neural signals to estimate the optimal parameters of the neuronal network using causal Fisher information. This approach might become a useful tool to quantify the causal weight in the processing of informationwhen considering different areas of the cortex.

Computational Neuroscience
Poster Number 139 / Session 1

Phase-locking between individual spikes and the local field potential of hippocampal and entorhinal areas in behaving rats

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In rodents, hippocampal and entorhinal neurons encode the location of the animal in the environment. During exploratory behavior, these areas display EEG signals with prominent collective oscillations between 7 and 12 Hz (theta rhythm). By analyzing electrophysiological recordings obtained in awake, behaving animals, we determine the degree of phase locking between individual neurons and the theta rhythm, both in the hippocampus and the entorhinal cortex.

Computational Neuroscience
Poster Number 140 / Session 2

Spatially modulated balanced states

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Balanced networks provide a framework to understand the irregularity in the electrical activity of cortical neurons. Aimed at modelling optogenetic experiments, we stimulated a balanced network with spatially modulated stimuli. The firing rate as a function of the position in the network was computed and we also studied the conditions under which the network remains balanced.

Computational Neuroscience
Poster Number 141 / Session 3

A computational model on the goldfish Mauthner cell

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Integration of multimodal information is of key importance to generate adaptive behavior. However, our understanding of how multimodal integration is implemented at the dendritic level is still scant. We address this question in the Mauthner-cell, the "decision making element" of the startle escape network of goldfish. The Mauthner-cell has two main dendritic branches, lateral and ventral, where the former receives auditory input and the latter input from the visual system. Both dendrites are amenable to intracellular recording in vivo. Here, we used a Hodgkin-Huxley type of model with three voltage-gated ionic channels (one Na+ and two K+ channels) combined with an approximate model of the cell morphology to describe the cell behavior. We fitted the model parameters to intracellular recordings using two types of data: 1) Square pulses injected intracellularly at soma, and responses measured at the proximal lateral dendrite, and 2) Short excitatory pulses injected extracellularly at distal parts of the axon to induce an antidromic action potential, measured at the soma and several different locations along the dendrites. This model provides a simulation framework for testing the cell response to electrical input. Moreover, it will allow us to explore the conditions for successful signal propagation in the cell, such as determining whether purely passive dendrites are enough to explain its electrical behavior or if voltage-gated ion channels are necessary to describe it.

Computational Neuroscience
Poster Number 142 / Session 1

Measures of correlated activity, beyond pairwise interaction models

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To understand how information is processed by the brain we need to investigate how information is encoded by the activity of a population of neurons. Despite providing an accurate description of the neurophysiological behavior of the neurons in the retina, pairwise interaction models do not always provide a realistic characterization of the population dynamics in the cortex, and higher order interactions should be taken into account. In this work, we present an information theoretical approach by means of an analytically solvable model to formally estimate spike correlations up to third order within maximum entropy principle. Furthermore, we apply the current formalism to study functional interactions underlying the neural code dynamics in healthy and unhealthy tissue.

Computational Neuroscience
Poster Number 143 / Session 2

Electric fights: electroreception during agonistic encounters in Gymnotus omarorum

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Electric fish sense their environment by using passive and active electroreception. With passive electroreception fish perceive sources generated by other animals. With active electroreception fish perceive objects through the perturbation produced in the electric field generated by their own Electric Organ Discharge (EOD). The dynamics of agonistic encounters in Gymnotus omarorum showed that the evaluation phase lasts 30 s in average. Our working hypothesis is that G. omarorum uses active and passive electroreception to locate and assess its contender. To test this hypothesis, we modeled the passive and active electric images of dyads of electric fish during agonistic encounters using a computational method developed by our group. The data for these simulations were provided by two set of experiments. To analyze the approaching trajectory, we used 6 dyads of G. omarorum in an experimental tank of 110cm x 80cm x 25cm (big arena). To analyze the assessment strategy we used 6 dyads of G. omarorum in an experimental tank of 55cm x 40cm x 25cm (small arena). Fish used electroreception in the evaluation and location of their potential contenders, confirming that electroreception is the fundamental sense modality in this nocturnal species, even in complex social behaviors. We also found that the modification of the size of the experimental arena changed the dynamics of agonistic encounters.

Computational Neuroscience
Poster Number 144 / Session 3

The cells of the electrosensory lobe: connectivity, firing patterns and electrosensory modulation

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INTRODUCTION and METHODS. Weakly electric fish Gymnotus omarorum emits a pulsatile and stereotyped electric organ discharge (EOD) to sense the surrounding. The Electrosensory Lateral Lobe (ELL) is the first neural relay that processes self-generated electrosensory information. It is a cerebellum-like structure in which the cell physiology of its components and their behavior as a network are still poorly known. To unveil these subjects we are applying classical histology and tract-tracing techniques, extra and intra cellular cell recording methods, and developed a new method to record unitary activity in the chronically implanted, freely moving fish. Here we report ongoing results on the anatomy and physiology of the ELL neurons and their response to natural and artificial stimuli. RESULTS. We found several types of cells in the ELL and describe the external projection of some of them to the pra-eminentialis, torus semicircularis and contralateral ELL. In vivo, all units show a characteristic post-EOD probability profile, derived from a sparse response to the EOD. Four main profiles can be described: a) tightly phase locked; b) unimodal excitation c) inhibition; and d) multimodal excitation-inhibition patterns. Depending on the effect of the stimulus placed at the center of the receptive field we identified two types of cells, â€œcenter onâ€ and â€œcenter offâ€. These cells show opposite modulation by non-conductive and conductive objects. The effect of the stimulus intensity and pattern was different on the different neurons. While some of the cells are plastic, others are followers of the stimulus intensity. CONCLUSION. The electrosensory lobe shows a multiplicity of neuron types showing as a common denominator the presence of post-EOD probability firing patterns. These characteristics suggest that although morphology is similar to wave Gymnotiform species, sensory processing is alike to the African pulse mormyrids.

Computational Neuroscience
Poster Number 145 / Session 1

Time-Frequency analisys for patterns detection of neural code on multifiber recordings

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The vibrissae system is mainly formed by vibrissae or tactile hairs (located at both sides of the animal's snout) through which obtain tactile information. Such information transduction occurs in vibrissae follicles, while transmission is performed by the trigeminal nerve (peripheral) to the brainstem, soon to take various paths to the thalamus and cortex. Electrophysiological and behavioral studies in tactile discrimination agree in that the rats can distinguish surfaces of different roughness by whisking their vibrissae. Currently, tactile discrimination studies involve experimental protocols with high degree of specificity (simple stimuli, single-cell recordings in very specific places on the sensorial path), decreasing the big amount of involved variables in this complex sensorial task. With this, the inference of the results to the functional understanding of the system, may be complex. This work has proposed to implement a experimental protocol to capture the afferent information of the vibrissae innervation between different frictional situations (complex stimulus). An alternate method has been proposed to analyze the tactile information in the afferent nerves based on time-frequency plots and statistical methods. These procedures allowed to infer about possible codification schemes and the discrimination degree at peripheral level. The method´s results proposed were compared with the ones obtained from others authors showing the advantages and disadvantages of itself.

Motor Systems
Poster Number 146 / Session 2

Motor control of sound frequency in birdsong emerges from the synergistic interaction between different physiological parameters

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Oscine birds share with human the rare capacity of having learned vocalizations. Consequently, the study of birdsong has become a favorite animal model for studying this complex, learned, motor behavior.
Birds vocal organ, the syrinx, is a non-linear biomechanical device capable of producing a wide variety of sounds by means of the oscillation of a pair of vibrating tissues (known as labia) which are controlled by a set of intrinsic and extrinsic muscles. Sound generation involves respiratory control for generating airflow, control of the vocal organ to position the labia and regulate their tension as well as upper vocal tract structures to adjust the filter properties.
In this work, we explore different dynamical models of sound production that accounts for these biological features of the syrinx, in particular for canary's song (Serinus Canaria).
We use experimental and theoretical tools to test the hypothesis that the phonology of bird song production emerges from the synergistic action of different physiological gestures. For different models, we describe the structure of the isofrequency curves, which are sets of parameters leading to sounds presenting the same fundamental frequencies.
We discuss how different nonlinear effects affect their shapes, and report experiments that allow unveiling their features.

Motor Systems
Poster Number 147 / Session 3

A Mechanism for Frequency Modulation in Songbirds Shared with Humans

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In most animals that vocalize, control of fundamental frequency is a key element for effective communication. In humans, subglottal pressure controls vocal intensity but also influences fundamental frequency during phonation. Given the underlying similarities in the biomechanical mechanisms of vocalization in songbirds and humans, songbirds offer an attractive opportunity to study frequency modulation by pressure. Here, we present a novel technique for dynamic control of subsyringeal pressure in zebra finches. By regulating the opening of a custom-built fast valve connected to the air sac system, we achieved partial or total silencing of specific syllables. We also observed that more nuanced pressure variations over a limited interval during production of a syllable concomitantly affected the frequency of that syllable segment. These results can be explained in terms of a mathematical model for phonation that incorporates a nonlinear description for the vocal source capable of generating the observed frequency modulations induced by pressure variations. We conclude that the observed interaction between pressure and frequency was a feature of the source, not a result of feedback control. Thus, although there are separate brainstem pathways for syringeal and respiratory control of song production, both can affect airflow and frequency. We hypothesize that the control of pressure and frequency is combined holistically at higher levels of the vocalization pathways.

Motor Systems
Poster Number 148 / Session 1

Time course of motor memory consolidation in visuomotor adaptation

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In motor adaptation process our motor system adjusts movements to a novel environment. Although evidence points to the formation of long-term motor memories for this type of learning, several studies have failed at characterizing the time course of memory consolidation using behavioral protocols of retrograde interference. The present study approaches this issue through a protocol of anterograde interference (AI). Subjects performed pointing movements to targets displayed concentrically around the start position using a joystick. They adapted sequentially to two types of visuomotor rotations, which shifted the position of the cursor on the screen by 30º. Participants experienced a 30º visuomotor rotation (A), followed by a -30º visuomotor rotation (B). Considering the interval between A and B six groups were defined: 1min, 15min, 1h, 3h, 5,5h and 24h. This protocol allowed us to estimate the amount of memory consolidation based on the AI of the memory A on B throughout time. Both memory retention of A and rate of learning of adaptation to B were computed. The results showed strong AI at 1min, 15min and 1h that subsides at 3h and 5.5h, when the speed of learning was not different from that of A. Interestingly, AI re-emerges 24h later, although to a lesser extent. These results suggest that memories formed during visuomotor adaptation undergo an initial phase of consolidation that ends approximately 1h after the offset of learning and a 2nd phase of consolidation overnight.

Motor Systems
Poster Number 149 / Session 2

Neural control of ankle isometric torque

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A classical problem in motor control is to explore how the nervous system deals with the large number of degrees of freedom during force and movement generation. Our aim was to test the following hypotheses: 1) there are preferred muscle activation patterns to achieve a constant force during joint isometric action; 2) these patterns are dependent on chosen joint angle; 3) these patterns are modified by elongation maneuvers. In 2 tasks we simultaneously recorded the electromyographic activation pattern of the ankle muscles while angle and torque were maintained constant: a) the subject was instructed to voluntarily change the activation pattern while maintaining the torque. b) the pattern was the natural that subjects unconsciously chose. The electromyogram space was largely covered voluntarily. However, when freely performing the isometric force task, the chosen patterns showed characteristic co-activation patterns following specific trajectories for flexion and extension. These trajectories were shifted by changing the joint angle and elongation maneuvers. Using a simple model representing the muscles as springs whose resting length and stiffness may be controlled by electromyogram signals, we reproduced the obtained patterns and their changes with angle and elongation. Our results may imply a neural adaptation in response to the changes introduced by these maneuvers either in the passive stiffness curve of the muscle or in the explored point along this curve.

Motor Systems
Poster Number 150 / Session 3

Preliminar Electrocorticographic Study of Normal and Abnormal Gait in rats

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Electrocorticography (ECoG) is one of the main tools for the analysis of electrophysiological manifestations in the brain, evoked by sensory and motor activities. This work studies the electrocortical manifestations evoked by the normal and abnormal rat's gait. Adult Wistar female rats were used and performed to chronic nichrome electrode implants in the primary motor cortex (one in each hemisphere). Electrodes were implanted in specific locations of the primary motor cortex corresponding to the maximum sensitivity area for a given motor evoked response. Locations were determined by a topographic mapping technique with intracortical stimulation (ICMS). Was designed a sliding platform in which the normal gait of the rats was carried out. An abnormal gait was achieved anesthetizing the left hindlimb of the rat. ECoG records were obtained through a BIOPAC system at 500Hz sampling rate and bandwidth of 0.05Hz to 250Hz. Subsequently, a time-frecuency analysis was performed to the ECoG records in both experimental situations. Results show temporal and spectral patterns evoked by the normal gait, which significantly changed during abnormal gait.

Motor Systems
Poster Number 151 / Session 1

CSF Trace-Elemental Analysis of Amyotrophic Lateral Sclerosis Patients by X-Ray Microfluorescense Whith Synchrotron Radiation

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Amyotrophic Lateral Sclerosis (ALS) is the most common adult-onset motor neuron disease but its etiology still remains a mystery. Analysis of biological samples provides a powerful strategy for investigating pathological processes and extensive studies indicated an important role of trace elements in ALS disease. We investigated trace element levels of ALS CSF samples. ALS (10) and control (6) CSF samples were treated for trace elemental analysis by X-ray microfluorescence with synchrotron radiation. Measurements were carried out at the XRF beam line at the Synchrotron Light National Laboratory (Campinas, Brazil). In this study, the following elements were analyzed: aluminium, bromine, calcium, chlorine, copper, chromium, iron, potassium, phosphorus, nickel, rubidium, silicon, sulfur and zinc. In ALS CSF samples we observed significative increased concentration of calcium, chlorine and potassium when compared to control samples. Excitotoxicity is one of many factors implicated in ALS pathogenic process. The intracellular calcium influx seems to contribute to neurodegeneration in multiple pathways, conducing cell to death. Activation of potassium and chlorine channels by increased calcium level was already described and prolonged efflux of both could be involved in apoptosis. The elevated levels of these three elements in CSF can reflect an abnormal activation of potassium and chlorine channels, indicating a possible molecular pathway involved in ALS pathogenic process.

Motor Systems
Poster Number 152 / Session 2

Reconstructed motor gestures unveil different dialects in Zebra Finch songs

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Songbirds are an ideal animal model for studying the mechanism that are involved in the learning, control and production of a complex behavior.
Our group has been developing in the last years mathematical models describing the biomechanics of the avian vocal organ, including the motor gestures that control both the sound source and the vocal upper tract.
In this way we reduce the dimensionality in the description of the singing dynamics, giving rise to a description of the behaviorin terms of simple motor gestures. In this work we implement this model and apply it songs from birds from different Zebra Finch colonies. We report that many of the features of the reconstructed motor gestures were present in all the colonies. Others ,were present in only one of them, giving rise to different dialects in the Zebra Finch song. In this way, we provide a quantitative tool to address the issue of which of the components needed to achieve this complex behavior present signatures of learning.

Motor Systems
Poster Number 153 / Session 3

Extinction interferes with the retrieval of visuomotor memories through a mechanism involving the sensorimotor cortex

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Savings is a fundamental property of learning. In motor adaptation, it refers to the improvement in learning observed when adaptation to a perturbation A (A1) is followed by re-adaptation to the same perturbation (A2). A common procedure to equate the initial level of error across sessions consists of restoring native sensorimotor coordinates by inserting null -unperturbed- trials (N) just before re-adaptation (washout). Here we hypothesized that the washout is not innocuous but interferes with the expression of the new memory at recall. To assess this possibility, we measured savings following the A1NA2 protocol, where A was a 40 degree optical rotation. We have previously shown that the washout reduces the level of savings measured based on an exponential fit of the initial portion of learning. Here, we investigated the anterograde effect of the washout on later stages of adaptation. For this purpose, we used a different analytical approach based on the cumulative percent increment in learning. This metric is more sensitive to detect savings towards the last portion of training, when differences in slope are rather small or undetectable. Our results indicate that the washout interferes with memory retrieval throughout the whole learning sessions. We speculate that this pattern reflects the consolidation of a memory for null trials into re-adaptation.

Neural Circuit Physiology
Poster Number 154 / Session 1

Compensatory changes occurring in medial prefrontal cortex (mPFC) through adolescence leads to an underconnected adult circuit in a mouse model of schizophrenia

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Ablation of NMDA receptors (NMDAr) in cortical and hippocampal parvalbumin interneurons during early postnatal development results in schizophrenia-like phenotypes after adolescence in mice. This delayed onset reflects an interaction between NMDAr ablation and normal development occurring during adolescence. mPFC circuit undergoes refinement during adolescence, with synaptic pruning of local and distant inputs, including hippocampal ones. To elucidate the pathophysiological changes leading to the observed phenotypes in our schizophrenia mouse model we analyzed the functional connectivity between ventral hippocampus (vHP) and mPFC before and after adolescent maturation. We evaluated the amplitude of the short latency evoked response in the local field potential recordings from mPFC to different stimulation intensities in vHP in anesthetized juvenile and adult, control and mutant mice. To explore circuit plasticity we used LTP/LTD stimulation protocols. KO mice present normal functional connectivity in juvenile stages that deteriorates in adulthood, evidenced by a diminished maximal evoked response. KO mice also present opposite alterations in plasticity forms before and after adolescence, with a higher susceptibility towards LTP in juveniles and LTD in adulthood. We propose that early ablation of NMDAr in interneurons triggers compensatory changes during normal development taking place during adolescence and resulting in an under connected mPFC circuit in adults.

Neural Circuit Physiology
Poster Number 155 / Session 2

Divergent neuronal circuitries underlying orexigenic effects of circulating or cerebrospinal fluid ghrelin: critical role of brain accessibility

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Ghrelin is a hormone that stimulate food intake via activation of growth hormone secretagogue receptor (GHSR). This study was aimed to delineate the neuronal circuits that mediate the orexigenic effect of ghrelin. First, we analyzed the c-Fos induction in the brain of mice centrally or systemically treated with ghrelin. We found that peripherally administrated ghrelin dose-dependently increased food intake and number of c-fos positive cells in the hypothalamic arcuate nucleus (ARC) and solitary tract nucleus. In contrast, centrally administrated ghrelin increased food intake and number of c-fos positive cells in most nuclei expressing GHSR. To determine which nuclei are directly affected by ghrelin, we centrally or systemically injected mice with fluorescein-ghrelin (F-ghrelin). We found that peripherally injected F-ghrelin only accessed to the ARC while centrally injected F-ghrelin reached most GHSR-expressing brain areas. Then, we tested ghrelin effects in ARC-ablated mice. These mice failed to respond to peripheral ghrelin but fully responded to centrally administrated ghrelin. ARC-ablated mice showed similar ghrelin-induced c-fos expression as seen in control mice, but in the ARC, where no c-Fos was found. Thus, circulating ghrelin mainly accesses to the ARC, which is required for orexigenic effects of the hormone. Cerebrospinal ghrelin accesses to a variety of nuclei, which can mediate the orexigenic effects of the hormone even in the absence of the ARC.

Neural Circuit Physiology
Poster Number 156 / Session 3

Unraveling the excitatory pathway of a neuroautonomic regulation in the crab Neohelice granulata

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The fear, flight or fight response serves as the fundamental physiological basis for examining an organism's awareness of its environment under an impending predator attack. Although it is not known whether invertebrates posses an autonomic nervous system identical to that of vertebrates, evidence shows invertebrates have a sympathetic parasympathetic-like response to regulate the internal environment and ready the organism to act behaviorally to a given stimuli. The goal of this work (which is still in progress) is to examine the excitatory neural and neurohormonal extrinsic pathway that modulates the cardiac response in the crab Neohelice. The immunohystochemical localization of tyrosine hydroxylase has revealed the presence of dopaminergic processes restricted mainly to the Y-shaped ganglionic trunk and forming a network around the large neurons. Injection of any one of the three aminergic neurohormones (OA, DA, and 5-HT) into resting animals brought about a significant increase in the heart rate that was maintained for more than 30 min. Furthermore, as this physiological response can be feasibly measured and acts as a biological index for the animal's internal state we mean to examine the autonomic response during social interactions and environmental disturbances that may increase heart rate taking into account that environmental stimuli of diverse modality previously tested have proven to result cardio inhibitory.

Neural Circuit Physiology
Poster Number 157 / Session 1

The synaptic connectivity of the PDF circuit suffers circadian structural remodeling

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In our laboratory we are interested in understanding the relevance of specific neuronal circuits in the circadian control of behavior in Drosophila. We have previously shown that sLNvs neurons, a circuit key to control rest-activity cycles in Drosophila, undergoes circadian remodeling of its axonal projections, and we have put forward the hypothesis that this structural plasticity provides the substrate for the circadian control of activity and connectivity of the PDF circuit. Here we show that this remodeling implies daily changes in presynaptic markers of active zones, opening the possibility that the connectivity is indeed changing daily. By expressing two complementary fragments of GFP tethered to synaptic membranes, we revealed that PDF axons contact different synaptic partners along the day, extending the impact of core pacemaker neurons to circuits outside of the circadian network. We propose that this plasticity is capable of affecting the synaptic output in a circadian fashion, by means of these structural changes. In order to test this hypothesis we are currently performing live whole brain optical imaging experiments to test if the putative synaptic partnerships identified through GRASP are indeed functional. To answer this question we will use two binary systems of expression such as GAL4/UAS and lexA/lexAop that will allow us to specifically activate the PDF neurons, while concomitantly expressing a reporter of activity on the putative post synaptic partners.

Neural Circuit Physiology
Poster Number 158 / Session 2

Detection of Beta oscillation in Striatal and Motor Cortex in freely moving mice

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A wide range of oscillatory phenomena is present in the Basal Ganglia. Different rhythms occur during exploration and may play a key role in the coordination of neural circuit dynamics. We focus our attention on Beta oscillations since they are a prominent rhythm in the Basal Ganglia and enhancement of this frequency range is described in Parkinson's disease. In this study we introduce a practical method to identify and analyze beta events (oscillations between 15 and 25 Hz). The method combines both Fourier- and Hilbert-based signal analysis increasing thus method's precision.

By means of 4-wire-electrodes (tetrodes) we acquired field potential activity in the Striatum and Motor cortex simultaneously. By applying this method we were able to specifically separate oscillations in the beta range from other oscillations (i.e. gamma oscillations -30 to 90 Hz). Then we looked for behavioral parameters correlating with beta oscillatory activity (i.e. movement onset). Furthermore, we plan to analyze the relationship of beta oscillations with other oscillations.

These results are the first steps in a better understanding of these phenomena and in a more general view will allow us to understand how different Basal Ganglia oscillations play a role in the coding of cortical information during the performance of various tasks.

Neural Circuit Physiology
Poster Number 159 / Session 3

Functional disconnection of striatal projection neurons of the direct pathway

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Although changes in the input connectivity to striatal projection neurons (MSNs) could be involved in the appearance of clinical manifestation of Parkinson's disease, how they correlate with different stages of dopaminergic depletion has not yet been evaluated. We used mice expressing fluorescent proteins under the control of the D1 and D2 dopamine receptors to identify neurons belonging to direct (D1-MSN) or indirect (D2-MSN) pathways. Immunohistochemical analyses show that Drd1-td tomato and Drd2-EGFP report D1 and D2 MSNs with high selectivity. We performed in vivo juxtacellular recordings in order to study the responses of striatal neurons to frontal cortex and thalamic stimulation in control, partially and fully dopamine depleted mice under anesthesia. In control animals, D1-MSNs respond more to cortical stimulation than D2-MSNs despite their lower intrinsic excitability ($p<0.05$; Day et al., J Neurosci 2008). Moreover, severe dopamine depletion markedly increases D2-MSNs responses to cortical and thalamic stimulation and decreases D1 MSNs responses as predicted by basal ganglia models. Preliminary findings show that D1-MSNs are less responsive to their main glutamatergic input after partial nigrostriatal lesions compared with sham. Overall, D1-MSN disconnection from their inputs emerges as a key factor in Parkinson's disease pathophysiology

Neural Circuit Physiology
Poster Number 160 / Session 1

Analysis of Brain Nuclei Accessible to Ghrelin Present in the Cerebrospinal Fluid

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Ghrelin is a stomach-derived peptide hormone that acts in the brain to regulate many important physiological functions. Ghrelin receptor, named the growth hormone secretagogue receptor (GHSR), is present in many brain areas with or without obvious direct access to ghrelin circulating in the bloodstream. Ghrelin is also present in the cerebrospinal fluid (CSF) but the brain targets of CSF ghrelin are unclear. Here, we studied which brain areas are accessible to ghrelin present in the CSF. For this purpose, we centrally injected mice with fluorescein-labeled ghrelin (F-ghrelin) peptide tracer and then systematically mapped the distribution of F-ghrelin signal trough the brain. Our results indicated that centrally injected F-ghrelin labels neurons in most of the brain areas where GHSR is present. Also, we detected F-ghrelin uptake in the ependymal cells of both wild type and GHSR-null mice. We conclude that CSF ghrelin is able to reach most of brain areas expressing GHSR. Also, we propose that the accessibility of CSF ghrelin to the brain parenchyma occurs through the ependymal cells in a GHSR-independent manner.

Neural Circuit Physiology
Poster Number 161 / Session 2

Characterization of neuronal activity of the striatum during a habit-inducing learning task

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Habits involve a structured action sequence that can be elicited by a particular context or stimulus. They are acquired by experience-dependent plasticity and once fixed, they are performed almost automatically. It is currently thought that synaptic plasticity in the striatum, the entrance gateway for cortical inputs to the basal ganglia, mediates habit formation. Theory says that signals produced by mesencephalic dopaminergic neurons and striatal cholinergic interneurons in response to reward related cues induce such plasticity and are essential for habit formation.

With the aim of characterizing striatal activity during the acquisition of a rewarded conditioning task, we recorded the local field potential and unit activity in the striatum of freely moving rats during task learning. Trials were initiated by a light signal delivered after a nose-poke. Water-deprived rats were rewarded with a drop of water in 50% of the trials after completion of eight licks, and could initiate a new trial after a two second interval. We are analyzing neuronal activity in relationship with different events of the task, like reward delivery and reward expectancy, and events occurring outside the task like impulsive nose-pokes during the ITI. Also, we study behavioral parameters of the task related to learning at different stages of training.

We plan to study task learning and neuronal activity in adolescent and adult rats under the hypothesis that behavioral control is immature in adolescents

Neural Circuit Physiology
Poster Number 162 / Session 3

Noradrenergic-dependent modulation of prefrontal cells activity in awake rats

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The prefrontal cortex (PFC) is a region within frontal cortex formed by a network of neurons connected to virtually all sensory and motor systems and some subcortical systems. One of the main functions of this cortex is to –along with other brain structures- organize behaviour in time, i.e. executive functioning. Attention, planning, task switching, decision making, are examples of executive functions that together determine the sequential organization of behaviour.
The locus coeruleus (LC) is a noradrenergic brainstem structure and the sole source of noradrenaline (NA) to the neocortex. One of its functions is to regulate waking and arousal by changing the level and mode of LC activity. During focused attention, LC cells exhibit phasic activation for target stimuli and a moderate level of tonic discharge whereas in inattentive states there is a very low level LC activity in general.
To further understand the role of the PFC in learning and decision making, single cell activity was recorded in awake rats, using a head restrained paradigm previously developed by our group. Local administration of drugs at the PFC was made through a novel arrangement of a glass electrode attached to the two wire-hexodes responsible for activity recording.
In this work we show how the activity of PFC neurons is affected under local delivery of yohimbine, a α2A noradrenergic receptor antagonist, whose action resembles the effect of a reduction of noradrenaline release in an attentional state.

Neural Circuit Physiology
Poster Number 163 / Session 1

Analysis of the GABAergic synaptic Inputs into mice Lateral Habenula

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Lateral Habenula (LHb) is a small epithalamic structure that exerts a powerful control over dopaminergic brain stem centers and conveys negative motivational signals. Physiological information about synaptic transmission in the LHb is scarce; particularly there is no information about physiology of inhibitory afferences over LHb. In this work we have begun to characterize them. We found inhibitory synapses over LHb to be clustered in two subpopulations one of big quantal size and another one of lower quantal size. High quantal size inhibitory synapses were present in half of the LHb recorded neurons, these neurons were also characterized by a higher frequency of spontaneous inhibitory synaptic currents. Functional consequences of activation of this high quantal inhibitory input are discussed.

Neural Circuit Physiology
Poster Number 164 / Session 2

Synaptic engineering: an ionic switch of behavior

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The unraveling of the human brain connectivity map is considered as an essential step in the understanding how the brain controls behavior. However, the connectivity map does not carry information about the sign of synaptic connections. Is it possible to reverse the behavioral output of a circuit by changing the sign of a synapse? Does the sign of a synapse provide constraints to the development and the specification of a connectome? Here, we address these questions using the neuronal circuit of the C. elegans escape response in which tyraminergic neurons coordinate the suppression of head movements with backward locomotion through the activation of the tyramine-gated Cl- channel LGC-55. Amino acid substitution allowed us to change the selectivity of LGC-55 from Cl- to Na +. Localization of LGC-55 cation channel is indistinguishable from wild-type LGC-55. Exogenous tyramine induces neck muscle relaxation and backward locomotion in wild-type worms, but induces neck muscle contraction and forward locomotion in transgenic animals that express the LGC-55 cation. Similarly, touch or optogenetically induced release of endogenous tyramine triggers opposite behavioral responses in animals that express the LGC-55 cation vs LGC-55 anion channel. Our data show that changing the nature of a synapse within a neural circuit can reverse its behavioral output and indicate that the C. elegans connectome is established independent of the nature of synaptic activity or behavioral output.

Neural Circuit Physiology
Poster Number 165 / Session 3

Neuronal Activity of the Interoceptive Insular Cortex in the Innate Fear

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Dozens of interoceptive receptors distributed in nearly every structure of the body send projections to the interoceptive pathway, and the insular cortex (IC) is the highest brain region in a hierarchy of nuclei and areas involved in the processing information about bodily needs and emotions. However, the function of IC in innate fear remains unknown. We tested the idea that the interoceptive IC (pIC) has a role in the expression of innate fear. To evaluate this hypothesis we exposed rats to cat fur odor, and evaluated their defensive behaviors: freezing, risk assessment, defensive attack, grooming, contact and exploration. Significantly stronger freezing and diminished defensive attack responses were observed in rats exposed to cat odor. We found a significant increase in Fos-ir neurons in both rostral IC and pIC as well as in subcortical nuclei involved in responses to a predator. We inactivated pIC with Neosaxitoxin, a long term Na+ channel blocker, immediately after the first exposure to the cat odor. We observed that pIC inactivation significantly decreased freezing behavior in all subsequent tests. The inactivation of pIC had no effect on defensive attack behavior. Ours results support the involvement of the neuronal activity of the pIC in the perception and expression of innate fear.

Neural Circuit Physiology
Poster Number 166 / Session 1

Neural circuits underlying motor behavior in the leech

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Crawling is a rhythmic locomotive behavior that the leech undertakes in shallow water and results from alternation between shortening and extension of the body. These movements are achieved by contraction and relaxation of longitudinal and circular muscles. The dorsal excitor 3 (DE-3) motoneuron (MN) and the circular ventral (CV) MN innervate these muscles, respectively.

The network underlying crawling is poorly understood. The goal of the present project is to study the structure of the central pattern generator (CPG).

Crawling can be induced in the isolated nerve cord using dopamime. The DE-3 MN activity is recorded extracellularly in the DP nerve and CV MN activity through intracellular recordings.

Previous results suggest that the MNs could be part of the CPG. We have observed that manipulations of the motoneurons AE and CV membrane potential affect the motor pattern indicating that these MNs are part of the CPG of crawling.

To be considered part of a CPG a neuron must oscillate with the motor pattern and must be capable of resetting the rhythm. We have done phase response curves analysis (PRC) that demonstrates that CV is part of the CPG.

Neural Circuit Physiology
Poster Number 167 / Session 2

Broadcasting from adult-born dentate granule cells to the hippocampal circuitry

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The dentate gyrus of adult mammals is a neurogenic region that continuously generates dentate granule cells (DGCs). New DGCs migrate, develop and integrate into the circuitry during a period of 6 to 8 weeks. Recently, we have proved that 4-week-old (immature) DGCs display low threshold for activation and high associativity to incoming inputs. Yet, the functional implication of these findings depends on the ability of immature DGCs to deliver information onto the target areas, and on the nature of the transmitted message. We are currently investigating whether immature DGCs can convey information to the hippocampal network and the nature of those signals. We combine retroviral transduction of neuronal progenitors with optogenetics to obtain cohorts of immature DGCs expressing channelrhodopsin-2 (ChR2). ChR2-DGCs can be activated by brief pulses of blue light delivered by a laser source. Acute hippocampal slices containing ChR2-DGCs were prepared and voltage clamp recordings were performed onto pyramidal neurons in CA3 and mature DGCs in the granule cell layer to monitor light-evoked postsynaptic currents (PSCs). In CA3 pyramidal neurons, light stimulation evoked excitatory and feedforward inhibitory PSCs, whereas mature DGCs only evidence light-induced feedback inhibition. Further experiments to establish the contribution of different cohorts of adult-born DGCs to information processing are currently underway.

Neural Circuit Physiology
Poster Number 168 / Session 3

Strategies of axonal guidance: study of commercial technologies

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The present work evaluates the cellular differentiation of a neuroblastoma (SH-SY5Y) to a neuron and its axonal guidance using physical and electrical methods. This include the use of gradient of pressure with commercial microfluidic chambers (E2dish and Axis chambers) and the use of electrical field employing commercial micro electrode array (MEAs) and silver electrode. Working on MEAs, we trying out different cleaning techniques and different coating, and cultures survived no more than a week. In the assay with the E2dish, only the 0.5% of the micro channels were occupied by a neurite, and the cells near to the channels died. On the Axis chambers, despite of cells died as in the previous case, at list the 10% of all the micro channels were occupied by neurites. Finally, proving silver electrodes, we stimulate with a weak electric field (pulse train of 10s and 50mV of amplitude), at list the 40% of the cells lined to the electrical field. As cells were not confined as in the previous cases, we avoid the apoptosis process related to the lack of space to grow. These factor, give enough time to finish the differentiation treatment. By the foregoing, electrical stimulation evidence that is, to our goal, the most appropriated technique, moreover it is not expensive and easily to apply method.

Neural Circuit Physiology
Poster Number 169 / Session 1

High Fat Diet Bingeing Activates the Mesolimbic Circuit and Requires the Orexin Signaling

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Many people suffering eating disorders display binge eating episodes, in which an excessive amount of palatable foods is rapidly consumed. Currently, little is known about the neuronal circuitries recruited by the acute ingestion of a rewarding stimulus. Here, we used a combination of immunohistochemistry, pharmacology and neuronal tracing analyses to examine the role of the mesolimbic system, in general, and the orexin neurons, in particular, in a simple experimental paradigm in which naïve mice are allowed to spontaneously eat a pellet of a high fat diet (HFD) for 2 h. We found that acute HF intake activates c-Fos expression in several reward-related brain areas. We also found that: i-HFD-mediated orosensory stimulation was required for the mesolimbic pathway activation, ii-acute HF intake activates dopaminergic neurons of the paranigral, parabrachial pigmented and interfascicular sub-regions of the ventral tegmental area (VTA); and iii-orexin neurons of the lateral hypothalamus (LHA) are responsive to acute HF intake. In addition, we found that orexin signaling blockage, with the orexin 1 receptor antagonist SB-334867, reduces acute HF intake and c-Fos induction in the VTA but not in other mesolimbic nuclei. Finally, we found that most orexin neurons responsive to acute HF intake innervate the VTA. Our results show that HFD binge recruits the mesolimbic system and that the manifestation of this eating behavior requires activation of the orexin signaling.

Neural Circuit Physiology
Poster Number 170 / Session 2

Synergistic role of synaptic plasticity and adult neurogenesis in dentate gyrus circuit remodeling

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Long-term potentiation (LTP) of synaptic transmission in the hippocampus is the primary experimental model for investigating the synaptic basis of learning and memory in vertebrates. In addition, during the past several years, evidence has accumulated suggesting a relationship between immature granule cells (GCs) born in the adult hippocampus and various types of hippocampus-dependent learning and memory formation. Mounting evidence that immature GCs are possibly more "excitable", with a stronger propensity for long-term potentiation than fully mature GCs, suggests that these cells may have a unique role in the processing of the dentate gyrus circuit. One hypothesis is that because of their unique physiological properties, developing adult-born neurons transiently serve as major mediators for experience-driven plasticity and become selectively integrated as special units within the adult circuitry where they contribute to specific brain functions over the long term. We set out to study the characteristics of activity-mediated synaptic plasticity revealed at level of neuronal ensembles, emphasizing the differences between the immature GCs and fully mature GCs that may be the basis for differential functional roles of these distinctive neuronal populations. For this purpose we are currently working in hippocampal slices from adult mice injected with a retrovirus to express RFP in newborn GCs. We are now combining calcium-imaging techniques with electrophysiological recordings to monitor changes in the activation profile of ensembles of young and mature neurons after induction of LTP by means of medial perforant path stimulation. We will then investigate the specific microcircuits underlying this type of network plasticity.

Neurochemistry and Neuropharmacology
Poster Number 171 / Session 3

Stoichiometry for Activation of Neuronal α7 Nicotinic Receptors

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Neuronal α7 nicotinic receptors are homopentameric ligand-gated ion channels (LGICs) that participate in cognition, synaptic plasticity and neuroprotection, and have emerged as therapeutic targets for treatment of neurological disorders. α7 often localizes distal to sites of nerve-released ACh, binds ACh with low affinity, and thus elicits its biological response with partial occupancy of its five identical binding sites. We therefore addressed the question of how α7 operates at these physiological conditions. To assess function of α7 when neurotransmitter occupies fewer than five binding sites, we generated α7 receptors with a different number of functional neurotransmitter binding sites. By measuring open-channel lifetime of individual receptors, we found that only one occupied site allows maximal response and that the additional sites allow enhanced agonist sensitivity. In contrast to α7, we found that open-channel lifetime of a receptor formed by the extracellular domain of α7 and the transmembrane region of 5-HT3A (α7-5HT3A) is dependent on the number of functional binding sites. Our results reveal that: i) the agonist binding domain is not sufficient to determine the relationship between agonist occupancy and open-channel stability and, ii) the distinctive ability of a single occupancy to elicit a full biological response adapts α7 to volume transmission, a prevalent mechanism of ACh-mediated signaling in the nervous system and non-neuronal cells.

Neurochemistry and Neuropharmacology
Poster Number 172 / Session 1

Stress and vulnerability to develop cocaine addiction: role of glial proteins in nucleus accumbens plasticity

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In this project we will use a cocaine self-administration (SA) model to determinate the behavioral interactions between chronic stress and cocaine, and neurobiological mechanisms associated to the neuropathology of cocaine abuse in cortical glutamatergic projections to basal ganglia. The restraint stress was implicated in the proactive influence of rewarding and stimulating properties of a non-contingent administration of amphetamine and cocaine (Esparza et al, 2012; Garcia-Keller et al, 2013). In this model we will evaluate: 1) influence of glial modulation (GLT-1) on the glutamate (Glu) homeostasis, 2) morphology of dendritic spines of nucleus accumbens (NAc) core and shell, 3) effect of ceftriaxone and minocycline (drugs that inhibit the glial activation and also affect GLT-1 levels). Our approach is that deregulation of glutamate homeostasis by stress and cocaine self-administration consist of a marked increase of Glu in core (extrasynaptic and synaptic), consistent with a decrease of GLT-1 glial protein and changes in density and morphology of dendritic spines in NAc core. Thus, we expect to determinate neurobiological mechanisms to demonstrate rationally how stress promotes substances consume. At the same time, pharmacological studies will allow us to evaluate drugs effects which are based upon the restoration of glial homeostasis and thereby repair the plasticity of glutamatergic synapses and the changes induced by stress or drugs in cocaine self-administration.

Neurochemistry and Neuropharmacology
Poster Number 173 / Session 2

Role of Wnt/b-catenin signaling pathway in the expression of cocaine induced sensitization

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The Wnt/b-catenin signaling pathway is activated by the interaction between the Wnt factors and their receptor Frizzled. While Wnt signaling pathway is essential for mammalian brain development, little is known regarding its role in adulthood. Recently we found that b-catenin levels are increased in the Nucleus Accumbens (NAcc) after cocaine induced sensitization. Our main goal was to investigate the relevance Wnt/b-catenin pathway in the expression of cocaine induced sensitization. In order to do that, adult male Wistar rats received daily injections of cocaine or saline for a week and then a challenge three weeks later. Locomotor activity was recorded on Day 1, 7 and 28. As it was expected, only rats chronically treated with cocaine showed a significant increase in locomotor activity on Day 28 compared to Day 1. Rats were sacrificed 24 hs after cocaine challenge on Day 28, and brains areas were dissected to study b-catenin expression levels. Our data showed that NAcc b-catenin is increased only after a cocaine injection while no changes were found after saline injection on Day 28. Furthermore, the increase in b-catenin only happened in sensitized animals while no changes were found in non-sensitized rats. In summary, our data showed that the increase in b-catenin in NAcc is induced by cocaine only when animals expressed locomotor sensitization, suggesting an important role of b-catenin in the expression of cocaine induced sensitization.

Neurochemistry and Neuropharmacology
Poster Number 174 / Session 3

Flumazenil-insensitive modulation of GABA--Aρ receptors by benzodiazepines

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GABA-A receptors are ligand-gated ion-channels that mediate most of the inhibitory neurotransmission in the CNS. They can be allosterically modulated by benzodiazepines (BZ) to produce anxiolytic and sedative effects in vivo. GABA-A receptors with diverse subunit composition and arrangement arise from particular combinations of five subunits, each belonging to different classes (α, β, γ, δ, ε, π, θ, ρ), which impart distinctive pharmacological and electrophysiological properties to the receptor subtypes. γsubunits are critical for the typical pharmacological potentiating effects of BZs on GABA-$A_{\alpha\beta\gamma}$ receptors to happen, while the retinal homomeric GABA-A_{ρ} receptors still are considered insensitive to these drugs. However, preliminary experiments from our lab suggested that this may not be the case. We expressed GABA-$A_{\rho1}$ receptors in *Xenopus laevis* oocytes and recorded, using two-electrode voltage-clamp, the GABA-evoked chloride currents in the presence or absence of diverse BZ. Diazepam, a common minor tranquilizer, significantly potentiated GABA-$A_{\rho1}$ receptor mediated responses. Meanwhile, the atypical anxiogenic BZ 4´-chlorodiazepam exhibited a biphasic effect depending on the GABA concentration (potentiation below 1µM GABA and inhibition above that concentration). All BZ actions were dose dependent and occurred in the µM range; BZ effects were also easily reversible and voltage independent. Co-application of the selective antagonist flumazenil had no effect on BZ modulation.
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Neurochemistry and Neuropharmacology
Poster Number 175 / Session 1

Establishing C. elegans models of human congenital myasthenic syndromes

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The free-living nematode Caenorhabditis elegans is a model for the study of human neurological diseases and drug testing. In humans, gain-of-function mutations in muscle nicotinic receptor (AChR) subunits lead to slow-channel congenital myasthenic syndromes. We here explored if homologous mutations in C. elegans subunits mimic the molecular and functional changes observed in patients. In the essential UNC-38 and UNC-29 subunits of the levamisole-sensitive AChR (L-AChR) we mutated residues at position 9' of M2, which forms the gate of the channel, and position 12', which mimics a mutation found in a patient. We generated transgenic worms expressing the mutant AChRs in muscle using both wild-type and null-mutant strains as backgrounds. Electrophysiological studies show a dramatic increase (14-fold) in the open duration of L-AChR channels, and a decrease in the desensitization rate of macroscopic currents elicited by ACh, similarly to the changes detected in human mutant AChRs. Unexpectedly, no significant changes in locomotion and levamisole-sensitivity of transgenic worms occur. Overall, our results show that mutant subunits are incorporated into functional L-AChRs and lead to kinetic changes similar to those observed in vertebrate AChRs, thus revealing a high degree of conservation of functional roles of amino acids between C. elegans and human AChRs. These results open doors for establishing C. elegans models for human myasthenic syndromes.

Neurochemistry and Neuropharmacology
Poster Number 176 / Session 2

Exploring a novel pathway in Levodopa induced dyskinesia

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Parkinson's disease (PD) is a neurodegenerative disorder which results from the selective death of nigroestrial dopaminergic neurons. The administration of L-DOPA is the most effective symptomatic pharmacological therapy. Despite of its benefits, most patients develop side effects known as L-DOPA induced dyskinesias (LID). The current great challenge in PD therapy is to control LID. To reach this goal it is necessary to better comprehend the multiple cellular and molecular mechanisms that take place during LID. Although some protein and gene changes have been described into the dyskinetic striatum, the functions and/or mechanism on which they are involved are not fully understood . In our laboratory we have shown that Pleiotrophin and its receptor RPTPz/b are upregulated as a consequence of dopaminergic loss and L-DOPA treatment. RPTPz/b belongs to the post synapsis density complex, where it interacts with PSD95 and regulates the protein kinase Fyn. Several evidences point Fyn as a potential candidate involved in LID. To test this hypothesis, we have analyzed the amount of Fyn protein and its phosphorylation state in the striatum of dyskinetic rats. We have also developed a LID model in Fyn KO mice. We found that Fyn is highly phosphorilated in dyskinetic striata while Fyn KO mice show less dyskinesia than wt controls. Our evidences support a role of Fyn in LID, yet further work is still necessary to determine the mechanism on which it may be involved.

Neurochemistry and Neuropharmacology

Poster Number 177 / Session 3

Differential effects of a chronic treatment with Pregabalin on mature and immature adult hippocampal granule cells

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Pregabalin (PGB) is an anticonvulsant, analgesic, and anxiolytic drug used in patients with epilepsy, neuropathic pain, anxiety disorder and migraine. Though PGB clinical use is widely extended its physiological mechanism of action is not completely understood. PGB targets the α2δ subunit of the voltage dependent calcium channel shown to be involved in synaptogenesis and adult neurogenesis in dentate gyrus a brain area related to some of the pathologies that are currently treated with PGB.

Animals were cronicaly treated with PGB and the morphological and functional properties of adult and new GFP labeled neurons were studied. We found that the application of PGB increased the frequency of miniature excitatory post-synaptic potentials, the action potential repolarization amplitude and the AMPA/NMDA ratio. All these effects are consistent with the accelerated neuronal development. The degree of maturation of newborn DGCs was determined by measuring the proportion of BrdU cells expressing DCX and Cb. These results are in agreement with the electrophysiological recordings described above.

We found PGB to affect differentially mature and immature DGCs. In immature granules cells both electrophysiological and morphological parameters are compatible with an acceleration of development via PGB. On the other hand, in mature DGCs, PGB seems to decrease glutamatergic transmission excitability and to reduce network activity.

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Neurochemistry and Neuropharmacology
Poster Number 178 / Session 1

Molecular mechanisms involved in benzodiazepine tolerance

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Chronic treatment with benzodiazepines produces tolerance to their pharmacological effects. Tolerance to the sedative effects in rats occurs after a 7 day-treatment with diazepam (15 mg/kg, subcutaneous injections) whereas tolerance to the anxiolytic effects develops after a 14 day-treatment, suggesting different mechanisms. The aim of this work was to study the molecular mechanism of tolerance to benzodiazepines. Chronic diazepam administration during 7 and 14 days in rats (Sprague-Dawley) induced a decrease in the potentiation of [3H] flunitrazepam binding by GABA, named uncoupling. It has been previously reported that chronic benzodiazepine administration produces selective alterations in the levels of GABAA receptor subunits, without changes in the number of receptors. In order to investigate whether tolerance is mediated by a change in the receptor subunit composition, we performed receptor immunoprecitation experiments followed by western blot assays. Results from these experiments showed that diazepam administration during 14, but not 7 days, induced an increase in the percentage of alfa1/gamma2 receptors. In conclusion, our results suggest that tolerance to the sedative and anxiolytic effects of benzodiazepines is associated with an uncoupling of GABA and benzodiazepine sites. Tolerance to the anxiolytic actions of benzodiazepines is also accompanied by a change in receptor subunit combination.

Neurochemistry and Neuropharmacology
Poster Number 179 / Session 2

Can early protein malnutrition facilitate cocaine relapse?

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Previously we demonstrated that perinatal protein deprivation increases the rewarding effects of cocaine, and facilitates the development of behavioral sensitization to this drug. This study evaluated if the increased reactivity evidenced in deprived (D) versus control (C) rats is also evident during the reinstatement of conditioned place preference (CPP), a useful animal model to study relapse. In order to assess the reinstatement of a cocaine-induced CPP, different groups of C- and D- rats were submitted to 4 conditioning sessions with cocaine (10 mg/kg, i.p.). In order to induce extinction, following the CPP test, animals were paired with saline for 3 or 4 days. Three days of extinction training did not induce CPP extinction. After 4 days of training, both groups of rats showed a significant decrease in the time spent in the drug-paired compartment. The day after the extinction test, rats received a priming injection of cocaine (2.5 or 5 mg/kg) to analyze if cocaine-induced CPP could be reinstated. Only D-rats showed reinstatement of preference for the drug-paired context after a priming injection with the lowest dose of cocaine used (2.5 mg/kg). Furthermore, CPP could be reinstated with 5 mg/kg of cocaine in both C- and D- groups. These preliminary results extend previous reports from our lab that clearly demonstrate that early nutritional insult during early life brings about alterations in the rewarding neural circuits that modify the reactivity to drugs of abuse.

Neurochemistry and Neuropharmacology
Poster Number 180 / Session 3

Study of the long-term influence of a single restraint stress on glutamate uptake and synaptic plasticity in nucleus accumbens

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Disrupted Glu homeostasis is observed 21 days later in the nucleus accumbens (NA) core, but not shell, following a single session of restraint stress (Garcia-Keller, et al 2012). The aim of our study was to determine in the cross-sensitization model of stress and cocaine the following: I) Firstly, the functionality and expression of Glu transporter GLT-1 and synaptic plasticity by measuring AMPA/NMDA (A/N) ratio in the NA core. II) Secondly, to determine whether ceftriaxone (200 mg/kg i.p (Cef)) can restore compromised Glu transport and reverse alterations in synaptic plasticity in pre-stressed animals. Male Wistar rats (250-350 g) were restrained for two hours, while control animals were left undisturbed in their cages. On day 16 following the stress episode, animals from non-stress and stress groups were divided in two groups which were administered with five daily injections of vehicle or Cef (200 mg/kg). Twenty-four hours later, the animals were sacrificed to determine GLT-1 expression or functionality (by western blot or glutamate uptake) in NA core, and synaptic plasticity (A/N) in NA. Our results demonstrate that Cef restores the altered Glu homeostasis increasing the functionality and the expression of the GLT-1 in the pre-stressed animals, but there was no change in synaptic plasticity showed by the A/N with only 5 days Cef treatment in the stressed rats.

Neurochemistry and Neuropharmacology
Poster Number 181 / Session 1

Involvement of cannabinoid CB1 receptors within nucleus accumbens in stress-induced reinstatement in extinguished cocaine–conditioned animals

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Relapse to drug abuse after long periods of abstinence is a common feature of drug addiction. Stress is considered an important factor that induces drug abuse relapse in human that can be modeled in laboratory animals. At this respect, it has been demonstrated that an acute stress exposure in animals that extinguished the cocaine-induced conditioned place preference triggers reinstatement in drug-associated contexts. One of the paradigms widely used in laboratory animals to study the relapse to compulsive drug intake is the reinstatement of the cocaine conditioned place preference. Previous results from our lab demonstrated that in extinguished cocaine-conditioned animals evaluated in a conditioned place preference test (CPP), the restraint stress was able to reinstate the cocaine conditioned place preference. In relation to the neurotransmission systems involved in these behaviors, there are evidences related to the participation of glutamatergic in relevant neural circuits for the drug action and stress impact on addiction. More recently, it has been demonstrated that endocannabinoid system, primarily through their actions at CB1 receptors, is implicated in the relapse in extinguished drug-conditioned animals. Moreover, several studies suggested that Nucleus Accumbens (NAc) is one of mesocorticolimbic brain regions involved in the reinstatement in cocaine-conditioned animals. The present project has been designed to evaluate the involvement of CB1 receptors within NAc Core and Shell, in restraint stress –induced reinstatement, in extinguished cocaine-conditioned animals.

Neurochemistry and Neuropharmacology
Poster Number 182 / Session 2

Boldine decreases the locomotory side effects induced by intracerebral hemorrhage in rats

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Intracerebral hemorrhage (ICH), which results from the spontaneous rupture of an intracranial vessel, is a subtype of stroke with high morbidity and mortality accounting for about 15% of all deaths. Boldine ((S)-2,9-dihidroxi-1, 10-dimetoxi-aporphine), an alkaloid obtained from Peumus boldus Molina, is known by its antioxidant and cytoprotective properties. Motor function and morphological parameters were accessed from male Wistar rats submitted to collagenase VII-induced ICH followed by a single intraperitoneal injection of boldine four hours after the lesion. In the open field test the animals treated with the higher doses of boldine (50 mg/kg and 75 mg/kg) showed results similar to those observed in the control group. In the footfault test assessed 96 hoursafter ICH recovery was increased in the animals treated with the higher doses of boldine. In the beam walking test, performed 48 and 96 hours after ICH, animals submitted to ICH slipped at least three times crossing the beam, being boldine able to partially reverse these slips. Western blotting analysis showed that boldine was not able to reverse the ICH-induced reactive astrogliosis, as evidenced by GFAP increase. These data suggest that boldine administration recovers motor function in this experimental model, although no significant morphological changes were observed after 96 hours.

Neurochemistry and Neuropharmacology
Poster Number 183 / Session 3

Decrease of nNOS expressing neurons in prenatally stressed male rats

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A great amount of evidence has shown that prenatal stress (PS) induces alterations in learning and memory. However, the mechanisms underlying these changes are partially understood. Nitric oxide (NO) is a diffusible and rapidly acting molecule involved in many processes, such as learning and memory formation. Our aim was to study the role of NO in a model of PS.
Pregnant rats were restrained in plastic devices three times a day during the last week of pregnancy. Its male offspring was evaluated at 90 days of age in the inhibitory avoidance task and the open field test. Another set of animals was used for immunohistochemistry and for NADPH diaphorase (d) staining.
We found impairments in associative learning in PS rats. No differences in locomotor activity and habituation memory were found. Observation of slices obtained by immunohistochemistry showed a decrease of neuronal nitric oxide synthase and glucocorticoid receptor levels in the hippocampus. We also found a decrease in NADPHd positive neurons in PS rats.
Extensive evidence has shown a role for NO in associative learning, and recent papers have involved GR hippocampal expression with inhibitory avoidance learning. Our results point to a participation of NO and the HPA axis in the behavioural alterations induced by PS. (UBACyT M20020100100633, ANPCyT-PICT 2011-1015).

Neurochemistry and Neuropharmacology
Poster Number 184 / Session 1

Pharmacological consequences of adaptive evolution of the α9α10 nAChR

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The α9 and α10 nicotinic acetylcholine receptor (nAChR) subunits form the receptor that mediates efferent inhibition of vertebrate cochlear hair cells. A phylogenetic analysis of the genes coding for each subunit showed signatures of positive selection only for the mammalian α10 subunits (Franchini & Elgoyhen, 2006). Here, we assayed the functional consequences of the acquisition of non-synonymous substitutions in α10 by comparing the pharmacology of recombinant chicken and rat receptors heterologuosly expressed in Xenopus Laevis oocytes.
Cholinergic agonists such as Choline (Ch) and DMPP showed higher efficacy on chicken α9α10 receptors (Ch:88±6%;n=6, DMPP:32±3%;n=5) compared to rat α9α10 nAChRs (Ch:37±2%;n=10, DMPP:0,6±0,3%;n=6). Moreover, responses to Ch were 72±3% (n=3) of the maximal response to Ach in chicken hair cells chicken. Finally, the heterologous expression of hybrid interspecies receptors revealed that the efficacy of Ch is mainly determined by α10 subunits (Rα9Cα10: 87±3%; n=5, Cα9Rα10: 57±4%; n=2).
Taken together, these results suggest that the aminoacid changes that accumulated on mammalian α10 subunits resulted in the pharmacological differences observed. Most importantly, we propose that the efficacy of choline (the main synaptic metabolite of ACh) to elicit a response may lay behind the selection pressure that shaped mammalian α10 subunits.

Neurochemistry and Neuropharmacology
Poster Number 185 / Session 2

Enkephalinergic system is involved in cocaine induced behavioral sensitization and the associated increase in brain-derived neurotrophic factor in nucleus accumbens

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The behavioral sensitization involves a complex interplay between (DA) and others as glutamate (Glu), opioid peptides and brain-derived neurotrophic factor growth (BDNF).
BDNF regulate drug-induced long-term neuroadaptations that encompass alterations in molecular components at the synapse and changes in gene expression. BDNF is reported to alter Glu and DA transmission in the brain areas associated with cocaine-induced sensitization. The main goal of this study was to demonstrate the involvement of the enkephalinergic (enk) system in cocaine-induced behavioral sensitization, and their association with changes in BDNF and its receptor. Male C57B/6J wild type (WT) and preproenk knockout (KO Penk) mice were daily treated with cocaine (15mg/Kg i.p.) and vehicle for 9 days. On day 21 of the treatment the following experiments were done: 1) Immunofluorescence: BDNF and TrkB levels were determined in PfC, NAc, Dorsal Striatum and VTA in response to saline and cocaine challenge. 2) Western blot: for pTrkB levels in these brain areas. We found that chronic cocaine administration increases BDNF and pTrkB levels in NAc and VTA compared to controls animals. These effects are absent in KO mice Penk (-/-).These results demonstrate that enk system is involved in cocaine- induced alterations in neurotrophic factors in the NAc and indicate that preproenk-derived opioid peptides are strongly involved in the long-term plastic changes underlying behavioral sensitization to cocaine.

Neurochemistry and Neuropharmacology
Poster Number 186 / Session 3

Ethanol withdrawal decreased the expression ofGABA-A α1-subunit in basolateral amygdala and elicits a memory trace resistant to labilization after recall

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We have recently reported that withdrawal from chronic ethanol (ETOH) administration facilitated the formation of contextual fear memory, which is resistant to the disruptive effect of propranolol (PROP; β-adrenoceptor antagonist) and midazolam (MDZ; positive allosteric modulator of GABA-A receptors) following memory reactivation. In addition, d-cycloserine (DCS, NMDA partial agonist) administration before memory reactivation promoted vulnerability to the disruptive effect of PROP (intra-BLA or systemic administration) on fear memory reconsolidation in ETOH rats. MDZ was also ineffective in DCS pre-treated ETOH rats. Here we examine whether the lack of the amnesic effect of MDZ in ETOH withdrawn rats could be attributed to changes in the total and/or surface expression of GABA-A receptor α1-subunit in BLA. Male Wistar rats received an ETOH containing liquid diet (6% v/v) for 14 days. On the 3rd day of withdrawal, animals were sacrificed for Crosslinking BS3 assay and then analyzed by Western Blot. A significant decrease of total and surface protein expression of α1-subunit in BLA was observed in ETOH withdrawn rats respect to control animals. Our finding indicated that the resistance to MDZ's disruptive effect on fear memory reconsolidation in ETOH withdrawn rats may be due to, at least in part, to the decrease of total and surface protein expression of GABA-A α1-subunit in BLA induced by chronic ethanol administration/withdrawal.

Neurochemistry and Neuropharmacology
Poster Number 187 / Session 1

An heterobifunctional probe with allosteric properties on the nicotinic acetylcholine receptor

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An heterobifunctional probe (AC4-ASA) was developed as a tool for the study of cholinergic receptor binding sites. Acetylcholine was derivatized at its alkyl end and, through a short spacer, with a photoactivatable aryl-azide group. The probe was able to specifically interact with the muscle nicotinic receptor and has a considerable selectivity for its α/δbinding site.
This ligand showed the capability of modyfing the affininty of (-)-[3H]-nicotine for the muscle-type nicotinic receptor through, at least, one new allosteric binding site, different from the typical orthosteric binding sites.
A detailed study involving in-gel digestion of alpha and delta subunits followed by mass spectrometry was carried out with the objective of delineating such binding site. Moreover, preliminary automated docking studies were performed between AC4-ASA and a refined structural model of the Torpedo californica nicotinic acethylcholine receptor. Results obtained, taken as a whole, allowed us to suggest the localization and structural aspects of the allosteric binding site.

Neurochemistry and Neuropharmacology
Poster Number 188 / Session 2

Perinatal protein malnutrition facilitates morphine´s cross-sensitization to cocaine in adult rats: a behavioral study

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In order to evaluate the influence of early malnutrition on the development of behavioral cross-sensitization to rewarding properties of cocaine in adult rats, different groups of control (C) and deprived (D) rats were pretreated twice a day for three days with increasing doses of morphine (5, 10 and 20 mg/ kg, s.c.). After the sensitization phase, the rewarding effect of cocaine was assessed in D-rats and C-rats using the Conditioned Place Preference (CPP) paradigm. Dose-response curves to cocaine (3, 5, 7.5 and 10 mg/kg i.p.) revealed in D-rats a conditioning effect with doses of 5, 7.5 and 10 mg/kg, whereas 3 mg/kg did not show conditioning effect.In C-rats, cocaine licited place preference only with the higher dose of 10 mg/kg.Thus, when the animals where pretreated twice a day for three days with escalating doses of morphine only D-rats showed sensitization to the conditioning effect with low doses of cocaine (5 and 7.5 mg/kg i.p.).These results suggest that a deficient nutritional status during early life may induce in adult subjects a lower threshold for developing a behavioral cross-sensitization to cocaine.The possibility that changes in reactivity may be due to pharmacokinetic alterations induced by early undernutrition may be ruled out, since similar brain and plasma morphine / cocaine levels were found in both groups of rats.

Neurochemistry and Neuropharmacology
Poster Number 189 / Session 3

Modafinil and Methamphetamine differentially activate c-Fos and FosB in the mouse striatum

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Modafinil (MOD) is an antinarcoleptic drug used off-label to treat psychostimulant addiction. High doses of METH can induce neurtoxicity in different brain areas. In the present study we aimed to explore MOD and METH acute effects on c-Fos and Fos-B activation (immediate early genes used as an index of neuronal activation) in striatal tissue. Female C57/Bl-6 mice were treated with a METH binge protocol (4x5mg/kg, i.p., 2 h apart) co-administrated with MOD (2x90 mg/kg, i.p., 1 h bef. 1st & 3rd METH inj.). We also investigated the effects of both psychostimulants in locomotor activity, catecholamine striatal content (by HPLC). METH and MOD administration induced hyperlocomotion compared to salines ($p<0.05$), with a different temporal profile. MOD+METH group exhibited locomotor activity values different from the METH group ($p<0.05$, ANOVA). One hour after last METH injection, an increase in striatal c-Fos- and FosB-positive cells was observed in METH-treated group ($p<0.01$, ANOVA). MOD co-administration was not able to counteract METH induction of c-Fos/FosB ($p<0.01$, ANOVA). Six days after METH binge dopamine content was decreased in the METH group and MOD co-administration was able to counteract this effect ($p<0.01$, ANOVA). These data show that MOD and METH have differential effects on c-Fos and Fos-B activation in the striatum. Even if MOD was able to interfere with METH-induced striatal toxicity, MOD did not counteract METH-induced activation of immediate early genes.

Neurochemistry and Neuropharmacology
Poster Number 190 / Session 1

Regulation of astrocyte glycogen metabolism by nitric oxide

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CNS glycogen is predominantly localized in astrocytes, where it is converted to lactate and shuttled to axons as an energy source. Thus, any event affecting glycogen metabolism, will affect the normal function of neurons. Several CNS disorders are characterized by excessive nitric oxide (NO) production. The exposure to NO results in S-nitrosylation of protein thiols which can alter protein function. It was previously established that S-nitrosoglutathione (GSNO) is a viable intercellular S-nitrosylating agent in CNS. In previous studies using C6 astroglioma cell line we have shown that glycogen accumulation was inhibited by NO but without affecting cell redox status. Here we have extended the studies using rat astrocytes primary culture and intact cells of rat spinal cord. Results have confirmed that glycogen levels are regulated in the presence of NO in all system tested, with generation of S-nitroso-proteins, and S-nitrosylation of some enzymes involved in glycogen and glucose metabolism. Since astrocyte glycogen plays an important role in supporting neuronal activity, this study would be relevant to those CNS diseases characterized by excessive NO production like multiple sclerosis, stroke, Parkinson's and Alzheimer's diseases.

Neurochemistry and Neuropharmacology
Poster Number 191 / Session 2

Inhibitory activity of natural ciclic ketones on the GABAA receptor. Citotoxicity studies

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The GABAA receptor is the main inhibitory receptor of the Central Nervous System. It possesses binding sites for drugs other than the neurotransmitter GABA, including benzodiazepines, barbiturates, and the convulsant picrotoxine which behave as allosteric modulators or channel blockers. The study of this last site is especially relevant since it constitutes the action site of widely used neurotoxic organochlorine pesticides. Considering the anticonvulsant activity of thujone, by blocking of chloride channel associated to GABAA receptor, in the present work we analyzed the effect of five cyclic ketones structurally similar, on the GABA stimulated increment of [3H]flunitrazepam binding. The assays were done by using primary cultures of cortical neurons. The results showed that not only thujone but also all the ketones included in this research, were able to reduce the GABA induced increment of the [3H]flunitrazepam binding. Taking into account the action mechanism associated to thujone on the receptor, we can suggest that the ketones studied would also recognize the picrotoxine site in the GABAA receptor. However, this last hypothesis should be confirmed by using specific ligands of that blocking site. All ketones did not affected neuronal viability and red cell integrity.

Neurochemistry and Neuropharmacology
Poster Number 192 / Session 3

Motor and cognitive deficits in a progressive animal model of Parkinson's disease

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive death of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Studies have shown that cognitive impairment may precede motor changes. However, animal studies are mostly conducted with an acute neurotoxin injection that leads to severe motor impairment, precluding the investigation of cognitive performance. We aimed to mimic the progressive nature of PD through the repeated administration of 6-hydroxydopamine (6-OHDA). Treatment on alternate days (i.c.v., 10 µg in 1.0 µl of 0.2% ascorbic acid) induced progressive motor deficits, as shown by catalepsy, oral movements and open-field tests. The treatment also induced memory deficit in the novel object recognition task, which appeared before the motor alterations. The rats also showed anxiety- and depression-like behaviors (decreased exploration of the open field center and reduced sucrose preference). These changes were accompanied by a progressive decrease of in tyrosine hydroxylase (TH) levels in the SNpc, ventral tegumentar area, locus coeruleus, dorsal striatum, prefrontal cortex and hippocampus. The alterations were still present 20 days after the last injection. The results indicate a possible application of repeated treatment with 6-OHDA in the study of the non-motor symptoms and the progressive nature of PD.

Neurochemistry and Neuropharmacology
Poster Number 193 / Session 1

Pretreatment with LiCl blocked development of cocaine induced sensitization by restoring bcatenin levels in specific brain areas

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Wnt factors are cysteine rich secreted proteins that interact with their receptors: Frizzled, Ryk, and Ror. As a result of their interaction, Dishevelled is activated, and consequently, one of three pathways: Wnt/bcatenin, Planar Cell Polarity, or Wnt/calcium pathways. Wnt signalling pathways are essential for mammalian brain development. However little is known regarding its role in adulthood. Recently, our lab showed that cocaine induce sensitization is associated with a decrease of bcatenin protein levels in Prefrontal Cortex (PFC), Amygdala (Amyg) and Dorsal Striatum (DS). Moreover, bcatenin levels were also decreased in PFC nuclear fraction suggesting that Wnt/bcatenin pathway may be inhibited in cocaine induced sensitization. Therefore our main goal was to elucidate if changes in bcatenin are necessary for locomotor sensitization. Since it is known that Lithium Chloride (LiCl) increases bcatenin levels by inhibition of GSK3b, we administered LiCl or saline i.p. before each cocaine injection. Twenty four hours after testing the behavioral response animals were sacrificed and brain areas were dissected. So far our results showed that systemic LiCl injections blocked cocaine induced sensitization by restoring bcatenin levels in PFC, Amyg and DS, as well as in PFC nuclear fraction. In summary our data showed that changes in bcatenin are essential for cocaine induced sensitization suggesting that Wnt/bcatenin pathway may be involved in cocaine induced neuroadaptations.

Neurochemistry and Neuropharmacology
Poster Number 194 / Session 2

Neurochemical changes in mouse DRGs and spinal cord after pelvic nerve axotomy (PNA)

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Peripheral neuropathies result in chronic pain and associated changes in the neurochemistry of primary afferent neurons. Most animal models on peripheral neuropathies target non-visceral nerves, while visceral ones are much less studied.
In this study, lumbar 6 and sacral 1 spinal nerves, major tributaries of the primarily visceral pelvic nerve, were axotomized in BalbC mice. Sham animals were also included. Immunohistochemical expression of calcitonin gene related peptide (CGRP), transient receptor potential cation channel subfamily V member 1 (TrpV1), and cyclic AMP-dependent transcription factor 3 (ATF3), was analyzed seven days after surgery in L4-S2 dorsal root ganglia (DRG) and spinal cord.
PNA resulted in a significant downregulation of CGRP- and TrpV1-immunoreactive (IR) L6-S1 DRG neuron profiles (NPs), in contrast to their abundant expression in uninjured DRGs (sham animals and contralateral to PNA). PNA also resulted in strong ATF3-IR DRG NPs upregulation. Small increases in ATF3-IR NPs were detected in sham animals and contralateral DRGs of some PNA mice. A modest decrease in CGRP like-immunoreactive primary afferents terminating in the dorsal horn of the spinal cord was observed ipsilateral to the lesion.
Neurochemical alterations in mouse DRGs after injury of a predominantly visceral nerve are shown for the first time. If changes in these and other pain-related molecules contribute to pain associated to the injury of a visceral nerve, it remains to be established

Neurochemistry and Neuropharmacology
Poster Number 195 / Session 3

Early protein malnutrition facilitates depressive-like behaviors in rats that experienced maternal separation

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This study was performed to evaluate the influence of early undernutrition on the behavioral consequences of maternal separation in adult rats. To this aim, half of the animals submitted to a protein malnutrition schedule at perinatal age (D-rats) and well-nourished animals (C-rats), were separated from dam daily for 180 min from postnatal day 1 (PND 1) until PND 10 (MS-group). The other half remained undisturbed (NMS-group). Using animal models commonly employed to assess depressive-like or anxiety-like behaviors, different groups of adult rats were subjected to the sucrose preference test, forced swim test, behavioral sessions for ambulatory activity and elevated plus maze. Thus, sucrose preference significantly decreased in D-MS and D-NMS group compared with C- rats (MS and NMS). Moreover, rats in D-MS group exhibited higher immobility time in the forced swim test and lower ambulatory activity than rats in other groups (D-NMS, C-NMS and C-MS). No differences were found in the time spent in the open arms of the elevated plus maze. These results suggest that the early nutritional insult could increase the risk of occurrence of anhedonia, a core symptom of depression, and facilitates depressive-like behaviors during adulthood in rats exposed to maternal separation.

Neuroendocrinology and Neuroimmunology
Poster Number 196 / Session 1

Revealing the role of CRF neurons of the CeA with a novel transgenic mouse model

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The corticotrophin releasing factor (CRF)-producing neurons of the central amygdala (CeA) have been implicated in mediating behavioral and physiological responses associated with fear, anxiety, stress and reward. However, difficulties in identifying CRF neurons of the CeA have previously complicated the study of this set of neurons. To overcome this problem, we report a novel transgenic mouse line in which humanized green fluorescent protein (GFP) is under the control of the CRF promoter (CRF-GFP mice), rendering CRF neurons readily recognizable. Using c-Fos as a marker of neuron activation we explored the response of CeA CRF neurons under different experimental paradigms. As expected, CeA CRF neurons were activated in mice exposed to a social defeat protocol, confirming their role in stress responses. We then explored a number of different conditions also known to activate the CeA. In particular, CRF-GFP mice were exposed to either: 1-ghrelin treatment, 2-melanocortin 4 receptor agonist treatment, 3-a conditioned taste aversion paradigm, 4-a high fat diet binging paradigm, 5-a high fat diet withdrawal paradigm. Despite most of these strategies caused a significant increase of c-Fos in the CeA, we could not detect a significant increase of c-fos expression in CeA CRF neurons. Hence, thus far, our results suggest that CeA CRF neurons are solely involved in stress-induced responses. Overall, this novel CRF-GFP line is a promising tool to dissect the role of this CeA subset.

Neuroendocrinology and Neuroimmunology
Poster Number 197 / Session 2

GABA transporters in human lymphocytes

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GABA is the main inhibitory neurotransmitter in CNS and is associated to several neurological disorders. GABA transporters (GATs) play a critical role in GABA level regulation by allowing re-uptake of neuronal secreted GABA. Four GAT subtypes (GAT 1-3 and BGT-1) have been described in humans. Previously, we reported a complete GABAergic system in lymphocytes. Here, we studied the modulation of the expression and activity of GATs in human lymphocytes by the mitogen phytohemagglutinin (PHA). We determined mRNA GAT expression in activated and resting cells (with and without PHA, respectively). GAT 3 was not detected under any condition, whereas GAT 2 and BGT-1 were detected in all activated cells. Expression of GAT 1 was variable among samples and conditions. In line with these observations, incubation with PHA also increased [3H]GABA uptake. To evaluate the physiological role of GATs we determined cell proliferation by PHA in the presence of nipecotic acid (NA), a GAT inhibitor. Cell proliferation was negatively modulated by NA. In addition, secreted GABA was detected only in supernatant from activated lymphocyte cultures. Taken together, our results show that lymphocytes express functional GATs whose expression is modulated by PHA, GATs regulate cell proliferation, and lymphocyte cells have the ability to secrete GABA. Pharmacological modulation of GATs present in lymphocytes could be a new target to modulate immune response.

Neuroendocrinology and Neuroimmunology
Poster Number 198 / Session 3

Effect of progesterone on the nigrostriatal metabolic activity of hemiparkinsonian male rats

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Previously we reported that hemiparkinsonian (HP) male rats have motor dysfunctions and alterations in the striatal neuronal activity. We also demonstrated that progesterone (P4) s.c. reverts some of these effects. We hypothesize that those changes could affect the metabolic activity (MA) of left corpus striatum (lCS) and left substantianigra (lSN). In this work we evaluated the MA in lCS and lSN of HP male rats obtained by lesion with the neurotoxic 6-OHDA. We used the method of chemical reduction of 3-(4,5-dimetyltiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). The groups we used were: G1) Sham rats; G2) HP rats and G3) HP rats treated with P4 s.c. for 3 consecutive days (4 mg/kg/day). Eight weeks after lesion, the rats were killed, their lCS and lSN dissected out and used for MTT assay. The results were expressed as MA per mg of protein (media ± SEM) and analyzed by ANOVA 1. In lSC the MA was reduced in G3 regarding G1 and G2 ($p<0.05$ and $p<0.01$ respectively). In lSN the MA was decreased in G2 regarding G1 ($p<0.01$) and P4 induced a trend of reversion of this later effect. The results suggest that the reduced MA in lSN could be due to the loss of dopaminergic neurons induced by the neurotoxic 6-OHDA and that P4 would be neuroprotective. Furthermore, the P4-induced reduction of the MA in lCS prompts us to propose the involvement of inhibitory tones. We conclude that the MTT assay is an efficient technique to evaluate functional neuronal changes in neurodegenerative models.

Neuroendocrinology and Neuroimmunology
Poster Number 199 / Session 1

Immune responses in a mouse model of autism spectrum disorder

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Autism spectrum disorders (ASD) consist of a heterogeneous group of neurodevelopmental disorders defined behaviorally by abnormalities in social, verbal, and nonverbal communication. It is widely agreed that a subset of patients with ASD show abnormal immunity. Furthermore, it has been proposed that autoimmunity may play a role in the pathogenesis of ASD. However, immune findings in ASD patients are often inconsistent likely due to the heterogeneous, behavior-defined subject groups.
Rett Syndrome is an ASD caused by mutations in Methyl Cytosine Binding Protein 2 (MeCP2) and mouse models of Rett have been widely used for studying ASDs. The main goal of our project is to use this monogenic model of ASD, which also shows a highly reproducible pathologic phenotype, in order to evaluate the role of altered immunity in the pathogenesis of this disorder. First, we evaluated the presence of autoantibodies against CNS proteins, as well as markers of neuroinflamation in two different mouse models of Rett. While the patterns of CNS autoantibodies change along development (2-7 weeks) for all the groups analyzed, we did not detect striking differences between WT and MeCP2 mutant mice. However, we did observed an increase in activated microglia in MeCP2 mutant mice, suggesting neuroinflammation could be implicated in the neuropathology of this syndrome. Future studies will characterize immune responses at later stages of the disease and how this could affect neuronal development.

Sensory Systems
Poster Number 200 / Session 2

Temporal patterns and surfaces properties in texture discrimination coding

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Studies in tactile discrimination agree that rats are able to learn a rough-smooth discrimination task by actively touching (whisking) objects with their vibrissae. This behavior induces specific patterns of temporal encoding at different levels of the whisker pathway.
In the present work we characterized the relation between temporal patterns extracted from the one vibrissal nerve and the surfaces roughness profile. We have used five sandpapers of different grain size as roughness discrimination surfaces and we obtained their roughness profiles by using a Hommel Tester T1000. We quantified all surface texture taking into account certain intrinsic characteristics, such as the simple roughness amplitude parameters, roughness spacing parameters, roughness hybrid parameters and statistical parameters. In addition, we propose here a new texture parameter: the DBLP (distance between local peaks) by using a threshold detection algorithm. The Inter-event time (IET) analysis allowed us to extract the temporal patterns from the afferent discharge.
The best fit between IET analysis and texture measurements were obtained for Sm and La parameters (R2= 0.97) and for the parameter proposed here, DBLP (R2= 0.98). These results show that the temporal patterns are related with the texture discrimination coding and that these coding would mainly describe texture spacing parameters.

Sensory Systems
Poster Number 201 / Session 3

Different features of visual motion stimuli give rise to different escape response velocities in a crab

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The visual world presents an abundance of information that animals break down into features, such as colour, direction of movement, size, contrast, etc. Crabs are highly visual animals that display complex visually guided behaviours. In nature, these animals are preyed on mostly by gulls. In order to avoid being preyed, the crabs have to sense and integrate different characteristic of the visual stimuli.
By using a walking simulator device, we studied animal's escape response when it was confronted with computer-generated visual stimuli. The stimulation consisted of figures which differed in speed, contrast or size. A black figure moving at different speeds triggered a Gaussian like curve response with its maximum at 30º/s. Figures which differed from white to black against a grey background showed a sigmoid like curve response with surprising low responses for clear figures and high responses for dark ones. The presentation of bars with different angular sizes provoked greater escape responses as the angular size increased.
By performing calcium imaging in vivo we have recently shown that the activity of small field columnar neurons feeding wide field giant neurons determines the habituation of the animal escape response. Our next step is to study if the visual tuning sensitivity of these columnar neurons also determines the animal´s proneness to escape from visual danger stimuli.

Sensory Systems
Poster Number 202 / Session 1

Effects of neonatal hypoxia-ischemia on cerebellar glutamatergic and GABAergic cell populations in the rat

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Premature birth and/or hypoxia-ischemia (HI) in the perinatal period are among the risk factors for cerebellar pathologies. The characterization of neonatal brain reactions to injury is of great importance in order to understand endogenous repair and survival strategies. We assessed the effects of HI on the postnatal developing cerebellum by studying the expression of NeuroD1 and GAD67 in glutamatergic and GABAergic neurons, respectively, via immunohistochemistry (IHC) and Western blot (WB). The treatment was performed at postnatal day 8 (P8) with sampling at P15. We detected a significant decrease of NeuroD1(+)-migrating cells in the molecular layer (ML) of lesioned (L) cerebella, which may be associated with abnormalities observed in radial glial fibers. These effects were accompanied by a reduction in the number of cells in the internal granular layer (IGL). A substantial change in the number, morphology and spatial orientation of Purkinje cells was also observed. Atypical cells displayed altered features; such as less-developed dendritic arborization towards the ML, mis-orientation, and smaller nuclei stained intensely with propidium iodide, indicating high chromatin compaction. In agreement with the IHC results, quantifications by WB showed significantly diminished NeuroD1 and GAD67 levels in the L group. In conclusion, we hypothesize that these changes could be related to mechanisms of adaptation to the lack of oxygen during a crucial moment in cerebellar development.

Sensory Systems
Poster Number 203 / Session 2

Understanding the roles of the efferent system in the inner ear

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Hearing loss affects about 10% of the overall population and 42% of the population above 75 years of age. Such impairment is usually permanent and results from a variety of causes, including loud sounds. Here, we intend to address the issue of noise-induced hearing loss and the role of the efferent olivocochlear system in this process. To this end, we are using a murine model of enhanced noise protection, the Chrna9L9â€™T knock-in, a mouse in which the Î±9 nicotinic receptor subunit bears a mutation and leads to enhanced medial efferent activity.

We tested how efferent innervation is rewired after noise trauma in wild type, Chrna9L9â€™T knock-in and Î±9 knockout mice. We exposed mice to loud sounds (1-16 kHz, 100 dB SPL, 1hr) and measured auditory brainstem responses (ABR), which reflect synchronized discharges from neurons along the auditory pathway. To test outer hair cell function, we recorded the distortion product otoacoustic emissions (DPOAEs). After trauma, knockouts and wild types showed large ABRs and DPOAEs threshold shifts. Suprathreshold ABR amplitudes were reduced, even in animals with almost normal threshold sensitivity. However, Chrna9L9â€™T knock-in mice were resistant to the same noise exposure. We used immunohistochemistry to visualize efferent neurons and found disorganized terminals after trauma compared to controls. These findings will contribute to the understanding of how normal hair cell function is affected by loud noise and the role of the efferent system.

Sensory Systems
Poster Number 204 / Session 3

Nitric oxide pathway to modulate feeding behaviour in a blood-sucking insect

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Gustatory sense provides animals with reliable information about the quality of a food source, contributing to discriminate nutritious from harmful food. Taste receptors located in the oral cavity are responsible for a primary evaluation of food. Nitric oxide (NO) is a neuromodulator that participates in many physiological processes in living organisms, including chemosensory perception. In insects, NO modifies sensory inputs and behavioural responses associated to chemical stimuli, both olfactory and gustatory. In this work, we studied the role of NO in the food assessment capacity by Rhodnius prolixus. Insects were treated (or not) for 1 min with a NO donor (SNAC) at different concentrations prior to a feeding test with an appetitive solution (AS) and the weight gained after 10 min was registered. Food intake significantly decreased in insects treated SNAC, suggesting the activation of an antiappetitive pathway. NO triggers the production of GMPc due to the activation of a soluble guanylyl cyclase (sGC), therefore we treated insects with analogues or inhibitors of this pathway. We observed that bugs treated with a GMPc analogue also provoke an inhibitory effect. Additionally, the inhibitory feeding of NO was prevented by adding a sGC inhibitor to the pre-treatment. Our results suggest that NO could act through a sGC that bears the production of GMPc and ultimately the NO might exert a peripheral gustatory modulation affecting insect's final decision about feeding.

Sensory Systems
Poster Number 205 / Session 1

Identification of the parabigeminal nucleus in the diurnal octodontid rodent Octodon degus

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The vertebrate isthmic complex, a collection of nuclei that establish reciprocal connections with the optic tectum, have an acethylcholine transferase (ChAT) immunopositive division. In birds the ChAT+ nuclei are n. isthmi pars semilunaris (SLu) and n. isthmi pars parvocelularis (Ipc), the later is thought to play a central role in attention and stimulus selection, as it selectively boosts the transmission of visual activity from the tectum to higher visual areas. In mammals this division corresponds to the n. parabigeminalis (PG). Whether the PG is functionally equivalent to Ipc, SLu or both is presently unknown. To investigate the role of the isthmotectal circuit in mammalian vision we used tracing and immunohistochemical techniques to characterize the PG in a diurnal rodent with a well-developed visual system the Octodon degus.

We found that the PG is a compact cell group located in the lateral wall of the midbrain tegmentum, ventral to the brachium of the inferior colliculus. Like in Ipc and SLu, PG cells are ChAT+. Injections of neural tracer CTb in the superior colliculus (SC) produced ipsi and contralateral retrograde cell labeling in restricted areas of PG, indicating a topographic projection. Additionally, ipsilateral filled cells are surrounded by CTb+ terminals, showing the reciprocal connectivity between SC and PG. We conclude that the PG in O. degus is well suited to investigate the precise homology between PG and Ipc/Slu, and the PG role in mammalian vision.

Sensory Systems
Poster Number 206 / Session 2

Pattern of tectal projections and VGluT1/2 staining in the caudal pulvinar of a diurnal rodent, the Octodon degus

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The retino-tectofugal pathway is present in all amniotes. In birds this pathway is characterized by a massive bilateral and diffuse projection from layer 13 of the optic tectum to different subdivisions of the thalamic nucleus rotundus (Rt). In rodents the caudal division of the pulvinar complex (Pulc) is considered the mammalian homolog of Rt, sharing a similar afferents pattern from the superficial tectal layers (superior colliculus SC). However, compared to birds, the tectopulvinar pathway is poorly understood. We studied the organization of this pathway in a diurnal rodent, the Octodon degus, by injecting the neural tracer CTb in the SC and by performing inmunohistochemistry for the vesicular glutamate transporters 1 and 2 (VGluT1 and VGluT2). Large and restricted CTb injections both produced intense bilateral labeling in Pulc, filling the whole nucleus, thus confirming the diffuse organization of this projection. The immunohistochemical results indicated that the full extent of the Pulc is rich in VGluT2+ terminals while just the anterior half is rich in VGluT1+ terminals, suggesting a differential cortical innervation. In addition, we found that the posterior, poor VGluT1+, aspect of Pulc have retrogradely filled cells after CTb injections. Therefore, as its avian counterpart, the Pulc seems to have differentially aferented divisions. Whether these aferents have a similar origin and the functional consequences of this hodological heterogeneity remains to be elucidated.

Sensory Systems
Poster Number 207 / Session 3

Reversal photoisomerization of all-trans retinal in primary cultures of chicken retinal ganglion cells

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In previous studies, we demonstrated the presence of intrinsically photosensitive retinal ganglion cells (ipRGCs) expressing the photopigment melanopsin (OPN4) in the wild type chicken retina. Furthermore, we found that the inner retina of chicken has the capability of synthesizing 11-cis retinal in a light dependent manner in the present study; we investigated the ability of primary retinal ganglion cell (RGC) cultures to take up all-trans retinal from the medium and to isomerize it upon light stimulation. RGC cultures were obtained by immunopanning with a OPN4X antibody to specially enhance the amount of ipRGCs from chicken retinas at embryonic day 8. After that, cells were irradiated with white light or maintained in the dark. Retinoids were extracted and analyzed by HPLC. Primary cultures obtained were highly enriched in RGCs expressing different neuronal markers with a typical RGC morphology displaying long processes after 4 days. Other retinal cell types were not significantly detected in the cultures. After cells were fed all-trans retinal 3 hours and exposed to a 1 h light pulse, we found detectable levels of 11-cis retinal in the cultures by HPLC. As we had previously reported in the chicken inner retina, the RGC cultures exhibit the capacity to isomerize 11-cis retinal from all-trans retinal under light stimulation strongly suggesting the presence of a photoisomerase activity in these cells that would be responsible for the light conversion of retinal in the RGCs.

Sensory Systems
Poster Number 208 / Session 1

Treatment With Bone Marrow Pluripotential Cells Prevent The Development Of Hyperalgesia In Rats With Sciatic Nerve Crush

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We previously described, in rats undergoing sciatic nerve crush, that systemic administration of bone marrow mononuclear cells (BMMC) results in their selective accumulation in the injured site and accelerated re-myelination of the affected nerve. The aim of the present work was to evaluate if improved myelin regeneration influences pain-like behaviour.To this end Wistar male rats subjected to sciatic nerve crush, were transplanted either with BMMC or bone marrow stromal cells (BMSC). Mechanical hyperalgesia was evaluated using the Von Frey`s test at different survival times. Inmunohistochemical expression of the cyclic AMP-dependent transcription factor 3 (ATF3), typically upregulated in neurons whose axons had been injured, was evaluated in dorsal root ganglion (DRG) neurons. Animals with sciatic nerve crush exhibited mechanical hyperalgesia from day 7 up to 28 days after injury. In contrast, animals treated with BMMC or BMSC exhibited higher withdrawal thresholds than the crush group, and almost complete recovery at 49 days survival. BMSC seemed to be more efficient in preventing mechanical hyperalgesia. ATF3 was strongly upregulated in DRG neurons after sciatic nerve crush, showing a peak 14 days after injury. BMMC treatment resulted in a considerable reduction in ATF3 upregulation at 14 days. BMMC as well as BMSC treatment appears to prevent the development of hyperalgesia in animals with sciatic nerve crush, consistent with their remyelination fostering effect.

Sensory Systems
Poster Number 209 / Session 2

Associative learning shapes mixture representation and improves perception of relevant odors

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Odors in nature are complex mixture, in which irrelevant components may hide the presence of relevant ones. In the present work we ask how olfactory experience increases the ability of animals to detect the relevant odors. The olfactory system of insects provides a good model for this study. The antennal lobe is the first processing center for olfactory information in the insect brain. The local network conformed by excitatory and inhibitory local neurons transforms the olfactory information before it leaves the antennal lobe to other brain areas. We train bees to pure odors and perform calcium imaging in projection neurons of the antennal lobes to measure neural activity patterns elicited by pure odors and mixtures that contain these odors.
We found a general decrease in the activity elicited by odors in the trained animals and one increase in the coherence of the code of the mixture and the untrained odor. Also on the basis of patterns obtained for naïve animals we assayed different algorithms that allow accurate prediction of the pattern elicited by the mixture. The prediction algorithms were later applied to animals that have been trained on appetitive conditioning using as conditioned stimulus one of the components of the mixture. We found that the representation of the mixture in trained animals deviates from the mixture predicted for naïve animals. This deviation is in favor of the representation of the rewarded odor.

Sensory Systems
Poster Number 210 / Session 3

The role of visual information in the protective effect of enriched environment on the retinal damage induced by ischemia

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Enriched environment (EE) consists on an environment with favorable conditions for visual, exploratory and cognitive activity, as well as physical exercise and social interaction. Recently, we demonstrated that EE housing protects the retina from ischemic injury. The aim of this work was to analyze the involvement of visual information in the protective effect of EE against acute ischemic injury. Adult male Wistar rats were submitted to retinal unilateral or bilateral ischemia by increasing intraocular pressure to 120 mm Hg for 40 min. Immediately after ischemia, rats were housed in a standard environment (SE) or EE. EE consisted of big cages with food hoppers, wheels and objects repositioned once/day and fully substituted once/week. The retinal function (electroretinography, ERG) and histology were analyzed at 1, 2 and 3 weeks post-ischemia. In rats housed in SE, ischemia induced a significant decrease in ERG a- and b- wave amplitude, and in the number of retinal ganglion cells (RCG), in a similar manner for animals with unilateral or bilateral ischemia. In rats with unilateral ischemia, EE housing significantly prevented retinal dysfunction and RCG loss, whereas in rats with bilateral ischemia, the ischemic injury was similar to that observed in ischemic retinas from rats housed in SE, at functional and histological level. These results suggest that the processing of visual signals is a necessary condition for the protective effect of EE against retinal ischemic damage.

Sensory Systems
Poster Number 211 / Session 1

Primary cultures of chicken retinal horizontal cells express the photopigment melanopsin X

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Retinal ganglion cells (RGCs) expressing the photopigment melanopsin (Opn4) display intrinsic photosensitivity. In the chicken retina, two Opn4 genes, Opn4x and Opn4m have been described of which, Opn4x shows its expression mostly in Prox1 (+) horizontal cells (HCs) by embryonic day 15 (E15). The aim of this work was to purify HCs from the chicken retina to obtain primary cultures enriched in these cells. Disaggregated chicken embryonic retinas at E15 were subjected to a discontinuous 1 to 4% bovine serum albumin (BSA) gradient. Cells collected from the different phases were cultured for 4 days and characterized by immunochemistry and morphology. Phases were examined with specific antibodies for HC´s and markers for other retinal cell populations. Prox-1 (+) cells from both the whole retina and the BSA gradient were quantified by flow cytometry. Also we analyzed HC primary culture mRNA expression by RT-PCR. The results show that only the fraction corresponding to 2.5% BSA contained most cells displaying PROX-1 and Islet-1 (+) immunoreactivities. Strikingly, Opn4x-immunoreactivity was observed in cultures from both the 2.5 and 3 % BSA gradient phases. 30% of cells from the whole disaggregated retina and 80% from the 2.5% BSA gradient phase were Prox-1 (+). In conclusion, by means of this method we selectively separated specific retinal cell types and obtained primary cultures highly enriched in HCs expressing the non-visual opsin Opn4x.

Sensory Systems
Poster Number 212 / Session 2

Should I eat or should I not? Bitter perception in a blood-feeding insect

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Food quality assessment is associated to an animal decision about feeding or not. Once triatomines reach a potentially suitable host, they walk over their skin in search of a good quality substrate (skin recognition phase) and then they pierce the skin until a venule or arteriole is reached. Subsequently they suck a small quantity of blood initiating the sampling phase of food. We show here that the fine assessment of gustatory preferences in triatomines occurs during both, the skin recognition phase and the sampling phase, independently. Triatomines have taste sensilla localized in the tip antenna that serve to determine externally the gustatory nature of the substrate. These taste sensilla showed electrophysiological sensitivity to bitter compounds like caffeine (CAF) and quinine (QUI). In feeding experiments we found that by adding CAF or QUI to the membrane of an artificial feeder offering an appetitive solution prevents insects from feeding. Additionally, the addition of CAF or QUI into the appetitive solution but not to membrane also caused an inhibition of the feeding behaviour of bugs. This modulation seems to occur by means of internal taste receptors placed in their alimentary canal (the epipharingeal organ). Finally, by applying a cognitive approach, we found that both, skin recognition and sampling phases, are modulated by experience. Results presented here highlight the relevance of bitter taste perception in the modulation of the feeding behaviour of insects.

Sensory Systems
Poster Number 213 / Session 3

Binocular Visual Integration in Neohelice granulata

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As most visual animals, arthropods possess two or more image-forming eyes. Perceiving visual information with more than one eye offers significant advantages (broadened visual field, better signal to noise ratio, estimation of distance by stereopsis, etc.). The crab Neohelice granulata (Chasmagnathus granulatus) is used as experimental model for study visually-guided behaviors. One of the benefits is that it offers the possibility of recording intracellularly the responses of individual neurons to visual stimuli in the intact animal. Recording from the third optic neuropil, we identified four classes of neurons, the Lobula Giants (LG) which seem to play a key role in the processing of visual information and the control of crab's behavior (Tomsic et al, 2003; Medan et al 2007). Additionally, we know that these neurons integrate information coming from both eyes, giving almost identical responses to ipsilateral and contralateral stimulation (Sztarker and Tomsic, 2004). We still don`t know how information coming from the other eye reaches the LGs. One possibility is that LGs from opposite sides are synaptically connected. To investigate this, we developed a preparation to do simultaneous recordings in the two eyes. Here, we present recordings of different pairs of LGs recorded from opposite sides of the brain. Results will reveal how the different classes of LG interact and allow a better understanding of this circuit known to be involved with decision-making in the crab.

Sensory Systems
Poster Number 214 / Session 1

A1 receptor distribution in rat retina and its modifications after continuous illumination

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Continuous illumination (CI) of rat retina produces photoreceptor degeneration. This model resembles human retinal degenerative diseases. Adenosine binds to four types of G protein coupled receptors named A1, A2A, A2B and A3. In the retina, A1 mRNA was reported in ganglion cell layer (GCL). A1-agonists have shown a neuroprotective effect in acute retinal injury hence our interest in the study of this receptor.

The aim was to map A1 in control (CTL) and illuminated (IL) rat retinas by immunocytochemistry.

Sprague Dawley rats were submitted to CI (12000 lux) during 1, 2, 5 and 7 days. The eyes of CTL (n=2) and IL rats (n=8) were fixed by immersion in 4 % paraformaldehyde. Peroxidase inhibition was performed prior to immunostaining by PAP method using a rabbit polyclonal antibody to A1 (Santa Cruz Inc).

CTL animals showed A1 immunoreactivity (A1-IR) in outer and inner plexiform layers and in ganglion cell layer (GCL). After 1 day of CI, A1-IR increased in GCL and in both plexiform layers. The increase of A1-IR persisted in GCL along the 7 days of CI, however A1-IR decreased in plexiform layers after 2 days of CI and increased again after 7 days of CI.

Our results in CTL animals match the description of A1 mRNA distribution and add A1-IR detection in plexiform layers. The peak of A1-IR at 24hs coexists with the previously determined maximum oxidative damage offering a suitable therapeutic target to protect the retina from CI damage. (Supported by CONICET PIP1098 and UBACYT 20020100100329).

Synaptic Transmission and Excitability
Poster Number 215 / Session 2

Purinergic modulation of acetylcholine release at the efferent-inner hair cell synapse in the developing inner ear

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Before the onset of hearing (postnatal day (P) 12 in mice) inner hair cells (IHCs) are transiently innervated by medial olivocochlear (MOC) efferent fibers. Acetylcholine released by these fibers activates α9α10 nicotinic receptors coupled to SK2 calcium-activated potassium channels, leading to inhibitory post synaptic currents (IPSCs). During this developmental period, IHCs fire spontaneous sensory-independent action potentials that are required for normal development of the auditory pathway. Recent studies suggest that this spontaneous activity is driven and/or modulated by ATP released from cochlear supporting cells. Recently, we showed that ATP (100 μM) decreases the quantal content (m) of evoked release (~50 %) in mouse IHCs at P9-P12, suggesting a pre-synaptic inhibitory modulating mechanism. In this work we investigated which ATP receptor subtypes are responsible for this modulation. IPSCs were evoked by electrically stimulating MOC fibers in the presence of different ATP receptor agonists and antagonists. Suramin (150 μM), a non-specific P2 antagonist, abolished the effect of ATP. PPADS (50 μM), an antagonist with a preferential effect on P2X receptors and TNP-ATP (10 μM), a specific P2X antagonist, did not modify ATP-induced inhibition. Furthermore, αβ-MeATP (50 μM), a specific P2X agonist, had no effect on m. Our results suggest that P2X receptors would not be involved in the modulation the MOC-IHC synapse, leading to a principal roll of P2Y receptors.

Synaptic Transmission and Excitability
Poster Number 216 / Session 3

An impedance technique to determine the onset of cellular damage in electrically excited cells

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Nerve cells can be artificially excited by electrical currents that depolarize the cell membrane. In fact, it is feasible to stimulate electro-active tissue from an extracellular microelectrode. This possibility is fully exploited in cochlear implants, and in novel prosthetic devices intended to restore the sense of sight. Both device types are being extensively studied in both experimental and clinical settings to determine, among other parameters, the maximum current amplitude that can be used for stimulation without producing cellular damage. Since a tradeoff between stimulation efficacy and safety is to be carefully considered, we are presenting in this work an electrical impedance technique which is able to establish the onset of cellular damage in cells exposed to a sequence of charge-balanced biphasic current pulses. An ad-hoc biophysical model of the cells-electrode interface allowed us to characterize cellular response to the stimulation protocol in terms of three adjustable parameters with physical correlates. Analyzing these parameters, we could determine the boundaries between three recognizable regimes for stimulation in a planar microelectrode array: a safe regime, a transitory cell change region (in which current amplitude values produced non-lasting alterations in the cells), and an unsafe zone.

Synaptic Transmission and Excitability
Poster Number 217 / Session 1

Intensity coding at the inner hair cell ribbon synapse is supported by a highly efficient recovery mechanism

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The auditory nerve represents the output of the cochlea and encodes intensity of acoustic stimuli in its firing rate. Sounds of increasing intensity produce a higher rate of action potentials. Inner hair cells (IHC) of the cochlea are the mammalian phono-receptors, transducing sound energy into graded changes in its membrane potentials (Vm). The IHC ribbon synapse is responsible for converting these changes in Vm into rates of action potentials in neurons of the auditory nerve. In this work, we investigated the time course of recovery of synaptic responses after 1 sec pulses at different IHC Vm. We observed a constant recovery process with an average rate per second of 0.25 of the initial response, when using pulses at -20 mV. A faster rate was observed after pulses at -30 mV (0.48 s-1). We also observed a higher intracellular calcium concentration in IHC with more positive Vm, as expected. Depletion of synaptic vesicles was consistently higher as presynaptic Vm increased. Therefore, recovery rate would depend upon the number of available release sites, but not on the presynaptic calcium concentration. This conclusion was further confirmed by evaluating recovery at individual time points after depleting pulses of different Vm. It can be calculated that recovery rate of the initial response matches with maximal release rate (~60 EPSCs/s). Increasing the extracellular calcium concentration (from 1.3 to 1.5 – 2.0 mM) produced a higher release rate for submaximal pulses only.

Synaptic Transmission and Excitability
Poster Number 218 / Session 2

New findings on the effects of the carbonic anhydrase inhibitor acetazolamide on transmitter release at the mouse neuromuscular junction

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Acetazolamide (AZ) is known to inhibit the action of carbonic anhydrase (CA), an enzyme responsible for regulating the extra- and intracellular pH. This drug is used as an anticonvulsant and for treatment of episodic ataxia type-2 patients, but its mechanism of action is still unknown.

Electrophysiology recordings done at the levator auris longus ex vivo muscles (NMJs) in bicarbonate solution showed a rise of spontaneous end plate potentials in muscles treated with AZ 100 uM (3.1±0.2/s AZ vs 1.92±0.06/s control), whereas quantal content measured at low high and burst stimulation showed no differences between treated and control NMJs.

We further investigated the mechanism of action of AZ by studying the dynamics of vesicle exocytosis/endocytosis. We used fluorescence FM 2-10 dye in bicarbonate buffer to load (20Hz) and unload (50Hz) nerve terminals. The amount of dye loaded in the presence of AZ was reduced to 48±9% of control. After loading the nerve terminal in the absence of AZ followed by unloading the dye during 9 min in the presence of AZ, different kinetics were evidenced with a fluorescence retention (fr) of 68±5% in treated NMJs in contrast to 8±4% in control.

To gain further insight about the role of CA in the AZ mechanism of action unloading experiments were repeated in a Hepes (10mM, pH 7.4) buffer. Experiments showed no effect of AZ in this condition:26±4% fr at treated NMJs vs 23±2% at control suggesting that AZ affects vesicle recycling through CA inhibition.

Synaptic Transmission and Excitability
Poster Number 219 / Session 3

Voltage-gated Ca2+ channels (VGCC) that mediate Acetylcholine (ACh) release at the transient efferent-inner hair cell (IHC) synapse during neonatal development

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During neonatal development IHCs are transiently innervated by medial olivocochlear (MOC) fibers. At postnatal days (P) 9-11, ACh release is supported by both P/Q and N-type VGCC and negatively regulated by L-type VGCC, coupled to the activation of BK channels. We previously reported that at P5-7, P/Q- but not N-type VGCC partially support ACh release and that BK channels reduce the quantal content (m) of evoked release. Our goal is now to determine which other type/s of VGCCs mediate ACh release at this stage and whether L-type VGCCs are coupled to the activation of BK channels. Postsynaptic responses were monitored in whole-cell voltage-clamped IHCs while electrically stimulating the efferent fibers in P5-7 mouse cochleas. Surpirsingly, both the L-type VGCC antagonist (Nifedipine) and the agonist (Bay-K) enhanced m (%increment = 161±21, 3 □M Nife; 294±26, 10 □M Bay-K). This suggests that L-type VGCC might be both supporting release and activating BK channels. However, occlusion experiments show that Bay-K has no effect on m after blocking BK channels with iberiotoxin (Ibtx) (m = 0.95, control; 2.7, Ibtx; 2.8, Ibtx + Bay-K). Moreover, Ibtx has no effect on m after incubation with L-type VGCC modulators (m = 0.8 ± 0.2 control; 2.49 ± 0.03 Nife; 2.9 ± 0.05 Nife+Ibtx; m = 0.7 ± 0.19 control; 1.9 ± 0.31 Bay-K; 2.1 ± 0.57 Bay-K+Ibtx). This shows that L-type VGCCs are coupled to BK channel activation. The paradoxical effect of Bay-K at this stage is being investigated.

Synaptic Transmission and Excitability
Poster Number 220 / Session 1

Acid-sensing ion channel 1A (ASIC1A) and its gender-dependent role in neuromuscular synaptic transmission

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CNS changes in extracellular pH (pHO) have considerable influence on the physiology of neurons. At the neuromuscular junction, H+ are co-release with ACh and are pump into the synaptic cleft after prolonged stimulation, contributing to muscle fatigue. Since acid-sensing ion channels (ASICs) have been recently identified and proposed to regulate neuromuscular synaptic transmission in response to acidosis, our aim was to investigate the modulatory role of ASIC1a on neuromuscular transmission and its dependence on gender.For that purpose, we initially studied the frequency of MEPPs in the absence or presence of either TTX or ASICs modulators.In males, we observed a considerable decrease in the frequency of MEPPs as a consequence of the genetic removal of ASIC1a. On the contrary, the frequency in females was significantly increased in KOs ($P<0.001$). Similar effects were found after the application of ASIC1a antagonists, such as amiloride and PcTx-1, although the changes were more pronounced when the non-specific blocker was used ($P<0.001$ vs. $P<0.01$). All these results were in accordance with some of our previous behavioural studies, which have shown an statistically significant difference in muscle performance between both genders.
Together our results suggest that ASIC1a may exert a differential role in modulating neuromuscular transmission in males and females, which may be crucial for understanding the divergence in muscle performance that exists between both genders.

Synaptic Transmission and Excitability
Poster Number 221 / Session 2

Recovery of Exocytosis Triggered by an Action Potencial Like Stimulus: Effects of Temperatura and Cytosolic Calcium Concentration

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The immediately releasable pool (IRP) is a group of ready release vesicles highly coupled to Ca+2 entry through voltage dependent channels. The participation of the IRP in physiological conditions might be questioned due to its slow recovery rate (tau=7 s). Applying a 5 ms action potential-like stimuli (APs), using whole-cell patch-clamp configuration, we measured the release of a subgroup of approximately 8 vesicles from the IRP, which was named as APP (for action potential associated pool). This pool recovers 7-8 fold faster than IRP, what would be enough for the complete refilling of APP during chromaffin cell basal physiological action potential frequency (0.5 Hz). The aim of this work was to analyze the effects of temperature and basal [Ca+2]i on APP recovery. The time constants for this process were 2.37±1.38 s and 1.24±0.46 s for 20oC and 25oC, respectively, while the ICa+2 integrals (IntCa) were 149±31 fC and 274±20 fC for the same temperature values. We applied 10 ms APs at 20oC to compensate for the change in IntCa, obtaining a IntCa of 216±26 fC. Unexpectedly, this condition increased the recovery rate of APP to 0.72±0.16 s. Next, we analyzed the effect of changing the [Ca2+]i on the recovery of APP. There was a clear effect of [Ca2+]i, resulting in time constants of 2,95±1,23 s and 0,49±0.29 s for 100 and 500 nM [Ca2+]i respectively. In conclusion our results indicate that internal Ca+2 concentration as well as temperature affect the recovery rate of APP.

Synaptic Transmission and Excitability
Poster Number 222 / Session 3

Intrinsic and synaptic factors interact to establish the firing mode of clock neurons in Drosophila

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Circadian rhythms have been extensively studied in the fruit fly where many clock genes that interlock through negative feedback loops and generate daily oscillations have been described. Clock genes are expressed in approximately 150 clock neurons in the brain, of which a particular subset, the pigment dispersing factor-expressing lateral neurons (LNvs) have been found to play a central role.
The firing mode of the large-LNvs (lLNvs) follows a circadian pattern, with a high activity bursting mode preponderant during the day and a lower activity tonic mode normally found at nighttime. This change in neuronal firing could be crucial to confer time of day information to other neurons by altering the release of neurotransmitters or neuropeptides, however, the mechanisms that allow this change in firing mode are not known. Ih (hyperpolarisation-activated cation current) provides a depolarizing current which contributes to resting membrane potential and opposes deviations away from the prevailing membrane potential. In the past, this current has been shown to participate in complex neuronal behaviors such as bursting. Using genetics and pharmacology coupled to whole-cell patch clamp electrophysiology in ex-vivo Drosophila brains, we show here that Ih is indeed involved in the bursting behavior of the lLNvs. We will also show that not only intrinsic, but also synaptic factors, such as Acetylcholine and GABA are contributing to the establishment of the lLNvs firing mode.

Synaptic Transmission and Excitability
Poster Number 223 / Session 1

Worm migraines: Characterization of a Gain-of-Function Mutation in the Voltage-Gated Calcium Channel, UNC-2/CaV2

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The fusion of synaptic vesicles with the cell membrane is initiated by the activation of presynaptic voltage-gated Ca++ channels (CaV2). C. elegans has a single presynaptic CaV2Î± subunit, UNC-2 . We identified an unc-2 gain-of-function (gf) mutant, which displays hyperactive locomotion. Animals that express the unc-2(gf) in the backward locomotion interneurons exhibit an increased reversal frequency, while expression in the hermaphrodite specific neurons produces hyperactive egg-laying, suggesting that the unc-2(gf) transgene can be used to hyper-activate selective neurons. unc-2(gf) mutants show an increased frequency of endogenous synaptic release events, indicating elevated levels of neurotransmitter release. Whole-cell recordings from HEK cells expressing the human CaV2.1Î± with the corresponding unc-2(gf) mutation revealed activation at lower membrane potentials. Our findings are similar to those reported for some mutations in the human CaV2.1Î± that cause Familial Hemiplegic Migraine (FHM1). Interestingly, animals that express unc-2 carrying corresponding FHM1 mutations display a phenotype similar to that of the unc-2(gf) mutants. Therefore, the unc-2(gf) mutants may provide an invertebrate model to study mechanisms underlying FHM1. To understand mechanisms of CaV2 function in vivo, we performed a screen for mutants that suppress the hyperactive phenotype of unc-2(gf) mutants. This suppressor screen may provide novel targets for the treatments of Ca++ channelopathies.

Synaptic Transmission and Excitability
Poster Number 224 / Session 2

A background current seasonally modified in a temperate zone electric fish (Brachyhypopomus gauderio)

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Electric organ discharge (EOD) of gymnotiforms is part of a sensory system and a communication signal. EOD waveform inform to coespecifics about sexual maturity, among others. Sex steroids during breeding season differenciate sexually the EOD waveform and that waveform is more resistant to changes caused by rapid increases of temperature. The thermosensitivity index (ITS), that is an indication of this property, when is ≤ 0.5 represent a "thermorresistant" fish. Specific EOD waveform is explained by: central mechanisms, organization of the electric organ (EO), membrane properties of the electrocytes (EC) and electrical properties of surrounding tissues. Two-electrode voltage-clamp was performed in electrocytes from isolated EO after blockage of main Na+, K+ and Ca2+ currents. In these conditions and under controlled temperature we recorded currents. Input conductance (Gin) and outward currents (Io) were significantly larger in thermoresistant fish during breeding season. Average Gin at 30°C in breeding fish (5.5±0.9 mS) is significantly larger than in no breeding fish (1.4±0.2 mS). Gin values had a good correlation with ITS (R2=0.49; p=0.008). Outward currents measured at +60 mV at 30°C were larger in thermoresistant fish (326.7±100.6 nA) than in thermosensitive fish (59.2±11.8 nA) and also had a good correlation with ITS (R2=0.53; p<0.005). These currents partially explained the seasonal changes in the excitability affected by temperature. Part. supp. by CSIC I+D C032-348.

Synaptic Transmission and Excitability
Poster Number 225 / Session 3

Margatoxin sensitive current regulates striatal cholinergic interneuron excitability

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Acetylcholine and dopamine are the main modulators of corticostriatal function, and disbalances in their availability may result in neuropsychiatric disorders like Parkinson´s disease. Acetylcholine is released by striatal cholinergic interneurons (ChIs). They have a tonic activity that depends on intrinsic mechanisms. Recent work showed hyperactive ChIs in a rat model of Parkinson's disease as a result of a lack of "accommodation". We study instrinsic properties of ChIs in mouse brain slices. Particularly, we try to identify the currents that regulate ChI excitability, using accommodation as an indicator. We used mice expressing the tdTomato fluorescent protein in ChIs (ChAT-Cre;rt) and made whole-cell recordings to study accommodation and the underlying current. We first validated the ChAT-Cre;rt model to be able to use it in the rest of the experiments. Our results show that margatoxin, a blocker of Kv channels with selectivity for Kv1.3 strongly reduced accommodation ($p<0.001$) and the underlying slow potassium current (>1500pA) in ChIs. Both were insensitive to UCL2077, a blocker of atypical KCNQ K+ channels. We have isolated and characterized the margatoxin sensitive current and found an activation voltage of -38+7mV and a V50 of -3+8mV. Immunohistochemistry revealed the presence of Kv1.3 channels. Our data suggest a novel voltage-dependent determinant of excitability in ChIs, which needs further validation as a therapeutic target in animal models of Parkinson's disease.

Brain Awareness Week Córdoba: Brain and Perception

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In March 2013 the Brain Awareness Week (BAW) was celebrated for the first time in Argentina. Three cities participated in the event. Our group of Young Neuroscience Researchers was in charge of hosting the BAW in Córdoba. Throughout the week we carried out an urban intervention under the title of "Brain and Perception". The activities were addressed to the general public and they were related to perception, attention and emotions. The format of the exhibition consisted of audiovisual stands where we exposed images and interactive games. The audience (estimated at approximately 2,500 people) played several games related with sensory illusions, and were guided through some of the main questions of contemporary neuroscience. Also, we handed out brochures with curiosities about the brain. After the official “Brain Awareness Week”, the exhibition continued over a month, associated with Cuatrociencia, the Science and Technology Fair from the National University of Cordoba. During this period, the BAW stand received approximately 120,000 visitors. In addition, we offered lectures about diverse neuroscience topics, as well as a photographic exhibition on neurons and the brain (“micro&Macro: Tu Mirada sobre las Neurociencias”). It was really gratifying for our group to interact with the people and to see how interested and amazed they were about the brain functions. We consider the activity a major success and we hope we can collaborate more often in this kind of initiatives.

BAW
Poster Number 227 / Session 3

Amazing brain!

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Neuroscientists visited a public school in Rosario to raise high school students' consciousness about the important role of the brain in our daily life. The activity included an interactive talk about how the brain works, what aspects of daily life it controls and what diseases are associated with poor brain function. The talk put a special emphasis on how scientific research in neuroscience has allowed us to advance the understanding of the brain in both health and disease. Namely, using a series of mental challenges to capture the students' attention allowed us to explain that there are different brain areas with specific functions. Then, through a series of guided questions and answers we explained how the brain works, how we learn and remember, how the brain controls different body functions, what happens to the brain during aging, etc. Immediately afterward we divided the students into small groups and explained them our research work through poster presentations that were specially designed to divulge the neuroscience research projects in our lab. Towards the end of the activity there were demonstrations of rat brain slices stained with various dyes to let the students watch different brain areas. Finally, it is important to highlight that both students and teachers were very enthusiastic about the whole activity. They showed their interest in the brain making questions and fully participating in each part of the activity.

BAW
Poster Number 228 / Session 3

Journey through the route of senses: interactive activities to primary school students

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In the context of the Brain Awareness Week, we visited primary schools to carry out activities with 3rd and 4th grade students (around 400 children between 8-9 years old). First they received an interactive lecture on neuroscience to reinforce previous knowledge of the Central Nervous System (CNS), focused on stories and anecdotes regarding the brain functions. After that, we conducted different tasks. For 3rd grade students the activity was “Remembering what we learned": groups of students had to find the words hidden, related to the CNS in a word search to the purpose to demonstrated their teamwork skills. For 4th grade students we performed subsequent activities: first they had to assemble a ‘neuro-puzzle’ that consisted in different parts of the human sense organs, muscles and brain. Once assembled, the structures had to be put on the correct place on a ‘giant doll’. The students showed great enthusiasm and curiosity about the actual anatomy of each organ. Finally, the students were located around the giant for the activity "A giant in the School". The students listened one story that told how the giant received sensory stimuli and responds to it. They had to follow the route from the sensory organs to the brain and from the brain to the muscles; using plastic balls as signals, and cords as pathways. The first Brain AwarenessWeek in Mendoza exceeded all our expectations, children and teachers showed great interest, and we are invited to repeat these activities.